UNIVERSITAT DE BARCELONA

Preferred Supplier: A Consensus Innovation Model for Health Equity

Marina Espriu Simon

PHD THESIS

PREFERRED SUPPLIER: A CONSENSUS INNOVATION MODEL FOR HEALTH EQUITY

MARINA ESPRIU SIMON

UNIVERSITAT DE BARCELONA

2024

PREFERRED SUPPLIER: A CONSENSUS INNOVATION MODEL FOR HEALTH EQUITY

PHD THESIS

MARINA ESPRIU SIMON

DIRECTORS
PEDRO GALLO DE PUELLES, PH.D.
JOAN BIGORRA LLOSAS, PH.D.

UNIVERSITY OF BARCELONA
FACULTY OF ECONOMICS AND BUSINESS
SOCIOLOGY DEPARTMENT

UNIVERSITAT DE BARCELONA

BARCELONA, 2024

Turn your face to the sun and the shadows fall behind you.

Maori Whakatauki

A Joel i Joana, per no deixar de cridar-me a sopar.

Acknowledgements

This work is born from an inspiration and a challenge. Thank you to Joan Bigorra for the vision on the former and Pedro Gallo for the rigorous support in the latter. Thanks to my angel, Laura Sampietro-Colom, for her generous encouragement along the way.

I want to deeply thank all the panellists who participated in the interviews and surveys of the study. Thank you for your openness in sharing your vision, insights, dreams and delusions… Thank you for being such stimulating travel companions. As journalists have commented, the secret of interviews is good preparation and listening to the interviewee, and if we had to choose one, listen, without a doubt.

Huge thanks to the colleagues of the ISGlobal 4S working group Adrián Alonso, Gonzalo Fanjul, Rafael Vilasanjuan and Joan Bigorra for their enthusiasm in the first publication of the model. I greatly appreciate Llorenç Quintó's open contribution to the statistical analysis of this work.

Thanks to ISGlobal for all these years together. Thanks to Pedro Alonso, Antoni Plasència, Núria Casamitjana and Manhiça Foundation for your trust. My particular thank you to the Innovation team and other colleagues for sharing this exciting journey.

We acknowledge support from the grant CEX2018-000806-S funded by MCIN/AEI/ 10.13039/501100011033, and support from the Generalitat de Catalunya through the CERCA Program.

My special thanks to my dearest family and friends for your unconditional love to make it happen.

Thanks to all the adventures lived and current.

Marina

PREFERRED SUPPLIER: A CONSENSUS INNOVATION MODEL FOR HEALTH EQUITY

ABSTRACT

Health areas with no commercial value are and will continue to be overlooked, while those that bring huge returns to the industry will not be sustainable for much longer. The current health innovation paradigm is pharma-led, profit-oriented, and does not always respond to social values and public health needs. Furthermore, the United Nations Sustainable Development Goals (UN SDGs) will not be achieved without innovation and the private sector doing its part.

Our hypothesis is that the public sector, as a major investor and purchaser, can shape health innovation to deliver improved and equitable health care by aligning incentives with priority health needs. Companies that engage in socially desirable environmental and health equity practices would get credit as Preferred Suppliers in a new fair play, promoting competition among the biomedical industry in its strive for excellence for the common good.

The Preferred Supplier model (PSM) proposes a public health investment and procurement system prioritising business with companies that fulfill the "4 Share" (4S) principles during the life cycle of research and innovation (R&I) sharing: i) Needs, ii) Results, iii) Risks and Rewards, and iv) Outcomes, promoting equitable innovation in exchange for incentives for health priorities. This PhD research aims to reach consensus on the values (normative preferences) that define the problem with the current biomedical R&I model and its causes, to then co-create a new consensus model based on the PSM, identify its barriers and enablers and outline policy recommendations.

The study considered early multi-stakeholder engagement with a constructive Health Technology Assessment (cHTA) to evaluate the different perspectives and reach consensus among twenty-seven global key informants. During in-depth interviews, experts' interpretive frames were reconstructed applying an adaptation of the Richardson model to contested values. A modified Delphi consensus method was applied with two cohorts and three rounds of scoring surveys.

The results showed the panel's unanimous desire for health equity. The experts significantly agreed on the PSM 4S principles, aligning public health needs with incentives and conditioning public investment and procurement to accredited providers according to ESG, an Access to Medicine Index-like and financial and scientific data sharing practices. The consensus co-created PSM would promote the hybrid risk-impact pricing model by balancing risk (involving disclosure of public R&I funds) and impact (revised value-based pricing) modulated by tier pricing according to the countries' ability to pay (i.e. GDP per capita). The key PSM enablers are its balance of risks and rewards as an incremental change in the system and the growing responsible innovation by the industry, likely driven by investors' demands for disclosure.

Overall, the co-created PSM reaches a multi-stakeholder consensus on the desirability (shared values) and plausibility (incentives and regulation) to accelerate equitable health innovation towards Planetary Health. It is recommended to further develop and pilot the PSM in the EU.

Keywords: equitable innovation, responsible innovation, health equity, health innovation, global health innovation, public health policy, value-based healthcare, common good, SDGs, ESG, ATMi, One Health, Planetary Health.

TABLE OF CONTENTS

LIST OF ACRONYMS

4S	4 Share principles of the Preferred Supplier model
AI	Artificial intelligence
AIDS	Acquired Immune Deficiency Sndrome
ATMi	Access to medicine index
B3W	Build back better world
BRICS	Brazil, India, Russia, China and South Africa
BT	Background theory
cHTA	Constructive health technology assessment
CEPI	Coalition for epidemic preparedness innovations
COVAX	COVID-19 vaccines global access
COVID-19	Corona virus disease 2019 caused by SARS-CoV-2
DNDi	Drugs for neglected diseases initiative
EC	European Commission
EHDS	European health data space
EHR	Electronic health record
EMA	European Medicines Agency
EU	European Union
FDA	Food and Drug Administration
GAVI	Global alliance for vaccines and immunization
GDP	Gross domestic product
GHS	Global health strategy
HIA	Health impact assessment
HiAP	Health in all policies
HIC	High income country
HIV	Human Immunodeficiency Virus
HTA	Health technology assessment
iHTA	Interactive health technology assessment
IPO	Initial public offering
IPR	Intellectual property right
JS	Judgement of the solution
KPI	Key performance indicator
LIC	Low income country
LMIC	Low- and middle-income country
MA	Market access
MEA	Managed entry agreement
MPP	Medicines patent pool
NP	Normative preferences
OD	Orphan drug
OECD	Organisation for Economic Co-operation and Development
OWS	Operation ward speed
PD	Problem definition
PREM	Patient-reported experience measure
PROM	Patient-reported outcome measure
PSM	Preferred supplier model
RCT	Randomised controlled trial
RD	Rare disease
R&D	Research and development

R&I	Research and innovation
RWE	Real-world evidence
SDG	Sustainable Development Goal
SME	Small and medium-sized enterprise
STMT	Statement
TT	Technology transfer
UHC	Universal health coverage
UK	United Kingdom
UN	United Nations
UNICEF	United Nations Children's Fund
US	United States of America
VBHC	Value-based healthcare
VC	Venture capital
WEF	World Economic Forum
WHO	World Health Organisation
WTO	World Trade Organisation

LIST OF TABLES

LIST OF FIGURES

LIST OF BOXES

1 INTRODUCTION

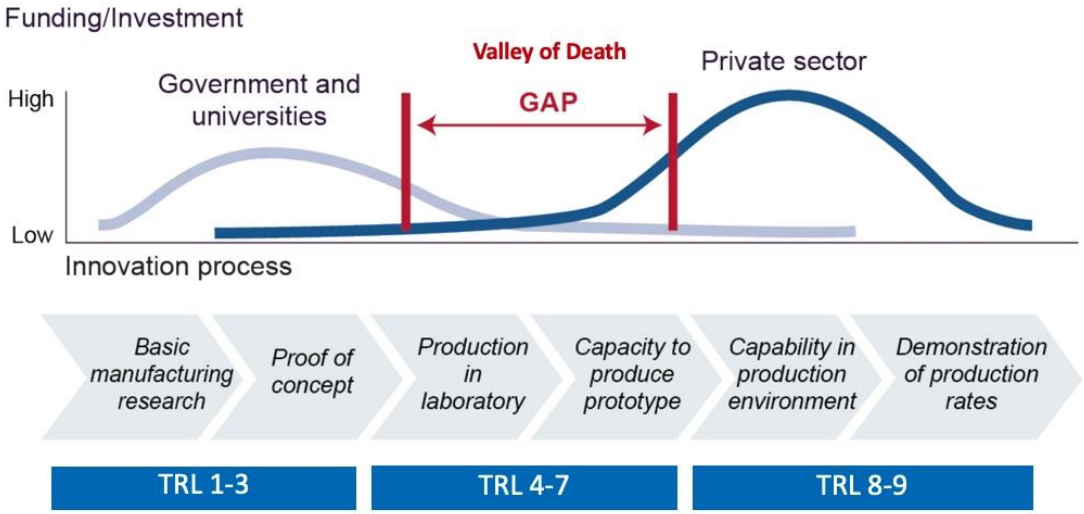
This PhD thesis aims to orientate health innovation towards global health innovation addressing the main health challenges worldwide. Innovation is a new, more effective way of solving a problem (Syeed et al., 2022; Rejon-Parrilla, Espin, Epstein, 2022). The WHO defines health innovation as "*a new or improved solution with the transformative ability to accelerate a positive health impact*" (WHO, 2023a). Health innovation is an iterative process that involves five phases: i) identification of the need, ii) research and development (R&D), iii) commercialization, iv) delivery, and v) dissemination (OECD, 2023). Innovation embraces new products, services, delivery methods, financing and processes that improve people's lives (USAID, 2020a). That is, health innovation comprises new pharmaceuticals (i.e. drugs), medical devices (i.e. point-of-care diagnostics) and digital health (i.e. solutions based on artificial intelligence, AI) (Brewer et al., 2020; Gupta et al., 2021; WHO, 2021b) involving new pricing and delivery methods.

In this research, health innovation comprises both the biomedical research and development (R&D) and the innovation technology transfer process to the market (including business model innovation), also referred to as research and innovation (R&I) (Rosati et al., 2023). Global health is *"an area for study, research, and practice that places a priority on improving health and achieving equity in health for all people worldwide"* (Koplan et al., 2009, cited in Smeeth and Kyobutungi, 2023). Global Health innovation are solutions to major health challenges that require the most attention and global cooperation such as antimicrobial resistance, the impact of climate change on health, the fight against non-communicable diseases (i.e. cancer, diabetes, heart diseases, mental health), emerging infectious diseases, strengthening healthcare systems, and artificial intelligence in health care, among others (Lucero-Prisno et al., 2023). It involves the identification of problems affecting the global population and vulnerable groups, and the equitable transfer of innovative solutions. As mentioned, in this PhD thesis health innovation refers to global health innovation with the co-creation of a new R&I model to overcome the main public health challenges on a global scale.

Current health innovation fails twice. First, to deliver solutions for those public health priorities that are not sufficiently lucrative. Second, to provide affordable products for both high- and low-and-middle income countries (HICs, LMICs) due to overprice (Bryan and Williams, 2021; Moreno and Epstein, 2019). This situation often leads to market failure for certain health challenges. This is the case for rare diseases (involving small populations), neglected tropical diseases (affecting populations with low ability to pay), new antibiotics against multidrug-resistant bacteria (restricted use) and cancer drugs (high prices) that require a collective action to address them (McPake et al., 2020). During the R&I product development, there is a "valley of death" between a good idea and a successful product covering an unmet need (Figure 1.1). According to Kampers et al. (2021), *"few biotechnology innovations make it through the valley of death to markets"*. This normally happens due to the lack of resources between the technology validated in the lab and the prototype demonstrated in operational environment, that is, technology readiness level (TRL) between 4 and 7, being TRL 9 ready for full commercial deployment. The focus of public funds on early-stage companies is the reason of unintended valley of death between early non-dilutive funding from government innovation agencies and production-level private sector investment (Williams and Tippit, 2022). Bridging this gap requires more than technology

innovation, that is, entails access to necessary resources in terms of capital, skilled workforce and infrastructure (Kampers et al., 2021; Lee, 2020) preferably in a cooperative ecosystem.

1 **Figure 1.1** R&I Product development: the "valley of death"



Source: Adapted from Williams and Tippit (2022)

In response to the global challenges, the UN SDGs were adopted by the global community in New York in 2015 as an ambitious agenda for a safer, fairer and healthier world by 2030 (UN, 2023; UHC2030, 2023). It carried forward the unfinished agenda of the Millenium Development Goals (Khetrapal and Bhatia, 2020; UN, 2023). Among the 17 SDGs, SDG3 aims to "*ensure healthy lives and promote well-being for all at all ages*" (UN, 2023). SDG target 3.8 specifically mentions the importance of achieving Universal Health Coverage (UHC) (UHC2030, 2023) with "*access to safe, effective, quality and affordable essential medicines and vaccines for all"* and SDG 3.b emphasises the need to develop drugs and vaccines to address persistent treatment gaps (Wirtz et al., 2017).

Barel, Boman and Morten (2020) summarise four failures of the current biomedical system, thereby undermining its potential to reach the SDGs. First, failing to respond to diseases that are not lucrative enough, focusing on diseases that affect rich people in wealthy countries, rather than those responsible for the heaviest burdens, such as HIV, tuberculosis and malaria that mainly affect disadvantaged populations (Plackett, 2020; WHO, 2021a). For instance, there is a large shortfall in global R&D spending for poverty-related and neglected diseases (PRNDs). As little as 1% of all global funding for health R&I is allocated to diseases mostly noted in LMICs (such as malaria, HIV/AIDS, tuberculosis, cholera, and Ebola) even though they account for more than 12.5% of the global burden of disease (WHO, 2023b). Furthermore, *"despite Africa carrying 25% of the global burden of disease, African-led research has contributed less than 1% of the scientific literature"* (De Olivera and Baxter, 2024). Second, failing to prioritise health needs, focusing on me-too drugs (as pharmacologically active compounds that belong to the same therapeutic class as the original first-in-class compound and used with the same therapeutic purposes) providing incremental benefit over the existing ones rather than truly innovative products (Aronson and Green, 2020). Although many me-too drugs have no significant advantages over their precursors, of all drugs listed in the WHO essential list, over 60% are me-too (Aronson and Green, 2020;

Krieger, Li and Papanikolaou, 2022). Third, failing to deliver affordable medical products, with products often overpriced, making them unaffodable for many populations and overwhelming healthcare budgets (Kesselheim, 2020; National Academies of SEM, 2018; Gronde, Uyl-de Groot and Pieters, 2017). Excessive pricing often responds to a lack of competition due to intellectual property rights (IPR) monopolies (i.e. patents) (Feldman, 2018), antitrust violations (Carrier, 2019) and lack of price bargaining power by public payers (especially in the US, the reference market) (Cubanski et al., 2023a). In particular, anticancer drugs are becoming exorbitantly expensive (Kwon and Kim, 2020) and, at the same time, fail to deliver clinically meaningful benefit (Cohen, 2017), leaving a large proportion of the population with unmet health needs. There is an urgent need to review both evidence for anticancer drugs prior to market approval (Cohen, 2017) and pricing to improve access globally (Fojo and Lo, 2016). Finally, failing to use scientific and financial resources efficiently and effectively. The current biomedical R&I process (discovery, development, manufacturing and distribution of medical technologies) is time and resource consuming, resulting inefficient and sometimes ineffective (Houston et al., 2021; Schlander et al., 2021; Yale CRIT, 2017). For instance, 90% of clinical drug development fails (Sun et al., 2022). This limitation is often due to the lack of data sharing (Ramstrand et al., 2019), redundancy in R&D and increased financialisation and underinvestment in the biomedical sector (Mazzucato and Roy, 2019). It hinders collaboration by encouraging scientists and industry to work in isolation rather than promoting information sharing in a cooperative ecosystem (Ellemers, 2021). According to Mazzucato (2023a), *"the SDG financing gap has increased from $2.5 trillion annually before the COVID-19 pandemic to between $3.9 and $7 trillion today"*. Health spending on SDG3 has increased, but not in all countries, although increases in spending do not always lead to better outcomes (Micah et al., 2020). Countries will likely need more funds to meet the target and will need to address other constraints, such as inefficient resource allocation, weak governance systems, and shortages of human resources and medicines (Micah et al., 2020).

In summary, the current biomedical R&I model is responsible for significant efficiency and efficacy issues that limit the ability to address global health challenges. It is worth recapitulating what are the main causes of this situation described in the literature. The current health R&I model is dominated by the biomedical industry which aims to maximize profits protected by a patent monopoly model resulting in market failures with significant unmet health needs (Annett, 2021; Ledley et al., 2020; Makurvet, 2021; Moreno and Epstein, 2019; Tenni et al., 2022). The biomedical industry comprises private funders, primarily venture capital (VC), and producers, companies developing medical technologies, which play a central role in translating research into healthcare innovation. In this current model, economic viability is a key driver for both actors (Chandra, Foroughi and Mostrom, 2022, cited in National Academies SEM, 2023).

As the National Academies SEM 2023 explains, VC investors are largely an American industry that has a major influence on funding innovation in all sectors of the economy. Investors are both drivers and gatekeepers through curated healthcare innovation investments in startups and SMEs (seed investment, series A, series B) based on what they believe is likely to be succesful (Chandra et al., 2022). Tipically, the investor exits when the new company is adquired by a large publicly traded firm or advances with an initial public offering (IPO) to become a publicly traded company. Companies come into play in two ways, in the initial development phase as start-ups seeking private funding for R&I, and later, as large publicly traded companies for approval and commercialization of the new product (Chandra et al., 2022). The market failure in the biomedical R&I system, which results in a lack of equity and

efficiency, is mainly explained by this competitive orientation to short-term profits of VC companies and by the fact that producers disregard the values and principles of other relevant stakeholders such as users and payers, among others (Barel et al., 2020; Bryan and Williams, 2021; Horne and Heath, 2022; Wouters, McKee and Luyten, 2020).

Ideally, any review of the health innovation model should consider early engagement of multiple stakeholders to reflect collective values and align the health system with public health needs. Stakeholder representation should encompass many other actors such as civil society, academia, the private sector, international organisations and government agencies involved in the R&I cycle. That is, a compendium of key actors involved in the R&I value chain that includes research, development, marketing, financing, procurement, evaluation and regulation of medical technologies. On the other hand, economic viability is a key factor for private funders and companies that develop and commercialise medical innovations. Any attempt to influence the decisions of these actors must be connected in some way to the final financial returns that may be generated (Chandra et al., 2022, cited in National Academies of SEM 2023).

Our hypothesis is that the biomedical market failure could be reduced by identifying the endpoint value, that is, *"what we, as society, want to achieve with the biomedical R&I and healthcare provision",* and defining the incentives and regulations of a new R&I model based on the market power of the public buyer. This new co-created health innovation model would address public health needs with a more inclusive and cooperative approach between public, private and social actors. It would result in a new R&I model to obtain equitable, agile and sustainable outcomes. In this sense, the Barcelona Institute for Global Health (ISGlobal) has proposed the "**Preferred Supplier" model** (PSM) as a new equitable and sustainable health innovation model. The foundations of the PSM have been published in a policy brief (Alonso, Espriu, Bigorra and Vilasanjuan, 2021a) and a discussion paper (Alonso, Espriu, Bigorra, Vilasanjuan and Fanjul, 2021b). The PSM proposes a public health investment and procurement system that prioritises business with those companies that comply with the principles of the "**4 Share**" (4S), that is, sharing needs, results, risks and rewards, and outcomes. By doing so, preferred supplier companies would be promoting access to innovative solutions as compensation for receiving public incentives for priority health challenges. More details on the 4S principles are provided in section 2.2.3.

The PSM is based on accreditation requirements and incentives for companies that *"share the mission, develop innovative and equitable solutions and get credit for it"*. The PSM aims to accelerate the transition from a shareholder primacy model to a **multi-stakeholder** approach to achieve equitable, agile and sustainable health outcomes. The present PhD thesis assesses the expected desirability and plausability of a co-reviewed Preferred Supplier health R&I model, proposing the necessary adjustments to the original PSM by seeking consensus among key actors on: 1) the social values that define the problem with the current health R&I model, 2) the causes of the problem, 3) co-creation of a new health innovation model based on the PSM, 4) identify its barriers and enablers, and 5) make policy recommendations. Ideally, this new consensus health innovation model would form the basis of a public health policy strategy in current health systems.

There are a series of highly relevant global trends that portray the scenario of health values. The massive global mobilisation to confront the COVID-19 pandemic represented a turning point, as well as a unique opportunity to increase social awareness about the value of global health for social prosperity (Prudêncio and Costa, 2020; WHO, 2023d). As a result, in July

2020, United Nations Secretary-General António Guterres called for a *"New Social Contract and New Global Deal"* in response to worsening international inequalities during the COVID-19 pandemic (Guterres, 2020; Perehudoff et al., 2022). In September 2023, the UN High-Level Meeting on UHC renewed the commitment to UHC with an action plan and investments that signal the importance of taking urgent steps towards health for all (UHC2030, 2023).

As for the private sector, in 2019 pre-Covid-19 era, the B Lab company that certifies B Corporations (which measure the social and environmental impact of companies) had already partnered with the UN to join forces with the private sector to address the SDGs. This agreement responded to B Lab's vision that the SDGs focus on countries, but the SDGs will not be reached without the acive participation of the private sector to reduce inequality and address climate change among member states (Feloni, 2019). In this sense, an example of responsible capitalism by the industry is Pfizer *ACCORD for a Healthier World* to improve health equity for 1.2 billion people in lower-income countries. This initiative was launched in May 2022 at the World Economic Forum (WEF) in Davos and provided patent-protected medicines and vaccines available in the US and/or the EU at a not-for profit price to 45 lower-income countries (Pfizer, 2022; Tanne, 2022).

Furthermore, one of the five takeaways of the 2023 World Economic Forum (WEF) meeting, as a public-private partnership forum, stated *"Global companies are finding that inclusion is helping them tap underserved markets, giving them a competitive edge"* (McKinsey, 2023). This quote refers to the principles that define the concept of **social business** about new social business models to provide products and services for an unmet need as a market opportunity, that is, making profit (Prahalad, 2019). According to a McKinsey report (Smit et al., 2022) on inclusive and sustainable growth "*The world has great potential to become more sustainable and inclusive by 2050. It will require solid economic growth to pay for huge investments in sustainability and inclusion. But growth alone will not be enough: innovation to find new solutions will also be critical and businesses are well placed to lead that innovation, as drivers of more than 70% of the total GDP [gross domestic product]".* As the McKinsey report points out, *"Two interrelated forces can help close the empowerment and sustainability gaps: business-led innovation that delivers affordable essential goods, higher productivity and incomes, and government and philanthropic resources that can shift private incentives"* (Smit et al., 2022). Therefore, one way to achieve a more sustainable and inclusive world could be for governments to identify priorities and define incentives and for industry to lead that innovation in exchange for social returns, including financial (profit) and non-financial (doing good) returns.

2 THEORETICAL BACKGROUND

The present research builds on the values that define health and how to reimagine health innovation accordingly to reach socially desired health goals. This chapter reviews the existing definitions of health values, as well as the models in healthcare that serve as a roadmap to develop the arguments applied in this reaseach.

The first section is a description of the principles of bioethics in healthcare, health values and policies in the European Union (EU), value-based healthcare (VBHC) and the economic approach to health value as a baseline theoretical framework to redefine health innovation. The models section presents the core theoretical foundations of this PhD thesis based on three theoretical healthcare models, two known models and a proposed new one. The first two are what we call the "public value" model, projected by researchers like Mazzucato, to oppose the traditional one, defended by DiMasi and others, which we call the "shareholder" model focused on maximising private profit. The third and new model builds on the "public value" model proposing the necessary incentives to attract private investors and industry to work for the unmet public health needs. This model is the so-called "Preferred Supplier" model (PSM) defined by ISGlobal in 2021 (Alonso et al., 2021a and 2021b) as the basic criterion that industry should comply with to become a preferred provider and a preferred recipient of funds of the public sector, as a prominent investor and buyer of healthcare innovation. Finally, the Access to Medicine Index (ATMi) is introduced as a reference indicator of health equity.

2.1 VALUES IN HEALTHCARE

2.1.1 Bioethics principles

Health is declared as a human right in the UN Universal Declaration of Human Rights (1948) and the legally binding UN International Covenant on Economic, Social and Cultural Rights (1967): *"every person has a right to the enjoyment of the highest attainable standard of health and the right to enjoy the benefits of scientific progress"*. The main current principles of bioethics are non-maleficence, beneficence, respect for autonomy and social justice (Henein and Ells, 2021; Varkey, 2021). Non-maleficence is the moral obligation of health providers not to harm the patient. Benefiance involves actively seeking the best possible outcomes for patients. It also includes the concept of pursuing economic **efficiency** in the health care delivery as an important ethical principle in utilitarism (Culyer, 1992; Marseille and Kahn, 2019). Efficiency is described as the maximization of health benefits under a budget constraint (Marseille and Kahn, 2019). According to Culyer (1992), it is ethical to be efficient, as inefficiency fails to achieve the ethical goal of maximising health benefits of available resources. The principle of autonomy is the right of patients to receive the necessary information and the freedom to make informed decisions about their health (Varkey, 2021). Finally, social justice in health care refers to the provision of quality care to all individuals.

There are four interrelated principles of social justice: **equity**, access, participation and rights. Health equity is concerned with creating equal opportunities for health and reducing health differentials to the lowest possible level in terms of utilities and quality-adjusted life year (QALYs) (Culyer, 2001). Health equity can also be defined according to Amartya Sen's (1993) capabilities approach as a person's opportunity and ability to generate health outcomes for well-being, involving individual factors (conversion) and the social environment (resources) (Hamilton, 2019). The capabilities approach comprises two norms: the freedom to reach well-being and that well-being must be understood in terms of functioning (valuable beings and doings). That is, *"Sen's capability approach is a moral framework that proposes that social arrangements should be evaluated primarily according to the degree of freedom*

people have to promote or achieve functionings they value" (Alkire, 2022). Functioning includes asset index, access to schooling, body mass index, income, and self-reported health. Sen, who was awarded the Nobel Prize in Economic Sciences 1998, argues that development should be seen as an enhancement of individual freedom rather than focusing only on indicators such as GDP or GDP per capita. Consequently, it is important to assess whether a health technology will promote well-being in terms of welfare (utilities, QALYs) or Sen's capabilities approach (Validate, 2019).

This PhD builds on equity and efficiency as the main ethical principles. That is, access to health care as a citizen's right regardless of individual socioeconomic characteristics (or the person's opportunity and ability to generate well-being, Hamilton (2019)), and the maximization of population health with the available resources (Culyer, 2001; Varkey, 2021). According to Marseille and Kahn (2019), *"efficiency quantified and promoted by cost-effectiveness analysis sometimes conflicts with equity and other ethical values, such as the 'rule of rescue' or rights-based ethical values"*. In these cases, efficiency is normally superior than the alternatives (Marseille and Kahn, 2019). Economic efficiency is a prominent principle in global health decision making (Jamison, 2018). The efficiency principle, which promotes human life and health, is a valid ethical standard applied by the utilitarism ethical theory focusing on outcomes through cost-effectiveness or cost-benefit analysis (Marseille and Kahn, 2019). Even though efficiency assessment is appreciated by policy makers seeking to maximize benefit from limited resources, it also raises concerns about fairness and reduction of disparities (Marseille and Kahn, 2019; Neumann and Weinstein, 2010). The representation of human wellbeing in monetary terms and decision making of life-saving interventions based on return on investment indicators often conflict with a range of ethical principles such as equity and human rights (Rutstein et al., 2017). However, when alternatives to efficiency, such as equity, are preferred, it is critical to quantify the trade-offs, particularly, the lost health benefits associated with deviating from rigorous efficiency measures (Marseille and Kahn, 2019).

2.1.2 European health values and strategies for social justice

The EU health systems are a central part of Europe's high levels of social protection and contribute to social cohesion and justice, and sustainable development (EU, 2006). The overarching values of universality, solidarity, equity and access to good quality care have been widely accepted in the different EU institutions (EU, 2006). Universality means that no-one is barred access to health care. Solidarity is closely linked to the financial arrangement of the national health systems and the need to ensure accessibility to all. Equity relates to equal access according to the need, regardless of ethnicity, gender, age, social status or ability to pay. The EU strategy to increase equity is by working on the **prevention** of illness by the **promotion** of healthy lifestyles as a strategy to reduce the economic burden on the national healthcare systems. Access to medicines refers to the patient's possibility to obtain medicines and is mainly influenced by availability and affordability. Regarding the former, regulatory policies have an impact on the availability of medicines among the EU member states involving pricing policies, lag-time between marketing approval and pricing, generic competition, and prescribing schedules. Regarding the latter, the affordability of a medicine is mostly dependent on the coverage by the health insurer. Reimbursement restrictions and co-payment deeply impact access (EU, 2006).

In terms of EU policies, the new EU Global Health Strategy (GHS) proposal**,** adopted on 30 November 2022 by the European Commission (EC), aims to improve health security worldwide and ensure better health for all (EC, 2022). It includes the commitment to health-related SDGs as part of the European Consensus on Development (EC, 2017). The GHS builds on the previous 2010 global health strategy and lessons learnt from the COVID-19 pandemic. It recognises that global health is affected by the **Triple Planetary Crisis** of climate change, biodiversity loss, and pollution and waste management (UN Climate Change, 2022). According to the UN, climate change is a first-level universal challenge referring to long-term changes in temperature and weather patterns that will completely modify the ecosystems of our planet. Human actions are the main driver of climate change with the use of energy, industry, transport, buildings, agriculture as the main responsible for greenhouse gases released into the atmosphere (UN Climate Change, 2022). The consequences of climate change are water shortages, droughts, wildfires, rising sea levels, floods, melting polar ice and declining biodiversity. Pollution is caused by a wide range of factors including factories, traffic, wildfire, and volcanoes, as well as indoor household activities such as cooking. Air pollution is the leading cause of disease and premature death wordwide, with seven million people dying prematurely each year from pollution. Nine out of ten people worldwide breathe air that contains levels of pollutants that exceed WHO standards (UN Climate Change, 2022).

The GHS positions global health as an essential pillar of the EU external policy, a critical geopolitical sector and a central aspect of EU's strategic autonomy as an essential component of the Global Gateway strategy to redefine its role as global actor (Rodríguez, Rocamora and Plasència, 2023). The GHS strategy focuses on three interconnected policy priorities in a framework leading to 2030, 1) better health throughout life, 2) strengthened health systems and universal health coverage (UHC); and 3) prevent and combat health threats, including pandemics, applying the One Health approach (European Parliament, 2023a). The first priority focuses on people's health, focusing on women and girls. It reinforces the "health in All policies" (HiAP) (Ramírez-Rubio et al., 2019) and coordination for impact aligned with the Team Europe approach. The second priority focuses on health systems, targeting 3 key drivers for better health: digitalisation, research and a skilled labor with specific actions to advance globally in these areas (EC, 2022). Finally, the third priority is related to global health security agenda building on the lessons learnt from the EU response to the COVID-19 pandemic with the focus on antimicrobial resistance (Rodríguez, Rocamora and Plasència, 2023). The GHS outlines 20 guiding principles, including: 1) prioritise addressing the root causes of ill health, with a focus on the rights of women and girls and vulnerable groups; 2) improve equitable access to essential health services; 3) promote global health research; 4) apply a One Health approach and intensify the fight against antimicrobial resistance, and 5) steer the new Global Health governance supporting a stronger, more effective and accountable WHO, in close cooperation with the G7, G20 and other global, regional and bilaterial partners.

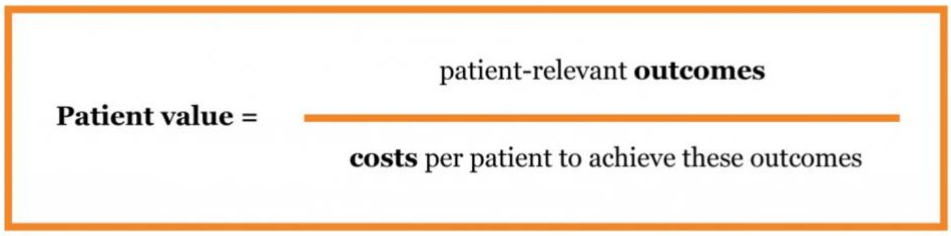
Regarding global partnerships, the EU is part of the UHC partnership and UHC2030 (EC, 2023a), supporting partner countries to identify needed health services and increase access to these services. In terms of EU legislation, the European Parliament approved on 10 November 2022 the mandatory disclosure of **Environmental, Social and Governance (ESG)** indicators with the Sustainable Finance Disclosures Regulation (SFDR) and the EU Corporate Sustainability Reporting Directive (CSRD) regulation. Moreover, the EC defined the new EU Pharmaceutical Strategy Regulation proposal on 26 April 2023 (EC, 2023b) to support innovation by increasing the attractiveness of the EU market and ensuring timely and

equitable access to medicines for patients across the EU. Finally, the NextGenerationEU recovery funds (EC NGEU, 2023) to overcome the economic and social damage of the COVID-19 pandemic, with more than €800 billion between 2021-2027, can contribute to adopting new measures to prepare a better future for the next European generation.

2.1.3 Value-based healthcare

Value in health care is defined as the *"improvement measured in a person's health outcomes by the cost of achieving that improvement"* (Teisberg, Wallace and O'Hara, 2020). That is, value-based healthcare (VBHC) is the equitable, sustainable and transparent use of available resources to achieve better outcomes and experiences for each person (Hurst et al., 2019). VBHC aims to improve patient outcomes while optimising the use of resources through a collaborative and evidence-based approach (Cossio-Gil et al., 2022). As shown in Figure 2.1, patient value is defined as patient-relevant outcomes divided by the costs per patient throughout the care cycle to reach these outcomes (Porter, 2010; Porter and Teisberg, 2006).

2 **Figure 2.1** Patient value in value-based healthcare (VBHC)

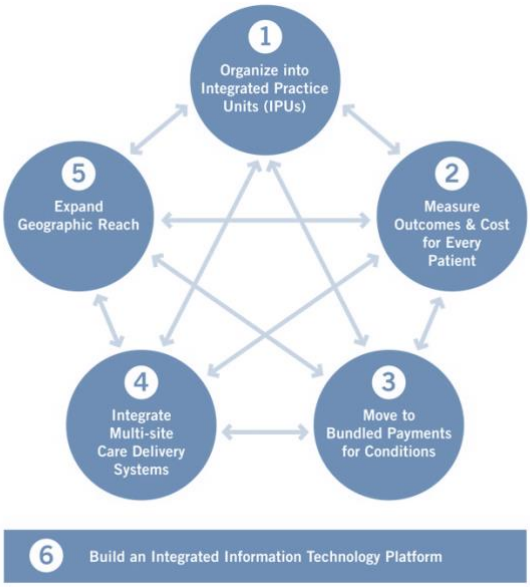


Source. Vintura (2023).

The principles of value-based competition (Porter and Teisberg, 2006) are as follows: 1) the focus should be on value for patients, not just cost reduction; 2) there must be unlimited competition based on results; 3) competition must focus on medical conditions throughout the care cycle; 4) quality care should be less costly; and 5) value is driven by provider experience, scale, and learning at the medical condition level. Porter's value agenda includes six core elements to implement the VBHC (Lee and Porter, 2013) depicted in Figure 2.2.

According to Teisberg, Wallace and O'Hara (2020), VBHC is a pathway to reachining the aspirational goals of the "triple aim", by improving the patient experience of care, improving the health of populations, and reducing the per capita cost of health care, according to the definition of the Institute for Healthcare Improvement. The triple aim can be expanded to the "quadruple aim" by including the goal of improving the working lives of health care providers (Haverfield et al., 2020).

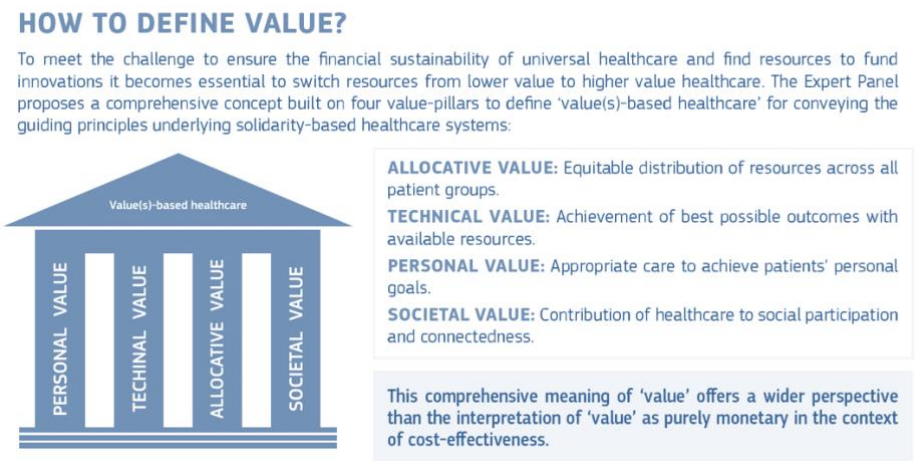
3 **Figure 2.2** VBHC core elements



Source. Harvard Business School.

At EU level, the definition of VBHC is summarized in Figure 2.3 by the EC report of the expert panel (EC, 2019). It includes appropriate care to meet patients' personal goals (personal value), achieving the best possible outcomes with available resources (technical value), the equitable distribution of resources among all patient groups (allocative value), and the contribution of health care to social participation and connection (societal value). The recommendations of the panel for high-value care are to create health awareness for an equal and fair society, develop a long-term strategy with a step-by-step plan towards culture change, support the R&I, encourage participation of health professionals, and promote learning communities.

4 **Figure 2.3** Defining value-based healhcare in the EU



Source. EC (2019).

2.1.4 Health as a public good, global public good and common good

Public good

Another approach is whether health is a public good as defined in economics. As Galea (2016) mentioned, the classic understanding of a public good in economics is based on Paul Samuelson's work on revealed preference were consumers are rational, so their behavior reveals their preferences (Samuelson, 1954). According to this, a public good is non-excludable and non-rival, where no one can be excluded from its use and where the use by one does not diminish the availability of the good for others. Classic examples of public goods include air, water, parks, and national security that are tipically managed by governments to avoid market failure, as the private sector does not have has sufficient incentives to provide universal access to these goods.

According to Galea (2016) *"health generally is not considered a public good, because non-paying individuals (for health insurance, healthy food, etc.) may not be able to achieve good health".* In this sense, efforts to introduce UHC in all countries will bring healthcare closer to being a public good (Galea, 2016). The adoption of social insurance or other publicly funded health insurance systems, where all citizens are insured and can use healthcare services regardless of whether they can pay for them, suggests that public insured health services become non-excludable and non-rival, approaching better a public good.

Global Public Good

Furthermore, Kaul el al. (1999) developed the concept of global public good in which national goverments cannot guarantee the provision of a public good because of global interrelationships that require international cooperation, international laws and incentives (Mazzucato, 2023). Kaul et al. (1999) define three types of global public goods: natural (i.e. climate), man-made (i.e. scientific knowledge) and policy outcomes (i.e. peace, financial stability). Accepting the basic elements of public health as a global public good can be the basis for developing and aligning effective investments for prevention, innovation and access to care (Abdalla et al., 2020; Galea, 2016).

Common Good

Finally, the economics of the common good was developed in Austria and Germany in 2010. It challenges the neoclassical economic theory (with 150 years of academic tradition) focused on the growth of the amount of goods produced as a measure of prosperity, which has shown to generate ecological and social imbalances (Dolderer, Felber and Teitscheid, 2021). Neoclassical economics builds on the positivism theory which claims to be completely objective based on individualism, rationality and general equilibrium of markets (Arnsperger and Varoufakis, 2006; Dolderer et al., 2021; Lawson, 2013). Instead, the common good is defined as *"a goal to be achieved together".*

The common good is different from a public good in that it is not "a correction of market failure with the public sector filling the gap of the private sector" (Mazzucato, 2023b). The difference with public and private goods is that the former is led by goverments and the latter by businesses, while common goods require **shared investment**, **ownership** and **governance**

(Deneulin and Townsend, 2007, cited in Mazzucato, 2023b; Sparkes, Kutzin and Earle, 2019). The difference between public goods and common goods is sumarised in Table 2.1.

1 Table 2.1 Public good versus Common good

Public Good	Common Good
Correction	Objective
Market Failure	Market Shaping
Outcome-Oriented	Outcome- and Process-Oriented
Governmental Action	Collective Interaction
Top-Down	Bottom-Up

Source. Mazzucato (2023b).

The common good focuses on a shared goal and a collective action to reach results, committed to principles such as transparency, reflexibity, value-orientation, participation, and plurality (Dolderer et al., 2021). That is, a mission and a process (the "how") to accomplish the desired outcomes together. The process includes how knowledge is shared during the R&I cycle, so coordination is key (Mazzucato, 2023 based on Dolderer et al., 2021; Murphy and Parkey, 2016). For instance, in the COVID-19 pandemic, the application of a common good principle would have led stakeholders to set global vaccination as a goal, rather than national targets. This objective would have promoted the inclusion of principles of justice and equity in investment, innovation and collaboration, leading to knowledge sharing (i.e. decentralising vaccine production) (Mazzucato, 2023b). In general, the common good involves **mission-** and **outcome-oriented policies, conditionality schemes, reward sharing**, and multistakeholder **co-creation** (Mazzucatto, 2023).

2.2 MODELS IN HEALTHCARE

This section summarises two main models in healthcare, the one called "public value" oriented to the needs of public health through the distribution of risks and rewards, as opposed to the conventional "shareholder" model focused on maximising the benefits of the private sector. This tension between the existing models serves as the basis for proposing the Preferred Supplier as an alternative model developed in this reaseach.

2.2.1 Shareholder model: Maximising industry profit

The traditional "shareholder" model advocated pricing based on the high costs of healthcare R&I. The pharmaceutical industry claims that they spend $2.6 billion on R&I of a new drug (Avorn, 2015). Although the average cost of developing a new drug is still a matter of debate, recent estimates using publicly available data range from $314 million to $2.8 billion (Wouters, McKee and Luyten, 2020). In this model, the patent-protected monopoly price is considered necessary to pay for the long and failure-filled R&I process involved in successfully bringing a therapy to market (DiMasi et al., 1991; DiMasi, Grabowski and Hansen, 2016). But this method, strongly supported by industry, has been criticized for the lack of transparency

about what counts as part of a firm's R&I costs, as well as the inclusion of opportunity costs (of capital), which represent almost half of the estimated total cost (Avorn, 2015).

Over a decade ago, the healthcare industry shifted to a **value-based pricing** strategy to *"give market value perceptions"* (Teisberg, Wallace and O'Hara, 2020). Value-based pricing is quantified and evaluated largely based on two health metrics, **cost-effectiveness** and **prevention**. In this definition, manufacturers are pushing to include the prevention value of new medicines by increasing the valuation of health innovations. Consequently, it tends to reward each incremental innovation with significant price increases (in many cases exceeding the scope of the therapeutic breakthrough), disproportionately rewarding end-stage value extraction by manufacturers and their shareholders.

According to Mazzucato and Roy (2019), the prevailing value narrative for health innovation can be summarised as follows "*higher prices represent the value of health improvements*", based on the logic that consumers are willing to pay more for better health outcomes, and that this payment will direct innovation towards the production of high-value therapies. As they point out, the problem is that consumers are not individual patients because the responsibility to "value" new medicines rests with the final buyers, that is, public health systems (Reinhardt, 2015). Alternatively, value can be reimagined in terms of value creation that foregrounds the long-term public leadership required for innovation (Mazzucato and Roy, 2019).

2.2.2 Public Value Model: Socialising risks and rewards

Some health economists are pushing to rethink health innovation in terms of the direction (meeting public health needs) and the accessibility (affordable low margin prices) of medical products given that the government, as a major investor and buyer in R&I, can shape and co-create markets. In other words, the public sector should not be relegated as simple regulator that corrects market failures but rather an active creator of new market spaces as a business opportunity (Laplane and Mazzucato, 2020; Mazzucato, 2016a; Mazzucato and Roy, 2019). In their view, value in health (R&I value chain) is determined by the collective investment between public, private and civil society organizations that define the pace and direction of value creation, rather than "market forces" oriented towards profit maximization for industry shareholders. They argue that the government must negotiate a better deal for publicly funded pharmaceutical research to deliver affordable and accessible therapeutics advances, reflecting the public contribution, so that taxpayers do not pay twice (publicly subsidized research and high-priced medicines). As a result, drug prices should not be much higher than manufacturing costs and should be transparent. That is, industry should disclose the cost of R&I and the source of funding, so that governments can ensure that prices reflect the burden of financial risk borne by taxpayers.

In this sense, health innovation can direct government-led "missions" for societal health needs such as healthy aging, antimicrobial resistance, cancer, and epidemic prevention, not just to de-risk private costs (Mazzucato, 2018). The public sector should then make the necessary investments in the **direction** of the "mission" together with the private sector, determining the **public-private investment mix**, and managing the **distribution of risks** and **rewards** to ensure sustainable and equitable outcomes (Mazzucato and Roy, 2019; Miethke et al., 2021). This socialization of rewards would promote a more equitable public–private partnerships to mediate asymmetric power relations, tensions and conflicting views among

stakeholders, as well as building a shared notion of the value and legitimacy of the role of the state (Laplane and Mazzucato, 2020).

In brief, in the "public value" model, health value is less defined in terms of comparative cost-benefit ratios of competing therapies, but rather in terms of directions, contribution to the value chain (dynamic divisions of the work and investment), and distribution of risks and rewards for innovation (Mazzucato and Roy, 2019), as follows:

1) Directed to fulfil social health needs and mission-oriented R&I coordinated by governments to address major global health challenges (i.e. SDGs, green economy), attracting public and private investment, implemented through decentralized public-private networks and creating new commercial opportunities while addressing crucial health needs (Mazzucato, 2021; Goyeneche et al., 2022; Sachs et al., 2019). Missions would be defined through public deliberation in a relatively top-down manner and policy instruments should allow for bottom-up creative experimentation in the innovative process.

2) Multi-stakeholder value creation as alternative ways to organise and incentivise innovative workforce by fostering disruptive innovation. Funding for such innovation would combine grants, milestone awards and contracts, with rewards focused on health benefits rather than patentability (Quigley, 2017). For example, pricing could allow the exchange of financial rewards for licensing of a new technology to a generic producer, bringing the price of new technologies closer to production costs rather than those expected by shareholders (Love and Hubbard, 2009). The GAVI The Vaccine Alliance public-private partnerships, the product development partnerships such as the Drugs for Neglected Diseases Initiative (DNDi), as well as innovative government agencies such as DARPA (Defence Advanced Research Projects Agency) and BARDA (Biomedical Advanced Research and Development Authority) in the US, are examples of such models that can be tested for wider areas of critical unmet health needs (Ikilezi et al., 2020; Liu, 2020; Mowbray et al., 2021; Singh et al., 2022).

3) Fair distribution of risk and rewards that sustains the process of value innovation through value creation, the long-termism, the willingness to fail and the diffusion and deployment of new technologies. This can be achieved with different strategies. First, the government receives royalties from companies in which public funding played an important role and reinvest them in future innovation (i.e. innovation funds) (Mazzucato, 2013; Mazzucato, 2016b). Second, the public sector retains a "golden share" of patents developed with public funding, with patents governed to be weak and narrow (rather than strong and broad) to stimulate greater use and innovation (Mazzoleni and Nelson, 1998). Third, public health systems pay prices that reflect both public contributions and the impact of new therapies on public budgets, with the price of new drugs linked to the possibility of universal access by health systems and patients (ICER, 2023). Fourth, changing the rules of the game in shareholder-driven, financial market-based economies so that companies are accountable to multiple stakeholders, including patients and health systems as part of the heatlhcare value constellation, rather than just shareholders (Lazonick, 2014; Pereno and Eriksson, 2020). These rule changes would direct profits generated through collective investment (crowdfunding) to be reinvested for the public benefit rather than held as cash stockpiles or stock buybacks deployed by large pharmaceutical companies (Palladino, Lenore and Lazonick,

2022). The challenge is to develop the incentive and regulation of this multistakeholder model.

Regarding the VBHC, unlike the "shareholder" model, the "public value" theory claims to demystify value as high prices that incentivize incremental advances over therapeutic breakthroughs. A broader deliberation on value (how it is created and how the creative process can be directed to reach public value) is required - not based on the assumptions underlying value-based pricing - to truly address the challenges faced by patients and populations in the future years. Furthermore, as Mazzucato (2023b) mentioned, *"the rewards of innovation and investment, sometimes as profits for business, must be shared as socially as the risks taken to solve the problem".*

The consideration of health value as a "public good" or a "common good" (Mazzucato, 2023b) (refer to 5.1.4) should encourage a radical rethinking of health innovation as it is currently conceived, with attempts to reform the dominant shareholder model while experimenting with paradigm shift strategies. Ultimately, because value creation is a collective process, discussions about directions of innovation and distributions of rewards must also be subject to proactive public deliberation (Mazzucato and Roy, 2019).

2.2.3 Preferred Supplier Model: Health innovation in the public interest

The massive global mobilisation to cope with the COVID-19 pandemic represented a turning point and a unique opportunity to increase social awareness of the value of global health to world prosperity. It also showed that an equitable distribution of vaccines, diagnostics and treatments did not consist only of increasing inputs, but redefining how different public and private actors interrelate (Alonso et al., 2021a and 2021b). **Public investment** and **procurement** can be a game-changer in the new health innovation model. Governments invest considerable resources in biomedical R&I through taxpayer-funded research, publicly funded grants and mechanisms that increase the rewards or reduce the risk of R&I. Most importantly, they are by far the largest purchaser of pharmaceuticals (WHO, 2020a). In the EU, more than 250,000 public authorities spend around 14% of the GDP (about €2 trillion) on the purchase of services, works and supplies (García-Altés et al., 2023) and many of them are found in the health sector. Thus, there is an opportunity to enhance the role of public procurement as a tool that shapes and creates markets for innovation, increasing efficiency and contributing to better health outcomes (Andrews et al., 2023; Bleda and Chicot, 2020; García-Altés et al., 2023; Torvinen and Jansson, 2023; Uyarra et al., 2020).

Therefore, as outlined in the "public value" model, governments can and should ensure that such innovations are designed in a more fair, efficient and effective way to respond to the public health needs of HICs and LMICs, guaranteeing access to medicines and, ultimately, access to health as fundamental human right (Cook, 2020; Moeckli et al., 2022). Public policy must drive industry to embrace new R&I approaches that deliver affordable solutions to unmet needs reducing the health equity gap.

ISGlobal's Innovation and Policy teams (Alonso et al., 2021a and 2021b) have proposed the fundamentals of a **Preferred Supplier Model (PSM)** for a public investment and procurement system. In the PSM, the public sector prioritises business with companies that comply with the **"4 Share" (4S) principles**, ensuring health needs are met. The PSM should be understood

as the basic criterion that the industry must meet to become a preferred provider and preferred investment recipient of the government. ISGlobal's proposal (Alonso et al., 2021a) reflects current procurement and supply practices in which the private sector applies **sustainability** and **ethical principles** – focused on the environment, human rights such as child labor, equality of opportunities and non-discriminatory treatment (Zhang, Pawar and Bhardwaj, 2017) – to redirect the research agenda and supply chain practices to address market failure.

As mentioned, an example of smart procurement practice by the industry is the international private B Corp certification to meet environmental, social and ethical standards and require suppliers to do so. Additionally, an example of smart public procurement is the Big Buyers initiative for Climate and Environment launched by the EC in 2018, under the small and medium enterprises (SME) Strategy, which pools the demand of public buyers to maximize market power and impact for sustainable innovation (EC, 2023c). The Big Buyer procedure is based on the "*winner-takes it all*" related to supply conditions in terms of price, timely delivery, green production and security, and continuity of supply.

The PSM aims to be the fundamental framework of health innovation policy, defining, not only the public investment and procurement system, but other policies such as the research and industrial policy to promote the public interest. The proposed model is fully aligned with the 2030 Sustainable Development Agenda, promoting R&I and access to quality essential medicines (UHC2030, 2023), targeting priority global health challenges such as antimicrobial resistance and epidemic preparedness and response, among others. According to Alonso et al. (2021a), interactions between public and private sector organizations should be based on the following PSM 4S principles:

- **Sharing needs**. To ensure that the medical research agenda prioritises the major public health needs, the Preferred Supplier should invest a tangible share of its R&I portfolio in addressing these needs.

- **Sharing risks & rewards**. To ensure a more balanced and transparent distribution of R&I risks and rewards throughout the development pipeline, a Preferred Supplier would acknowledge public resources received during the R&I cycle. The amount of public funding should affect the protection of IPR with the participation in the commercial profits associated with the final product, impacting its price.

- **Sharing results**. If public funds are invested in pharmaceutical R&I, they should be conditional on ensuring that the results (end products and knowledge generated) are accessible. A Preferred Supplier would provide access to clinical trial results, as well as access to all the information related to drug candidates that have ultimately been neglected. This data would be considered a public good.

- **Sharing outcomes.** Preferential access to public funds as Preferred Suppliers would be granted to companies that demonstrate compliance with the best environmental standards in manufacturing and distribution, health equity practices and fair financial management (reduction in stock buybacks and reinvestment of some profits in new R&I).

In return, the government would provide significant push and pull incentives for priority health challenges. Moreover, the size of the public partner market must be to be large enough for companies to adopt the proposed measures. More detailed analysis is needed to expand the principles, define indicators and desing the incentive and regulation scheme.

Regarding indicators, the present thesis will explore whether the PSM could build on the existing ESG (see section 2.1.2) and the Access to Medicine Index (ATMi). The ATMi ranks the world's 20 largest pharma companies based on their ability to expand access in LMICs, assessing: 1) governance (strategy), 2) R&I portfolio, and 3) implementation (price and delivery). Since 2008, the biennial index has been published by the Access to Medicine Foundation in the Netherlands, an independent non-profit organization funded by the governments of the United Kingdom (UK) and the Netherlands, the Bill and Melinda Gates Foundation, The Leona M. and Harry B. Helmsley Charitable Trust and AXA Investment Managers. For instance, the aforementioned Pfizer Accord initiative will likely significantly improve the company's upcoming ATMi ranking position. In the health sector, an index similar to ATMi could stimulate the industry to improve global access by getting credit as Preferred Suppliers. This access to medicine index like would stimulate competition among the pharmaceutical industry to create the most innovative products in terms of efficiency and equity for global health priorities. An adaptation of the ATMi could be adopted considering the PSM 4S principles and convert it into a KPI to be measured and audited at industry level.

According to Alonso et al. (2021a), the PSM approach needs transparency, international cooperation and governance. Regarding the former, confidentiality agreements between companies and public buyers are common, although this practice is progressively reversed (EC, 2021). Regarding the last two, the PSM 4S model cannot succeed without the support of influential governments, multilateral organizations and visionary industry leaders (Alonso et al., 2021a and 2021b).

3 OBJECTIVES

The objective of this research is to explore and define the most appropiate model to better connect the creation and translation of biomedical knowledge with the health needs of the population, promoting equity and a sustainable collaborative ecosystem that fosters efficiency. Overall, this research aims to stimulate a thriving public debate with alternatives to the *status quo*, inspiring further research into health equity models.

The ultimate goal of this research is to help close the gaps in health disparities in the world by breaking the vicious circle of poverty and disease and promoting the virtuous cycle of health and prosperity for all.

More specifically, the main objectives are shown below:

O1. Confirm, in the light of consensus social values, that the current biomedical R&I model has a health equity problem that needs to be addressed.

O2. Identify the main consensus causes that hinder health innovation from fulfilling the desired equity goals.

O3. Validate the principles and conditions of a co-created consensus equitable health innovation model based on the Preferred Supplier model (PSM).

O4. Prioritise a set of barriers and enablers for the implementation of the co-created consensus PSM.

O5. Make policy recommendations based on these findings.

4 RESEARCH QUESTIONS

The research questions posed in this PhD thesis are defined below.

Main research question: **Which would be the grounds and conditions for the success of a more equitable health innovation model?**

Specific research questions:

RQ1. Which moral dilemma prevents health innovation from realising socially desirable goals?

RQ2. Which are the agreed explanations by which health innovation is unable to fulfil the desired equity goals?

RQ3. Which could be the underpinning characteristics of a co-created consensus PSM for health equity?

RQ4. Which are the main ranked PSM barriers and drivers?

RQ5. Which policy recommendations arise from the consensus PSM?

5 HYPOTHESES

The main hypothesis of this research is that it is desired and feasible to co-create a new health innovation model building on the shared social values of different stakeholders and based on the market power of public buyers. This new biomedical R&I model would offer the appropriate incentives and risk leveraging practices resulting in a new fair play for more equitable, agile and sustainable outcomes.

The specific hypotheses aligned with the thesis objectives are the following:

H1. There is a moral dilemma in health innovation that, when incentives are not aligned with public health priorities, efficiency (in terms of commercial rewards) takes preference over equity, resulting in a health equity problem.

H2. Consensus main causes that prevent equitable health innovation are related to the lack of sharing needs, results, risks and rewards, and outcomes, in addition to the lack of governance.

H3. Governments, as major investors and buyers of biomedical innovation, are well positioned to drive industry toward environmental and health equity practices and get credit as Preferred Suppliers, by aligning incentives to public health priorities in accordance with the "4 Share" principles (sharing needs, results, risks and rewards, and outcomes) and adequate governance.

H4. The key PSM barriers are related to the health systems capabilities, the pricing scheme and the dominant position of the industry in health policies. The key PSM enablers are related to expanding ESG practices.

H5. Policy recommendations should consider appropriate incentives and regulation to promote the implementation of the consensus PSM.

Table 5.1 shows the research objectives, questions and hypotheses of this PhD thesis.

2 **Table 5.1** Research objectives, questions and hypotheses

Objectives	Research questions	Hypotheses
1. Confirm, in the light of consensus social values, that the current biomedical R&I model has a health equity problem that needs to be addressed.	Which moral dilemma prevents health innovation from realising socially desirable goals?	There is a moral dilemma in health innovation that, when incentives are not aligned with public health priorities, efficiency (in terms of commercial rewards) takes preference over equity, resulting in a health equity problem.
2. Identify the main consensus causes that hinder health innovation from fulfilling the desired equity goals.	Which are the agreed explanations by which health innovation is unable to fulfil the desired equity goals?	Consensus main causes that prevent equitable health innovation are related to the lack of sharing needs, results, risks and rewards, and outcomes, in addition to the lack of governance.
3. Validate the principles and conditions of a co-created consensus equitable health innovation model based on the Preferred Supplier model (PSM).	Which could be the underpinning characteristics of a co-created consensus PSM for health equity?	Governments, as major investors and buyers of biomedical innovation, are well positioned to drive industry toward environmental and health equity practices and get credit as Preferred Suppliers, by aligning incentives to public health priorities in accordance with the "4 Share" principles (sharing needs, results, risks and rewards, and outcomes) and adequate governance.
4. Prioritise a set of barriers and enablers for the implementation of the co-created consensus PSM.	Which are the main ranked PSM barriers and drivers?	The key PSM barriers are related to the health systems capabilities, the pricing scheme and the dominant position of the industry in health policies. The key PSM enablers are related to expanding ESG practices.
5. Make policy recommendations based on these findings.	Which policy recommendations arise from the consensus PSM?	Policy recommendations should consider appropriate incentives and regulation to promote the implementation of the consensus PSM.

6 METHODOLOGY

This chapter includes several sections on the methodology applied in this research, the desing of the expert panel, data collection, data analysis, and ethical considerations. The applied mixed methodology involves a constructive HTA (cHTA) approach as a social analysis to solve a policy problem (section 6.1). The cHTA comprises the analytical framework of the interpretive frames, Richardson's model for solving a moral dilemma with the specification of norms, and the technique of argumentation circles (section 6.2). Moreover, it applies a

modified Delphi method to reach consensus among a wide range of stakeholders (section 6.3). The design of the expert involves a social map and the choice of the expert panel membership (section 6.4). Data collection involves primary and secondary data, specifying data collection per objective (section 6.5). The data analysis includes the different consensus criteria applied to each round (section 6.6). Finally, bioethical considerations describe the ethical requirements that the present research meets (section 6.7).

6.1 HTA APPROACH

6.1.1 HTA methodology as a social analysis

This policy research focuses on the disparate access and equity outcomes of the current medical R&I model. It proposes the co-design of a new model to deal with the social challenges. The research work is based on the **Health Technology Assessment (HTA)** methodology applied to co-create a new R&I process in healthcare. Table 6.1 summarises the HTA definition according to INAHTA and HTA International (HTAi).

3 **Table 6.1** HTA definition according to INAHTA and HTAi

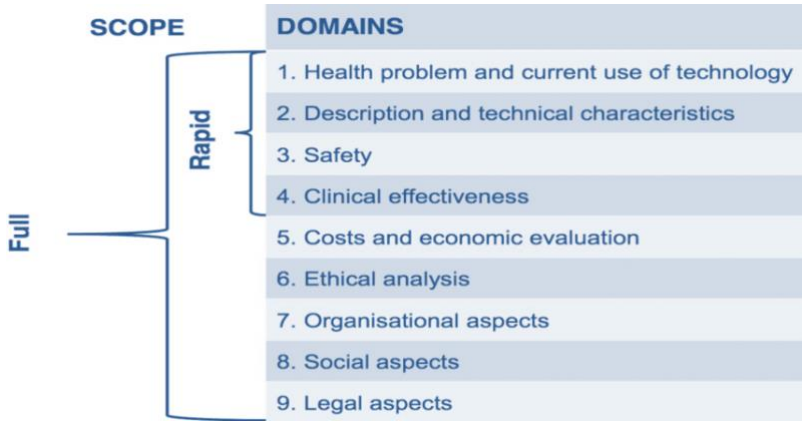
- *A multidisciplinary process that uses explicit methods to determine the value of a health technology at different points in its lifecycle. The purpose is to inform decision-making to promote an equitable, efficient, and high-quality health system.*
- *Intervention developed to prevent, diagnose or treat medical conditions; promote health; provide rehabilitation; or organize healthcare delivery. The intervention can be a test, device, medicine, vaccine, procedure, program or system.*
- *The process is formal, systematic and transparent, and uses state-of-the-art methods to consider the best available evidence.*
- *The dimensions of value for an HTA may be assessed by examining the intended and unintended consequences of using a health technology compared to existing alternatives. These often include clinical effectiveness, safety, costs and economic implications, ethical, social, cultural and legal issues, organisational and environmental aspects, as well as wider implications for the patient, relatives, caregivers, and the population.*
- *The overall value may vary depending on the perspective taken, the stakeholders involved, and the decision context.*
- *The assessment can be applied at different points in the lifecycle of a health technology (i.e.pre-market, market approval, post-market, and disinvestment).*

Source. O'Rourke et al. (2020).

HTA is a form of policy research such as the relationship between policy problems (i.e. unmet medical needs, health inequity) and solutions (i.e. new health innovation model) (Schon and Rein, 1994). Despite its policy goals, HTA must always be firmly rooted in research and the scientific method. HTA covers different aspects called "domains" developed by EUnetHTA (Kristensen et al., 2017) as shown in Figure 6.1.

The present research focuses on the desirability of social aspects (health equity) for a new biomedical R&I incentive model jointly constructed by the different interest groups. It applies an interactive HTA technique based on an adaptation of Grin, van de Graaf and Hoppe (1997).

5 **Figure 6.1** HTA core model domains according to EUnetHTA



Source. Kristensen et al. (2017).

6.1.2 Type of Policy problem

A proposed technology makes sense in light of how the problem it seeks to solve is framed. According to Grin et al. (1997), since HTA is an analysis of the relationship between technological or process developments (such as the R&I model) and political and social problems (such as health inequity) it has a very normative bias since the very start. The nature of the uncertainty of the research question is important for the choice of HTA. According to Grin et al. (1997), there are two types of uncertainty regarding:

Values: The different actors perceive reality through their own value systems and corresponding worldviews. These value systems focus actors' attention on certain facts and interrelationships, and help them to make sense of the facts. It represents the **direction** "*where we want to go*".

Facts: The cause of this uncertainty is the lack of information about issues that are relatively new or yet to arise in the future. The high costs (financial or social) of acquiring adequate information are also a source of uncertainty. It represents the **means** "*how to get there*".

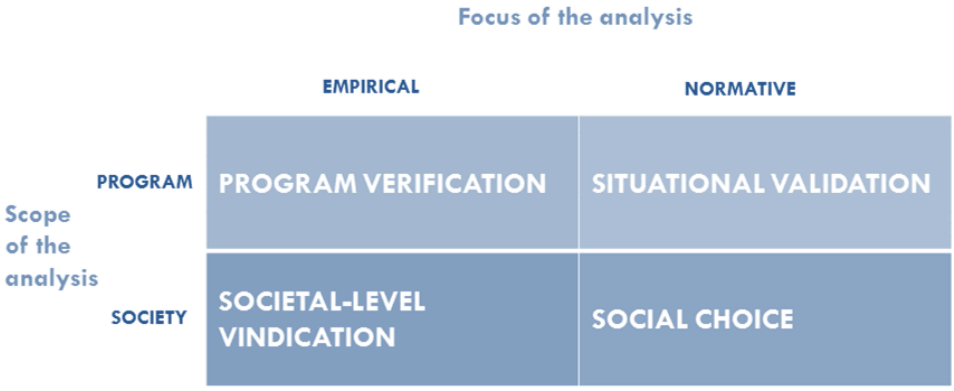
Uncertainty in both values and facts leads to an unstructured problem, which is a great challenge for researchers and policy makers because we, as society, do not know exactly where we want to go and we do not know how to get there. Reaching a more equitable health innovation model is likely a relatively **unstructured problem**. It inherently manifests the tension between industry's profit orientation and socially desirable public health goals and thus, the apparent **value dissent** (in terms of direction). Furthermore, the magnitude and severity of the problem and the main causes and measures likely to alleviate it can be seen as different among the stakeholders, pointing out a **fact dissent** (in terms of means).

According to the concept of policy as the co-creation of an appropriate response, in such situations, the problem must be truly understood from the various perspectives and explore any policy can be devised that is critical as well as respectful of these perspectives (Alford, 2014). As defined by Grin et al. (1997), in cases of value dissent, the debate between the adherents of the different value systems is necessary to structure the problem, but there is

the risk of degenerating into a *dialogue of the deaf* if the differences in underlying value systems are not made explicit. An **interactive HTA** (iHTA) applies a bottom-up approach, considering the **viewpoints** of all **interested parties** (Grin et al., 2017). The iHTA offers a necessary space for exchange to structure the problem and reach a certain development path (co-created solution) considered meaningful by all parties involved (Grin et al., 1997).

Moreover, different types of problems call for different approaches in terms of research and analysis to produce truly helpful policy advice. Figure 6.2 shows the four types of policy analysis described by Fischer (1995) according to the focus of the analysis (empirical "facts" or normative "values") and the scope (program or societal level). Where, in terms of focus, the normative framework is critically challenged (the values underlying R&I model are not shared by the stakeholders) and, in terms of scope, the analysis should be at societal level rather than at the program level (questions the organization and health care goals) a social choice analysis is appropriate. **Social choice** analysis focuses on the **concepts** and **assumptions underlying the problem** and has been applied in this study. The aim of the iHTA has been to help define a consensus social choice in terms of "*what we, as society, aim to achieve in terms of health*?" (direction), and consequently, "*which R&I model can help reach our health goals?"* (means).

6 **Figure 6.2** Fisher type of policy analysis



Source: Validate (2019).

6.1.3 Constructive HTA

iHTA stands for interactive health technology assessment in which the views of different stakeholders are considered. An iHTA is a kind of social experiment, an attempt to conduct a creative and innovative analysis in a space as free of power influences as possible. When the iHTA is conducted at an **early phase** of a technology or process development and aims to integrate normative aspects (values) in the design of this technology or process it is called **Constructive Technology Assessment** (cHTA). A cHTA with a mixed method research technique, combining qualitative and quantitative research elements, has been applied to assess the different **views, perspectives and attitudes** of the stakeholders representing the R&I ecosystem (Grin et al., 1997). Overall, the goal of the cHTA has been to consider early multi-stakeholder participation to co-create and reach consensus on a new equitable health

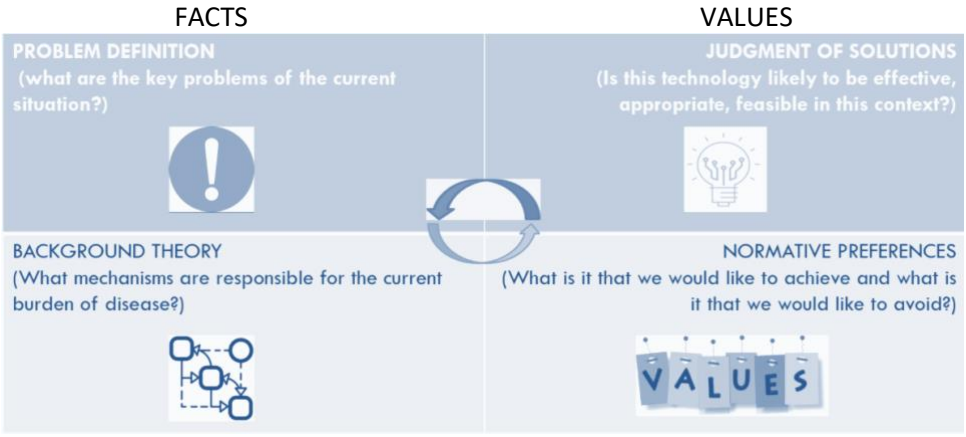
R&I model by making the necessary adjustments to the PSM in the light of a set of norms, principles and conditions (Grin et al., 1997).

6.2 cHTA Analytic framework

6.2.1. Interpretive Frames

The cHTA has applied the methodology of reconstructing the interpretive frames (Grin et al., 1997). Each participating stakeholder was asked open-ended questions about the 4 categories of interpretive frames: problem definition (PD), background theory (BT), normative preferences (NP) and judgement of solutions (JS), as shown in Figure 6.3. Problem definition and background theory represent "facts", whereas judgement of the solutions and normative preferences represent "values".

7 **Figure 6.3** cHTA Interpretive Frames



Source. Validate (2019) based on Grin et al. (1997).

The interpretive frames are the conceptual schemes that stakeholders use (often implicitly) to interpret a situation, and making them explicit helps to better understand the sources of discrepancies as a basis for working towards a joint construction agreed by all parties. Table 6.2 describes the four elements that define the interpretive frames.

4 **Table 6.2** Interpretive Frames analytical framework

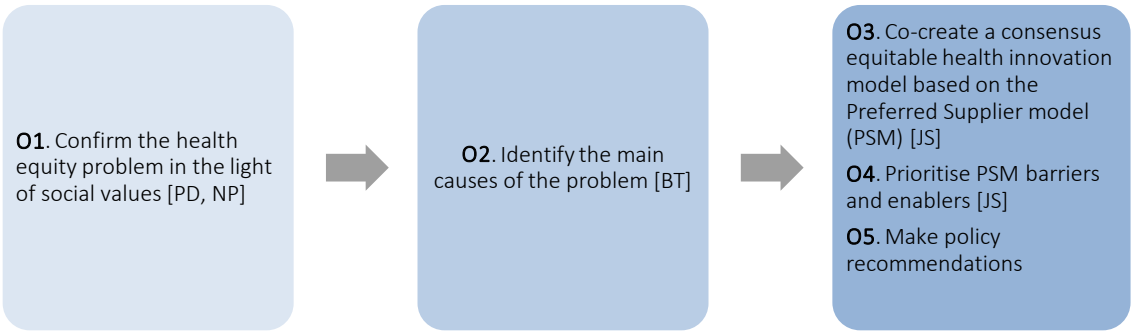
The interpretive frames consist of the following four elements: First beliefs (beliefs about the current and proposed R&I model) • **Judgment of solutions** (JS): whether the new proposed R&I model is considered appropriate (feasible, effective, desirable) to solve unmet needs and reach equity in healthcare. • **Problem definition** (PD): what is particularly problematic in meeting the health needs of patients, their families, providers and healthcare managers?

Second beliefs (underlying beliefs about the reliability and relevance of first order beliefs)

- **Background theory** (BT) (feasibility) what is possible / impossible (in terms of feasibility of the proposed R&I model), main causes or mechanisms underlying the current situation; why the current R&I model leads to health gaps?
- **Normative preferences** (NP) (relevance): what values should be observed in the R&I process? what actors want to achieve with the R&I model? what is desirable?

By reconstructing the interpretive frames of multiple stakeholders, differences in judgements of specific solutions (a new R&I model) can be related to differences in problem definition, background theory and normative preferences. The cHTA method with the reconstruction of the interpretive frames has facilitated learning between the actors, generating new conceptualisations, perspectives and approaches to define the problem and a reach a consensus solution. Figure 6.4 summarises the relation between research objectives and cHTA interpretive frames.

8 **Figure 6.4** Research objectives and cHTA Interpretive Frames

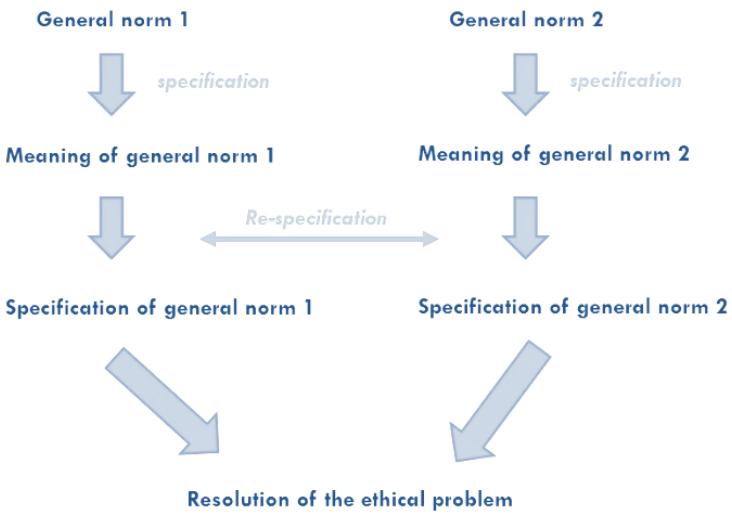


Note. Interpretive Frames: NP, normative preferences; PD, problem definition; BT, background theory; JS, judgement of solution. Source. Self-created.

6.2.2 Richardson model of specifying norms

The expected value dissent between stakeholders has implied a conflict of ethical norms generating an ethical dilemma. The cHTA has applied a modified Richardson model (Richardson, 2019) of specifying norms (revision of the definition of the norms) for the resolution of the moral dilemma (Figure 6.5). In other words, we have identified and specified the main ethical norms to achieve **normative consensus.**

9 **Figure 6.5** Richardson model of specifying norms



Source. Validate (2019).

6.2.3 Constructivism: Argumentation circles

The methodology for constructivist evaluations developed by Guba and Lincoln (1989; 2001) has been taken as a starting point. The constructivism theory states that humans construct knowledge through their intelligence, experiences and interactions with the world, therefore reality is subjective. For social constructivism, knowledge results from many social processes and interactions. It characterises knowledge as the set of **beliefs** or mental models people use to **interpret** actions and events in the world (Detel, 2015). The constructivist evaluation methodology consists of the **argumentation circle,** which must be repeatedly worked through. It is called the hermeneutic-dialectical circle and consists that the various participants' problem definitions and solution assessments are identified and brought into connection by the researcher and gradually grow into a joint construction that can be tested by the different participants.

There are two ways to apply the argumentation circle. In the first option, the researcher interviews a participant and then reconstructs their problem definition and the judgement of the solution. A second participant is interviewed in the same way. Subsequently the second respondent is introduced the problem definition and solution assessments of the first respondent. Based on the second respondent's views and the comments on the views of the first respondent, the researcher tries to create an initial joint construction until all the relevant participants have been interviewed. The joint construction can be tested and perfected in a second, and possibly third or fourth round. In the second option, the researcher first interviews all the participants and reconstruct their problem definitions and solution assessments independently. The researcher then formulates an initial joint construction that is presented to the diferent participants in a second, or even a third round. In the present research, an adaptation of the first option method, applying the triangulation technique to introduce prior respondents' feedback, has been applied to stimulate the iterative process driven by the stakeholders rather than the analyst. Table 6.3 displays some considerations on the argumentation circle method applied.

5 **Table 6.3** Argumentation circle method

• Participants have been interviewed as openly as possible to clarify their views, facts and assessments. • The researcher has combined openness and impartiality towards all participants with the determination to keep the process going and to take care for substantive closure. • All participants have been provided clarity about the methods and techniques used. • Repeatedly working through the argumentation has contributed to guarantee that the researcher's own knowledge, intuition and contribution have not 'sneaked in' biases. • The actors have been asked to evaluate the feasibility of certain ideas and to indicate enablers and challenges to bring them to reality. • A part from interviews, literature review has been considered.

Overall, the cHTA applied in this research aimed to find a joint consensus construction of the new R&I model based on the PSM that all parties judged positively (Grin et al., 1997).

6.3 DELPHI METHOD TO REACH CONSENSUS

Delphi is a scientific method for structuring expert discussion to **generate insights** and **reach consensus** on complex or controversial topics with limited information (Beiderbeck et al., 2021)**.** The Delphi method was originally designed during the 1950s by the Rand Corporation under the contract to the US government to predict the likely outcomes of the use of nuclear weapons in the Cold War (Avella, 2016; Sekayi and Kennedy, 2017). Its name comes from the ancient Greek city that housed the oracle of Delphi, where a priestess communicated with the gods to answer questions (deBoer and Hale, 2002, cited in Avella, 2016). The technique has been frequently used in various scientific disciplines ranging from health, medicine, education, business, engineering, social and environmental sciences (Habibi, Sarafrazi and Izadyar, 2014; Hasson, Keeney, McKenna 2000).

Key aspects of the Delphi method include the use of **experts**, **anonymity**, **rounds** and **controlled feedback** (Keeney, McKenna and Hasson, 2011). As Kobus and Westner (2016) described, the goal of a Delphi is to achieve the most reliable consensus among a group of specialists by questioning individual experts over several rounds, providing anonymous feedback from other experts between rounds, and avoiding direct confrontation. Aggregated group responses from previous questionnaires are provided with each new questionnaire, and the experts can reconsider their judgments on this basis, revising them as appropriate (Niederberger and Spranger, 2020). Table 6.4 describes the implications of the Delphi technique.

Delphi can be qualitative, quantitative and mixed methods approach (Sekayi and Kennedy, 2017). This study applied a mixed method approach, with a primary qualitative approach based on one-hour in-depth interviews with experts to get insights and obtain qualitative narrative statements that were then assessed by the panel of experts in quantitiative Delphi rounds (Sekayi and Kennedy, 2017).

6 **Table 6.4** Implications of the Delphi method

- **Iterative process with controlled feedback to participants** designed to combine expert opinion into group consensus (Lynn et al., 1998; Keeney, Hasson and McKenna, 2001; Keeney et al., 2011) and to reflect and revise judgements (Strasser, 2017).
- **Multistage** where each stage builds on the results of the previous one (Keeney et al., 2001).
- **Key informants** as group of specialists in their field or someone who has knowledge in a particular topic (Keeney et al., 2001) in a heterogeneous sample to ensure that the entire spectrum of opinion is determined (Moore, 1987).
- **Purposing sampling:** non-probability sampling, in which participants are not randomly selected, so representativeness is not guaranteed. The researcher selects participants to apply their knowledge to a certain problem based on criteria developed from the nature of the problem under investigation. Research knowledge about the population can be used to manually select cases for inclusion in the sample (Hasson et al., 2000).
- **Anonymity of participants and their inputs**: equal chance for each member of the panel to present ideas and react to them without prejudice of the identity of the other participants (Goodman, 1987). In this way, subjective bias is eliminated, since respondents do not know each other (Goodman, 1987; Jeffery, Hache and Lehr, 1995). For anonymity purposes, the Delphi method is more suitable than focus groups discussions, ruling out personal sensitivities between experts and thus avoiding potentially intimidating or destructive group dynamics (Beiderbeck et al., 2021).
- **The number of rounds** depends on the time available and whether the Delphi started with a broad question or a list of questions. Four rounds may be ideal, but difficult to obtain a high response rate (Keeney et al., 2001).
- **Statistical aggregation** of the group response: a quantitative and statistical treatment of these responses is carried out (Strasser, 2017).

According to the different types of Delphi research, defined by Kobus and Westner (2016) based on Paré et al. (2013), this study has applied a **modified policy Delphi.** According to Spranger et al. (2022), a policy Delphi is concerned with explicitly capturing a wide range of judgments or approaches to innovations or solutions. We apply a modified policy Delphi combined with a modified ranking-type Delphi (Strasser, 2017) to prioritise the main causes of the current equity problem, as well as the PSM main leading institutions and the main barriers and enablers to implement the new co-created model. Based on Fletcher and Marchildon (2014), Table 6.5 shows the five reasons why the Delphi method was selected as the consensus technique for this cHTA study.

7 **Table 6.5** Reasons for applying the Delphi method

- Delphi method is epistemiologically adapted in a participatory cHTA that values experts' **experiential knowledge** about the flow of the medical system over limited academic knowledge, mostly concentrated in specific parts of the system. Moreover, Delphi studies, like cHTA, produce information that can be applied by participants, making it useful for policy-and decision makers (Fletcher and Marchildon, 2014).
- The Delphi method allows for **confidentiality** and **inclusion**, which were necessary to generate knowledge about a controversial topic (Fletcher and Marchildon, 2014). Delphi technique allows the **anonymous** collection of narratives, in terms of the identity of participants and their responses. It represents a convenient way for participants to record their judgement through the level of agreement and disagreement level on a Likert scale.

It also provides an opportunity to produce open-ended feedback in the absence of dominant voices that may inhibit the expression of minority viewpoints during in-person meetings such as focus group discussions (Lazarus et al., 2022). Delphi surveys also avoid "group thinking" or "entrapment" and the reproduction of possible power structures (Niederberger and Spranger, 2020). The Delphi method has involved self-administered virtual scoring surveys with participants' anonymous statements in each of the three rounds. The digital environment of Delphi surveys has enabled the inclusion of participants from around the world during the COVID-19 pandemic and the post-pandemic period (Fletcher and Marchildon, 2014).

- Regarding the **sample size**, focus group discussions usually involve between six and ten participants while the Delphi technique is a structured group communication that accepts a higher number of participants, as is the case of the present study (Brown, 2018).
- The Delphi survey allows the researcher to perform a **quantitative analysis** of the questionnaire results reducing interpretation bias compared to the focus group technique also used in cHTA (Grin et al., 1997).
- Delphi requires researcher **accountability** to participants during rounds. In round 2 (R2), participants in cohort B were asked about the consensus statements from round 1 (R1) cohort A, and in round 3 (R3), consensus points of round 2 Delphi survey were provided to both cohorts prior to fill in the final Delphi survey (Fletcher and Marchildon, 2014).

In the present research, the cHTA has comprised a **modified Delphi** technique that included the following aspects:

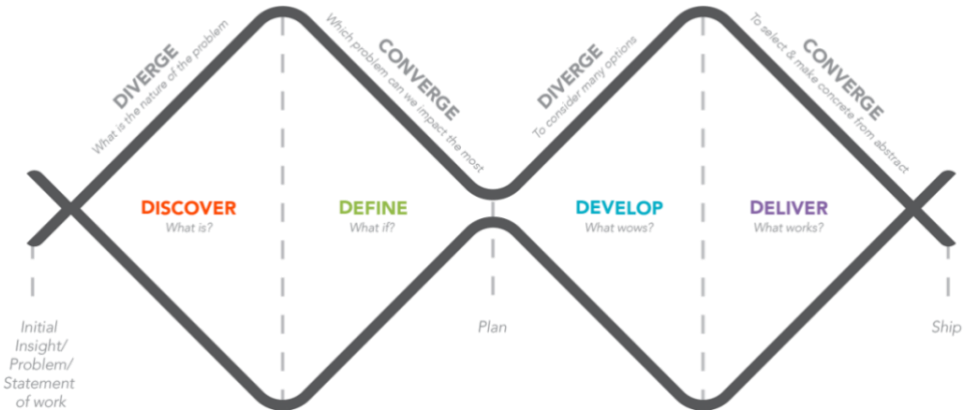
1) **Informational input provided to experts.** Additionally to the usual information on consensus points, the experts received these informational input briefing papers:
   - In **Round 0** (R0) experts received a **PSM policy brief** as a reference document for discussion. Before starting the R1 (cohort A) and the R2 (cohort B), experts received a policy brief (Alonso et al., 2021a) with the proposed principles of the PSM for more direction in the orientation of the discussion from the beginning versus a standard Delphi that tipically begins with a R1 brainstorming session (Keeney, 2001).
   - In **R3** experts received two feedback documents to help them to answer the final Delphi survey section 3 (co-created PSM). The first, on the R1 and R2 **consensus statements** and a second as the **summary of the proposed PSM** with the new ideas generated during the R2 interviews.
2) **Involvement of two cohorts of experts.** The study included a cohort A panel (with ten key informants) and a cohort B panel (with seventeen additional key informants), resulting in a **total panel of twenty-seven experts** representing the health R&I cycle. The two cohorts conformed a **sequential expert panel** in R1 and R2 and a **final total panel** in R3. The decision to distribute the key informants in two cohorts responded to two main reasons:
   - **Reduce the number of rounds** in which key informants participate given their limited time as high-profile experts and the complexity of the topic: R1 with cohort A, R2 with cohort B, and R3 with cohort A and B. So, each cohort participated in only two rounds out of a total of three rounds.
   - **Facilitate the triangulation of the statements** within and accross cohorts by increasing critical thinking, building on points of consensus and expanding

joint constructions to include points of disagreement and new ideas. R2 was created from R1 and R3 from previous rounds for a final statement rating by both cohorts.

To my knowledge the described technique of an iterative process with two sequential cohorts has not been applied as a consensus technique to solve the research question guiding the present PhD study.

3) **No formal review of statements.** The panellists did not formally review the statements or ranking items to establish preliminary priorities among the items. In qualitative Delphi studies, R2 normally consists on asking participants to review researcher-edited statements based on information provided in R1 (Hsu and Sandford, 2007; Sekayi and Kennedy, 2017), and only in R3 (and potentially in further rounds) final statements are presented to the panel for endorsement. Our study had not included a specific round of statement review, but used the in-depth interviews to elicit these statements that where directly introduced into the R2 and R3 scoring surveys. Panellists had the option of leaving comments on the "other" response option of the surveys that were analysed to refine the statements in the final round and incorporate them into the analysis of results.
4) **Delphi survey in each round.** The present study comprised a total of three Delphi endorsement surveys, one per round. In R1, cohort A performed a Delhi survey and the resulting consensus statements were presented in R2 to cohort B to score their level of agreement. In R3 both cohorts completed the final endorsement survey. As a result, each cohort performed a total of two rounds with two assessment surveys. An iterative process with at least two rounds defines the Delphi method compared to a regular one-shot survey (Jünger et al., 2017). The number and the definition of the statements have evolved during the rounds, incorporating new ideas, so the results of the different rounds are not directly comparable for all the statements.
5) **Inspired by the "Double Diamond" design thinking method.** The Double Diamond's discovery process is a design thinking method in the lean user experience (UX) that goes through a series of **divergent** and **convergent thinking** steps to ensure participants are not boxing themselves too quickly into a suboptimal solution, while focusing on the core topic (Gustafsson, 2019). As shown in Figure 6.6, the process involves 4 phases that define a double diamond: discover (diverge), define (converge), develop (diverge) and deliver (converge). The starting point of our study was the aforementioned PSM policy brief as informational input, then diverged to particularly frame the problem and initially target possible solutions (R1 cohort A initial survey and in-depth interviews). Then it converged to define common ground between the two cohorts (R1 cohort A Delphi scoring survey and R2 cohort B Delphi scoring survey of consensus points of R1). It then diverged again to discuss points of disagreement and develop new ideas (R2 cohort B in-depth interviews). Finally, R3 aimed to deliver a final convergent thinking that resulted in a jointly revised PSM (final Delphi survey for both cohorts).

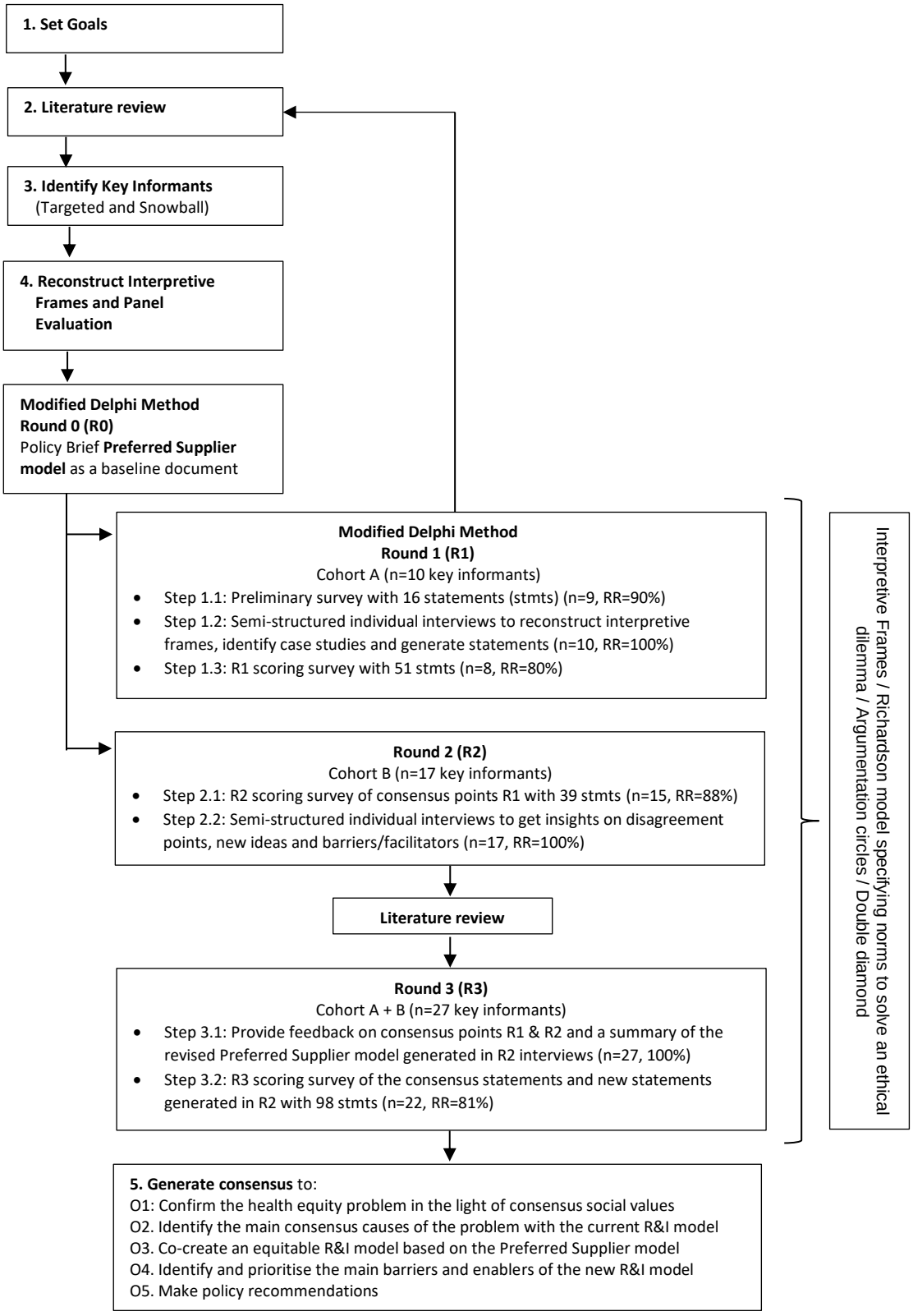
10 **Figure 6.6** Design Thinking "Double Diamond"process model



Source. UX Planet (2022).

In summary, the data collection methodology is shown in Figure 6.7 which describes the step-by-step plan of the participatory Constructive Technology Assessment (cHTA) methodology combined with a modified Delphi technique to reach consensus. The process involves an iterative data collection from two rounds of surveys and interviews (R1 and R2) to scope the topic and generate new ideas and a final survey round (R3) to reach consensus.

11 **Figure 6.7** Data collection methodology



6.4 EXPERT PANEL DESIGN

The cHTA participants have been high-profile **key informants** from around the world, chosen according to their extensive knowledge and experience and representative of the health R&I value chain. Therefore, the sample was non-probabilistic but purposive to better serve the objective of this research.

6.4.1 Social map

The first step was to identify the social map with the parties involved in the process (R&I model) (Grin et al., 1997). This included both parties who normally play an active role (developers, suppliers, sponsors, policy makers), and the affected parties who experience the positive or negative effects, who traditionally play a more passive role (i.e. patients and patient associations, environmental organizations) (Grin et al., 1997). In HTA, prioriy has often been given to the perspective of affected parties, as suppliers and funders were thought to already have sufficient influence.

The involvement of patients or patient organisations was supposed to ensure that the new process would meet their needs and be used in practice. The involvement of technological researchers and industry managers is supposed to help ensure that the priorities set are scientifically and economically feasible. As Grin et al. (1997) stated, without this contribution, there is little chance that the recommended proces will be developed and marketed. Policy makers need to be involved to ensure that outcomes can be incorporated into policy.

The health value chain is a circular process involving public and private actors that perform: research and development (discovery, pre-clinical and phase I-III clinical studies), regulatory approval, production and commercialization, prescription and evaluation of patient outcomes (i.e. phase IV clinical studies as post-approval follow-up studies).

The R&I social map categories are the following 4 **segments** (payers, performers, users and shapers) with a total of 9 **sub-segments**:

PAYERS

1. **Funders**: governments (national, supranational), private investors (i.e. venture capital), non-profit organisations (i.e. philanthropic foundations, civil society organisations), companies (i.e. R&I investment, corporate venture).
2. **Buyers**: government (i.e. national health systems, ministries of health), insurance companies, patients (i.e. out-of-pocket, co-payments), non-profit organisations.

PERFORMERS

3. **Developers:** academia, research centers, companies (start-ups, small and medium enterprises (SMEs), multinational), public-private partnerships, product development partnerships, non-profit organisations.
4. **Suppliers** (production and commercialization): mainly companies (multinational, SMEs).

USERS

5. **Users/Prescribers**: healthcare providers (i.e. hospitals, health centers), pharmacies.
6. **Beneficiaries**: patients, patient associations and representatives, caretakers.

SHAPERS

7. **Evaluators**: health technology assessment (HTA) agencies, academia, research centers, consultacy services.
8. **Regulators**: regulatory agencies, intellectual property agencies.
9. **Policy makers & Global governance**: governments (national, supranational), multilateral agencies.

6.4.2 Expert panel membership

The construction of the expert sample involved an iterative sampling approach to generate a knowledgeable and diverse Delphi panel considering the parameters of representativeness and saturation. According to Boddy (2016), the present work is primarily based on qualitative research in terms of aiming to capture attitudes, perceptions and narratives of key informants during interviews, particularly when carried out under a non-positivist paradigm that is, involving a constructivist research approach to generate great insight. Qualitative analyses require a smaller sample size than quantitative analysis, but at the same time be large enough to describe the phenomenon of interest and address research questions (representativeness) and up to a number that by adding more participants to the study it does not result in additional insights or information (attainment of saturation).

For qualitative Delphi research, Habibi et al. (2014) recommend including a group of 10 experts with different specialties. Sekayi and Kennedy (2017) point out that a careful selection of 20 to 30 panellists should provide sufficient diversity of perspective on most topics. According to Okoli and Pawlowski (2004), the literature review recommends 10 to 18 experts in the Delphi panel. The systematic review of Delphi studies done by Diamond et al. (2014) reveals that 40% of the studies have 11 to 25 participants in the final round and 24% between 25 and 50 participants, only 22% of the studies have more than 51 participants.

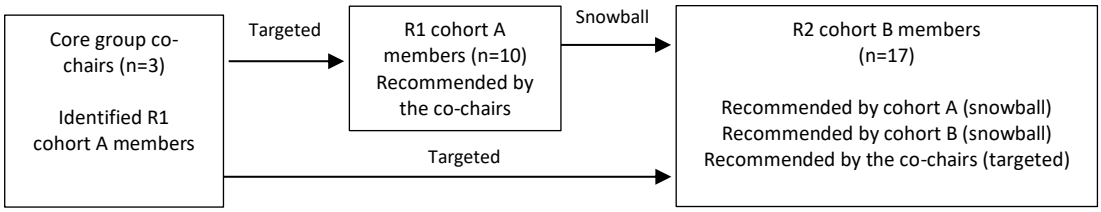
Our study resulted in twenty-seven key informants (n=27) distributed in two cohorts, cohort A with ten experts (n=10) and cohort B with seventeen experts (n=17). Three core group co-chairs (M.E, P.G, J. B[1]) initially identified the ten experts in cohort A. The seventeen experts in cohort B were identified by applying the snowball process with the cohort A recommendations, within the same cohort B, as well as the target participants recommended by the co-chairs (Figure 6.8).

Regarding the participant profile, the second step was to identify which type of actors from the R&I social map could participate in the cHTA process and in what proportion, as a purposive sample. The identification of the experts was based on multiple criteria. First, the 4 segments and the 9 sub-segment categories of the social map are represented. Second, the recommendation primarily from co-chairs and panel members due to relevant professional experience and commitment with the study. Third, gender balance. Fourth, institutional affiliation with a certain overrepresentation of the private sector versus the public sector, since the PSM proposes a new incentive scheme for health equity that must engage private

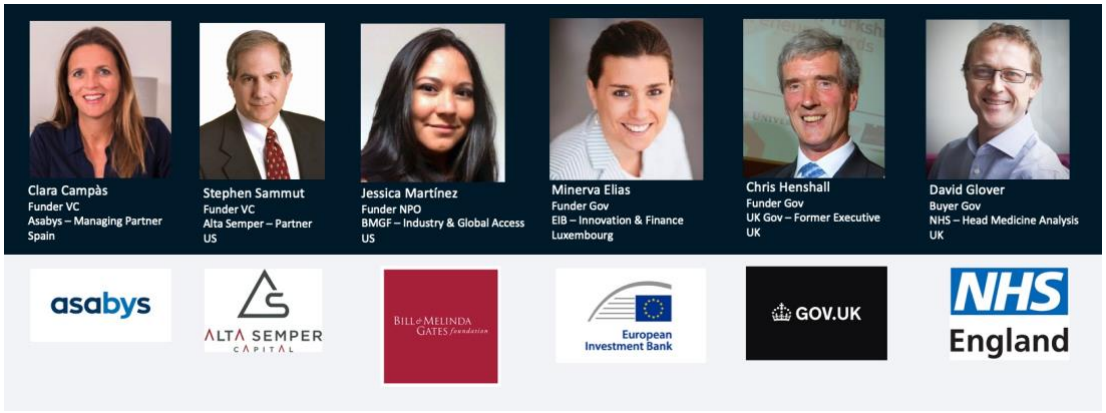
[1] *Co-chairs: Marina Espriu, Pedro Gallo De Puelles, Joan Bigorra.*
Espriu, M.: ISGlobal, Hospital Clínic - Universitat de Barcelona, Spain, Barcelona, Spain.
De Puelles, P.G.: Faculty of Economics and Business, University of Barcelona, Barcelona, Spain.
Bigorra, J.: ISGlobal, Hospital Clínic - Universitat de Barcelona, Spain, Barcelona, Spain.

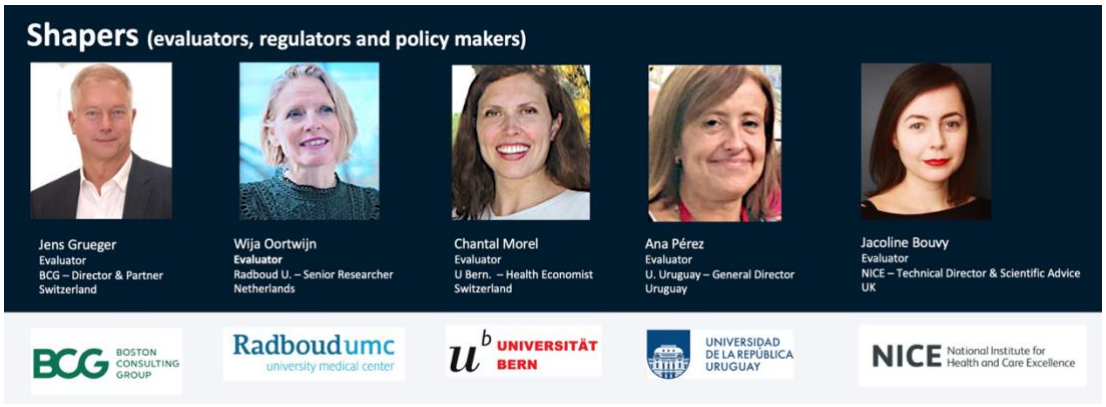
actors. Fifth, the geographical aspects related to place of work prioritising regions and countries leading R&I and at least one emerging country in R&I. Figure 6.9 summarises the expert panel profile.

12 **Figure 6.8** Panel generation methodology



13 **Figure 6.9** Expert panel profile





Tables 6.6 to 6.10 show details of the expext panel purposive sample.

Table 6.6 displays the main characteristics of the panel members, summarized as follows:

- **Gender balance. Gender parity** with equal number of women (13, 48%) and men (13, 48%) in addition to other (1, 4%).
- **Segments and sub-segments**. All four segments were represented in the sample with an overrepresentation of SHAPERS (10, 37%) and PERFORMERS (7,26%), followed closely by PAYERS (6, 22%) and USERS (4,15%). Regarding the nine sub-segments,

shapers are particularly represented with evaluators (5, 19%) and policy makers (4, 15%), performers with suppliers (4, 15%) and payers with funders (5, 19%). The reason is that actors with the most active role in medical R&I are funders, suppliers and policy makers and, to a lesser extent, developers (usually dependent on funders and suppliers). As our aim was to co-create a new model based on the PSM - which considers the public health interest, in conflict with the current for-profit market orientation - a larger representation of active actors has been included. Moreover, a higher proportion of evaluators, as an analyst profile, have been involved to increase the robustness of the new model, as they play a key role in providing evidence and advising policy makers. Furthermore, Cohort A (n=10) has an overrepresentation of PERFORMERS with developers and suppliers (5, 50%) to assess their initial level of agreement with the model as the main operational actors. Cohort B (n=17) has an overrepresentation of SHAPERS with evaluators, regulators and policy makers (9, 53%) given their assessment and decision-making role. In general, most of the participants are multi-profile enriching the analysis by considering different perspectives of the value chain. That is, participants may have significant experience in various roles (segment and sub-segment categories), for instance, as developers and suppliers or as payers and funders, or as performers and evaluators, acquired during their professional career. Four senior experts represent the profile of their former positions given their relevance and extensive experience in them

- **Institution type.** Active actors from the private sector have been overrepresented (16, 59%) compared to those from the public sector (11, 41%) to better assess their commitment to the resulting model. Greater representation of private funders (i.e. venture capital, private foundations) and private payers (i.e. private healthcare providers and insurance companies), and especially of suppliers (pharmaceutical and biotech industry) have been included in the study given their potential opposition to the PSM and a significant dominant position in shaping the market.
- **Sector of employment.** One third of the sample represented a governmental organisation (9, 33%), followed by large indrustry (4, 15%), non-profit organisations (4, 15%), academia and research (3, 11%), venture capital (2, 7%), and one representative (1, 4%) of each of the following sectors: SME, start-up, inter-governmental organisation, healthcare provider /insurance company and consulting services.
- **Global region and country of work.** Priority for regions and countries leading R&I with Europe (21, 78%), North America (3, 11%) and Latin America and the Caribbean (3, 11%) with a focus on the EU, UK, US and Switzerland, as well as Brazil as an emerging country.
- **Work experience.** Various seniority levels with 56% of the panel having more than 20 years of work experience (20-30 years, 30%; more than 30 years, 26%), 37% between 10-20 years, and 8% less than 10 years (2-5 years, 4%; 5-10 years, 4%).
- **Age.** Different age segments represented with 41% of the experts over 55 (55-64 years old, 19%; 65-74 years old, 22%;), 41% between 45 and 55 years old, and 18% under 44 years old (25-34 years old, 7%; 35-44 years old, 11%).

8 **Table 6.6.** Expert panel characteristics (n=27)

Characteristic	n (%)
Gender	
Woman	13 (48)
Man	13 (48)
Other	1 (4)
Segment	
Shaper	10 (37)
Performer	7 (26)
Payer	6 (22)
User	4 (15)
Sub-segment	
Funder	5 (19)
Evaluator	5 (19)
Policy maker	4 (15)
Supplier	4 (15)
Developer	3 (11)
Beneficiary	3 (11)
Buyer	1 (4)
Regulator	1 (4)
User/Prescriber	1 (4)
Institution type	
Private	16 (59)
Public	11 (41)
Primary sector of employment	
Governmental organisation	9 (33)
Industry (corporate)	4 (15)
Non-profit Organisations (Foundation, NGO, etc)	4 (15)
Academy / Research	3 (11)
Venture capital	2 (7)
Industry (SME)	1 (4)
Industry (startup)	1 (4)
Intergovernmental organisation (i.e. United Nations)	1 (4)
Healthcare provider/Insurance	1 (4)
Consultancy services	1 (4)
Global Region of work	
Europe	21 (78)
North America	3 (11)
Latin America and the Caribbean	3 (11)

Country of work	
UK	5 (19)
Spain	5 (19)
Switzerland	3 (11)
USA	3 (11)
Luxembourg	2 (7)
Brazil	2 (7)
Uruguay	1 (4)
Belgium	1 (4)
Denmark	1 (4)
Lithuania	1 (4)
Romania	1 (4)
Netherlands	1 (4)
Sweden	1 (4)
Years of work experience in biomedical R&D and healthcare	
2-5 years	1 (4)
5-10 years	1 (4)
10-20 years	10 (37)
20-30 years	8 (30)
>30 years	7 (26)
Age	
25-34	2 (7)
35-44	3 (11)
45-54	11 (41)
55-64	5 (19)
65-74	6 (22)

Given the importance of the key informants in this research, Table 6.7 details the composition of the expert panel, indicating their profile in terms of name, company, position and country of work.

9 **Table 6.7** Expert panel composition (n=27)

S	Name	Company	Position	Country
PY	Clara Campàs	Asabys Partners	Mananging Partner	Spain
PY	Stephen Sammut	Alta Semper VC	Partner	USA
PY	Jessica Martinez	Bill and Melinda Gates Foundation (BMGF)	Senior Officer Industry Engagement & Sustainable Access	USA
PY	Minerva Elias	European Investment Bank (EIB)	Senior Innovation & Alternative Finance Manager	Luxembourg
PY	Christopher Henshall	British Government	Former Executive	UK
PY	David Glover	National Health Service (NHS) England	Deputy Head Medecine Analysis Team	UK
PF	Seamus O'Brien	Global Antibiotic R&D Partnership (GARDP)	R&D Director	UK
PF	Marc Ramis	Ninevah Therapeutics	Co-founder & Chasing Science Co-founder & Partner	Switzerland/Spain
PF	Monika Paule	CasZyme	CEO & Co-founder	Liithuania
PF	Alexandra Clyde	Medtronic	Corp. VP GH Policy, Reimbursement & Health Economics	USA
PF	César Velasco	AstraZeneca	Innovation & Digital Strategy Director	Spain
PF	Alicia Granados	Sanofi-Aventis	Head of Global HTA Scientific Strategy	Spain
PF	Georgiana Cosoveanu	Janssen (Johnson&Johnson)	Senior Manager Governmental & Corporate Affairs	Romania
US	Joatam Silva	UnitedHealth Group	Research pe	Brazil
US	James Smith	Elrha Humanitarian Innovation Fund	Health Research Advisor	UK
US	Felipe Carvalho	Médecins sans Frontières (MSF)	Country Advocacy Coordinator	Brazil
US	Bettina Ryll	Melanoma Patient Network Europe	Founder	Sweden
SH	Jens Grueger	Boston Consulting Group (BCG)	Director & Partner	Switzerland
SH	Wija Oortwijn	Radboud University Medical Centre & HTAi	Senior Scientific Researcher & Vice-president HTAi	Netherlands
SH	Chantal Morel	University of Bern	Health Economist Infectious Diseases	Switzerland
SH	Ana Pérez	University of Uruguay	General Director	Uruguay
SH	Jacoline Bouvy	National Inst. Health & Care Excellence (NICE)	Technical Director & Scientific Advice	UK
SH	Xavier Luria	European Medicines Agency (EMA)	Former Head Safety & Efficacy of Medicines	Spain
SH	Sarah Garner	WHO EURO	Senior Policy Advisor	Denmark
SH	Jesús M Fernández	Spanish Parliament	Former member of the Spanish Parliament	Spain
SH	Antoni Montserrat	European Commission (EC)	Senior on Public Health & Expert Cancer & Rare Diseases	Luxembourg
SH	Matthew Hudson	European Commission (EC)	Former Dir. DG SANTÉ Res. Mgmt, Regulation, EU4Health	Belgium

S, segment; PY, payer; PF, performer; US, user; SH, shaper. Company: Inst, institute; VC, venture capital. Position: CEO, chief executive officer; Cor, corporate; DG Santé, Directorate-General for Health and Food Safety; Dir, director; GH, global health; HTAi, Health Technology Assessment International; Mgmt, management; Res, resource; VP, vice-president.

Tables 6.8 to 6.10 provide specifications of the expert panel by cohort.

10 **Table 6.8** Expert panel by cohort, segment and sub-segment (n=27)

C	S	Sub-segment	Sector	Pub/Priv	Region	Company
A	PY	Funder	VC	Private	Europe	Asabys Partners
B	PY	Funder	VC	Private	North America	Alta Semper VC
B	PY	Funder	NPO	Private	North America	Bill and Melinda Gates Foundation (BMGF)
B	PY	Funder	Gov	Public	Europe	European Investment Bank (EIB)
A	PY	Funder	Gov	Public	Europe	British Government
B	PY	Buyer	Gov	Public	Europe	National Health Service (NHS) England
A	PF	Developer	NPO	Private	Europe	Global Antibiotic R&D Partnership (GARDP)
B	PF	Developer	Industry (startup)	Private	Europe	Ninevah Therapeutics
A	PF	Developer	Industry (SME)	Private	Europe	CasZyme
B	PF	Supplier/Dev	Industry (corporate)	Private	North America	Medtronic
A	PF	Supplier/Dev	Industry (corporate)	Private	Europe	AstraZeneca
A	PF	Supplier/Dev	Industry (corporate)	Private	Europe	Sanofi-Aventis
A	PF	Supplier/Dev	Industry (corporate)	Private	Europe	Janssen (Johnson&Johnson)
A	US	Prescriber/Buyer	Healthcare Prov/Ins.	Private	LAC	UnitedHealth Group
A	US	Beneficiary	NPO	Private	Europe	Elrha Humanitarian Innovation Fund
B	US	Beneficiary	NPO	Private	LAC	Médecins sans Frontières (MSF)
B	US	Beneficiary	NPO	Private	Europe	Melanoma Patient Network Europe
B	SH	Evaluator	Consultancy	Private	Europe	Boston Consulting Group (BCG)
B	SH	Evaluator	Academia / Research	Private	Europe	Radboud University Medical Centre & HTAi
B	SH	Evaluator	Academia / Research	Public	Europe	University of Bern
B	SH	Evaluator	Academia / Research	Public	LAC	University of Uruguay
B	SH	Policy maker	Intergovernmental (UN)	Public	Europe	WHO EURO
B	SH	Evaluator	Gov	Public	Europe	National Inst. Health & Care Excellence (NICE)
B	SH	Regulator	Gov	Public	Europe	European Medicines Agency (EMA)
A	SH	Policy maker	Gov	Public	Europe	Spanish Parliament
B	SH	Pollcy maker	Gov	Public	Europe	European Commission (EC)
B	SH	Policy maker	Gov	Public	Europe	European Commission (EC)

C, cohort. S, segment; PY, payer; PF, performer; US, user; SH, shaper.Sub-segment: Dev, developer. Sector: Gov, government; Ins, insurance; NPO, non-profit organisation; Prov, provider; SME, small and medium-sized enterprise; VC, venture capital.

11 **Table 6.9** Expert panel cohort A (n=10)

S	Sub-segment	Sector	Pub/Priv	Country	Company
PY	Funder	VC	Private	Spain	Asabys Partners
PY	Funder	Gov	Public	UK	British Government
PF	Developer	NPO	Private	UK	Global Antibiotic R&D Partnership (GARDP)
PF	Developer	Industry (SME)	Private	Liithuania	CasZyme
PF	Supplier/Dev	Industry (corporate)	Private	Spain	AstraZeneca
PF	Supplier/Dev	Industry (corporate)	Private	Spain	Sanofi-Aventis
PF	Supplier/Dev	Industry (corporate)	Private	Romania	Janssen (Johnson&Johnson)
US	Prescriber/Buyer	Healthcare Prov/Ins.	Private	Brazil	UnitedHealth Group
US	Beneficiary	NPO	Private	UK	Elrha Humanitarian Innovation Fund
SH	Policy maker	Gov	Public	Spain	Spanish Parliament

S, segment; PY, payer; PF, performer; US, user; SH, shaper.Sub-segment: Dev, developer. Sector: Gov, government; Ins, insurance; NPO, non-profit organisation; Prov, provider; SME, small and medium-sized enterprise; VC, venture capital.

12 **Table 6.10** Expert panel cohort B (n=17)

S	Sub-segment	Sector	Pub/Priv	Country	Company
PY	Funder	VC	Private	USA	Alta Semper VC
PY	Funder	NPO	Private	USA	Bill and Melinda Gates Foundation (BMGF)
PY	Funder	Gov	Public	Luxembourg	European Investment Bank (EIB)
PY	Buyer	Gov	Public	UK	National Health Service (NHS) England
PF	Developer	Industry (startup)	Private	Switzerland/	Ninevah Therapeutics
PF	Supplier/Dev	Industry (corporate)	Private	USA	Medtronic
US	Beneficiary	NPO	Private	Brazil	Médecins sans Frontières (MSF)
US	Beneficiary	NPO	Private	Sweden	Melanoma Patient Network Europe
SH	Evaluator	Consultancy	Private	Switzerland	Boston Consulting Group (BCG)
SH	Evaluator	Academia / Research	Private	Netherlands	Radboud University Medical Centre & HTAi
SH	Evaluator	Academia / Research	Public	Switzerland	University of Bern
SH	Evaluator	Academia / Research	Public	Uruguay	University of Uruguay
SH	Policy maker	Intergovernmental (UN)	Public	Denmark	WHO EURO
SH	Evaluator	Gov	Public	UK	National Inst. Health & Care Excellence (NICE)
SH	Regulator	Gov	Public	Spain	European Medicines Agency (EMA)
SH	Pollcy maker	Gov	Public	Luxembourg	European Commission (EC)
SH	Policy maker	Gov	Public	Belgium	European Commission (EC)

S, segment; PY, payer; PF, performer; US, user; SH, shaper.Sub-segment: Dev, developer. Sector: Gov, government; Ins, insurance; NPO, non-profit organisation; Prov, provider; SME, small and medium-sized enterprise; VC, venture capital.

6.5 DATA COLLECTION

The present cHTA research includes primary and secondary data collection. Primary data consisted of a three-round iterative process that included a **preliminary survey**, **in-depth interviews** and **endorsement surveys** to reconstruct the stakeholders' interpretive frames and reach a joint construction. The Likert rating scales applied to the different rounds have been adapted to better capture the level of commitment in accordance with the objectives of the study (Box 6.1).

This approach was complemented by secondary data collection from the literature review, comprising academic papers, grey literature and opinion articles.

1 **Box 6.1** Likert scales applied in this research

In R1 and R2 the statements were presented to the panel using a **5-point Likert scale** with the following agreement-disagrement response options: **1, strongly disagree; 2, disagree; 3, neutral; 4, agree; 5, strongly agree**. Additionally, panellists could select "**other**" to make comments or respecify the statement. This five-point scale was chosen to provide better data quality compared to seven points or more in terms of increased response rate and response quality along with reduced respondents' frustration level (Revilla, Saris and Krosnick, 2013).

In R3 the statements were presented to the panel in a **4-point Likert scale**, according: **1, disagree; 2, somewhat disagree; 3, somewhat agree; 4, agree**, without the neutral option, in addition to a "**not qualified**", as well as "**other**" (open-ended) (Lazarus et al., 2022).

The reduction to a 4-point scale in R3 aimed to provide better quality of results considering:

- **Clear positioning**. In R3 the conditions changed from R1 and R2 as our aim was to obtain a clear agreement or disagreement statement by avoiding the neutral option neutral, but incorporating "not qualified" in case some key informants considered themselves not prepared to score a specific statement.
- **Evolve in results rather than comparing**. The objective was not to compare the change in R3 results with the results of previous rounds as the statements were redefined between rounds and incorporated new ideas.
- **Common practice for a final Delphi**. There is previous evidence that applies this 4-point Likert scale for final consensus (Lazarus et al., 2022). The survey required a response for each statement, limited to one possible rank value per statement and shuffled the order of the rows to avoid selection bias, and for checkbox questions a validation of answer with a maximum number of options selected.

6.5.1 Primary data collection

Box 6.2 summarises the primary data collection tools in each cHTA round described in Figure 6.7.

2 **Box 6.2** Primary data collection tools in cHTA rounds

R0

Step 0. Informational input PSM policy brief (n=27).

R1

Cohort A (n=10)
Step 1.1: **Preliminary survey** to generate initial ideas (15 minutes).
Step 1.2: **In-depth interview** to reconstruct interpretive frames, identify case studies and generate statements (60 minutes).
Step 1.3: **Delphi scoring survey** (20 minutes).

R2

Cohort B (n=17 additional participants)
Step 2.1: **Delphi scoring survey** with consensus points of R1 cohort A (15 minutes).
Step 2.2: **In-depth interview** to get insights on disagreement points, new ideas, and identify barriers and facilitators to generate additional statements (60 minutes).

R3

Cohort A and B (n=27)

Step 3.1: **Informational input** R1 and R2 consensus points and a summary of the new co-created proposed PSM with the new ideas generated in R2.

Step 3.2: **Delphi scoring survey** of consensus statements, non-consensus statements reformulated and new statements generated in R2 by cohort B (40 minutes).

Primary data collection involved digital communication channels with key informants such as email, videoconferencing and online questionnaires (see section 6.7 for further detail). The COVID-19 pandemic and the global geographical location of the key informants did not allow face-to-face interviews. The informational inputs and the surveys questionnaires were prepared by the researcher and reviewed and piloted by two other co-chairs (P.G and J. B) initially. Non-consensus statements (see section 6.6 consensus criteria) were analysed, redefined and incorporated in subsequent rounds. Data collection per round was carried out as follows:

R0 (n=27)

- **Step 0. Informational input.** Initial PSM policy brief (Alonso et al., 2021a) shared with key informants as a baseline document for discussion.

R1 (cohort A) (n=10)

- **Step 1.1. R1 preliminary survey** (n=9, RR=90%). A self-administered online baseline survey was a preliminary step to generate ideas and obtain some insights from key informants on the main challenges and limitations of the current health R&I model, as well as normative preferences and potential solutions. The survey had 16 questions, including 9 open-ended questions, organized in 3 sections as follows:

    - [Demographics (7 questions)].
    - **Scoping** (8 questions) on the main challenges, barriers, values and facts assessment.
    - **Looking for a solution** (4 questions) to detect the need for change and spontaneous solutions based on case studies.
    - **Alternative solution** PSM (4 questions) assessing the level of agreement/disagreement with the proposed model, stating advantages and disadvantages and a final open question for further considerations.

    Estimated completion time 15 minutes. Participants completed the survey prior to the interview.

- **Step 1.2. R1 In-depth interview** (n=10, RR=100%). As a second step, each participant in cohort A performed a **one-hour semi-structured individual interview** with open-ended questions to reconstruct the interpretive frames (NP, PD, BT, JS) and identify case studies. The interview was intended to capture the necessary adjustments of the proposed PSM and initial reactions to the views of oher stakeholders, and

preliminary joint constructions. The main contents of the interview of cohort A were the following:

- Review of the preliminary survey answers, asking for clarifications and justifications according to the interpretive frames ("*why"* questions).
- PSM proposed adjustments in the governance and the 4 Share principles (needs, risks and rewards, results and outcomes).
- Case studies as reference success stories for the new model.
- Facilitators for the new co-created model to be piloted and implemented.
- Feasibility of the new model to increase health equity.
- Probability of the new model to be implemented.
- Impact (how to measure the potential impact of the model).
- Supporters and Opponents.
- Potential cohort B interviewees.
- Any other consideration.

The method of triangulation was used by asking interviewees about their degree of agreement with the statements of other stakeholders, within the same profile and between different profiles (see argumentation circle in 6.2.3). Cohort A participants helped identify potential interviewees for cohort B.

Interviews were scheduled in 60-minute intervals per participant. A short post-interview questionnaire with final questions was emailed to seven participants. One participant preferred to have a second virtual interview to complete the remaining points.

- **Step 1.3. R1 Delphi scoring survey** (n=8, RR=80%). As a third step, each participant in cohort A answered a self-administered scoring survey. The process included the collecting narrative statements from each interview, generating clear and inclusive statements, and presentating anonymous final statements to the panel to indicate their level of agreement/disagreement with each statement. A **5-point Likert** scale plus the option "other" (see Box 6.1) was applied to confirm the level of **consensus** (Sekayi and Kennedy, 2017). The Delphi scoring survey had 4 sections according to the interpretive frames with a total of 51 statements (stmts) to endorse according**:**

  - [Demographic (1 question)]
  - **Problem definition** (18 stmts)
  - **Background theory** (9 stmts)
    - Gains to adopt the new model
    - Value-based pricing
  - **Normative preferences** (3 stmts) Norm 1, Norm 2, Norm 2 specified
  - **Judgement of the solution** based on the PSM (18 stmts):
    - Governance
    - Needs
    - Risk & Rewards
    - Results
    - Outcomes
  - **Enablers** (1 stmt – checkbox question)

- **Feasibility** (1 stmt)
- **Probability** (1 stmt)

Estimated completion time 20 minutes.

R2 (cohort B) (n=17)

- **Step 2.1. R2 Delphi scoring survey** (n=15, RR=88%) of R1 consensus points. Anonymous feedback of the consensus statements resulting from the R1 Delphi scoring survey (cohort A) was presented to the second cohort (cohort B) in a self-administered scoring survey to endorse their level of agreement on the same 5-point Likert scale plus "other" (open-ended). R2 survey had 4 sections with a total of 39 questions and statements to endorse**:**

    - [Demographics (7 questions)]
    - **Scoping** (10 questions and statements) on the main challenges (free text), main limitations (free text), values and facts equity assessment, reason for the equity gap (free text), need for change, priority elements to redefine the model (checkbox), success stories as case studies, level of agreement with the PSM.
    - **Scoring of the Consensus Statements of R1 cohort A** (27 statements):
        - Problem definition (6 statements)
        - Background theory (3 statements)
        - Normative preferences (3 statements)
        - Judgement of the solution:
            - Governance (3 statements)
            - Needs (3 statements)
            - Risk & Rewards (4 statements)
            - Results (2 statements)
            - Outcomes (3 statements)
    - **Facilitators** (checkbox) **and barriers** (free text) (2 questions)

- **Step 2.2. R2 In-depth interviews** (n=17, RR=100%). As a second step, cohort B participated in a **one-hour semi-structured individual interview** to get insights into points of disagreement in the R2 survey with cohort A and identify new ideas, as well as barriers and facilitators of the new model. The main lines of the cohort B interview were as follows:

    - Justification of the disagreement points with cohort A shown in the R2 scoring survey.
    - Identification of additional new ideas, especially:
        - Background Theory: particularly gains for the industry and deconstructing value-based care.

        - Proposed Solution: mainly governance, 4 Share principles (needs, results, risk and rewards, outcomes), regulation, push and pull incentives.
    - Case studies as reference success stories for the new model.
    - Enablers & Barriers (and how to overcome them).
    - Feasibility of the new model to increase health equity.
    - Pilot implementation and leadership.
    - Supporters and Opponents.
    - Potential cohort B interviewees.
    - Any other consideration.

Round 3 (cohorts A & B) (n=27)

- **Step 3.1. R3 Informational input** (n=27, RR=100%). In this final round both cohorts received anonymous written feedback from the R1 and R2 consensus points (annex E) and a summary of the new co-created proposed PSM (annex F) with the new ideas generated during the R2 interviews to facilitate the completion of the R3 survey.
- **Step 3.2. R3 Delphi scoring survey** (n=22, RR=81%). Both cohorts answered a self-administered scoring survey with consensus points, disagreement points, and new statements generated by cohort B in R2. The process included collecting narrative statements from each interview, generating clear and inclusive statements, and presentating the anonymized final statements to the expert panel for endorsement. It applied a **4-point Likert** scale, plus "**not qualified**" and "**other**" (open-ended option) allowing comments (see Box 6.1) to reach a **consensus** model (Lazarus et al., 2022). The R3 Delphi scoring survey had 4 sections with a total of 98 statements to endorse the level of agreement, as following**:**

    - [Demographics (7 questions)]
    - **Normative preferences** and **Problem definition** (8 stmts)
    - **Causes** of the problem (44 stmts)
    - **Co-creation** of the revised **PSM** (44 stmts)
    - **Barriers** and **Enablers** (2 stmts)
    - **General comments** (1 open question)

  Estimated completion time 40 minutes.

Among the R3 98 statemtents were 4 ranking questions (comprising main causes, PSM governance, barriers and enablers), 2 checkbox questions for PSM pull incentives (regulatory incentives and pricing models), as well as a final open question for general comments. The ranking questions are described in Table 6.11 and asked them to rank a series of statements, with 1 being 'Most important' and 5 being 'Least important'.

13 **Table 6.11** R3 ranking questions

Ranking question 1
2.44 Main causes of the problem. Please RANK these main CAUSES that prevent the current R&D system from fulfilling health equity goals in order of importance (5 items).

- Lack of alignment between incentives and public health needs
- Unequal distribution of Risks & Rewards
- Perverse use of patents and value-based pricing
- Lack of transparency in scientific and financial data
- Developers (academia/start-ups/SME) lack of funds and alignment for priority health challenges

Ranking question 2
3.42 PSM Governance. Lead organisations to pilot and implement the model. Please RANK these options (4 items).

- Big public-private consortium for a 360º view
- Reformulated WHO (more transparent and empowered)
- EU lead with EU Pharma Strategy Amendment, EU Health Data space, EU4Health, etc.
- USA lead as the main market, engaging MEDICARE and MEDICAID

Ranking question 3
4.1 PSM Barriers. Please RANK these options (9 items).

- Cognitive dissonance between the sectors
- Governments decentralized decision making
- Difficulty of global commitments to reward innovation based on the ability to pay
- R&D length of time. (i.e. a decade)
- US Venture led by short-term ROI
- Industry lobby in health policies
- Lack of academia preparation for Open Innovation
- Delay in data ownership and access legislation
- Lack of health system capabilities, especially in LMIC

Ranking question 4
4.2 PSM Enablers. Please RANK these options (9 items).

- Incremental change with balanced Risk and Rewards
- Compulsory ESG KPIs in different countries
- Investors requiring company disclosures
- Outcome standards with COMET & ICHOM for data aggregation
- Digital technology available
- Responsible capitalism by industry i.e. Pfizer with ACCORD (May 2022) providing patent-protected drugs and vaccines at non-for-profit price to 45 lower-income countries
- Access to Medicine Index as a reference
- Pharma leadership in front of Amazon, Google, Apple incomers
- WHO International Pandemic Treaty

Table 6.12 details the 2 checkbox questions for PSM pull incentives, one related to regulatory incentives and the other to pricing models. For each question, experts could only tick 4 boxes out of 8, plus the “not qualified” and “other” options. For the regulatory pull incentives

question the order of the items was not randomised (the shuffle option was not enabled) making it easier to understand the options to improve the quality of the survey responses.

14 **Table 6.12** R3 checkbox questions

Checkbox question 1

3.40 PULL Incentives. PSM best regulatory incentives (please tick only 4 boxes) (not shuffle option).

- Regulatory Fast Track
- Transferable Regulatory Fast Track (Priority Review Voucher)
- Regulatory FDA – EMA alignment
- Regulatory agency – HTA agency alignment
- Regulatory Exclusivity Extension" (EE) Market exclusivity for the priority product for a certain time
- Regulatory Transferable Exclusivity Extension (TEE) or Transferable Exclusivity Voucher (TEV)
- Managed Access Fund: conditional regulatory approval based on clinical trial Phase II with the commitment to perform the confirmatory phase III trials in a certain period of time
- Regional Regulatory Agencies in LMIC
- Not qualified
- Other

Checkbox question 2

3.41 PULL Incentives. PSM best new Pricing model incentives (Please tick only 4 boxes).

- De-link "Netflix" model: annual subscription fee de-linked from volume for a certain population for a period of time
- Financial-based Risk-sharing agreements (i.e. price-volume, budget cap)
- Outcome-based Risk-sharing agreements (i.e. conditional coverage)
- "Beyond the pill" embracing Prevention & Promotion
- "Bundle Payments" care pathways
- Advanced Market Commitment
- Pooled/Centralized purchasing especially for LMIC
- Renting production capacity (MH)
- Not qualified
- Other

6.5.2 Secondary data collection

The present research was complemented by secondary data collection with a non-systematic literature review, as the aim was to identify elements rather than provide evidence. All the panellists were invited to suggest relevant papers. The non-systematic literature review involved 485 references, among them 333 selected articles and 152 grey literature documents (including reports, white papers, evaluations, databases) on the main gaps of the current medical R&I model and possible solutions to create and translate knowledge into solutions for population health needs. It comprised purposely selected articles with critical appraisal of relevant evidence published in international indexed journals and grey literature, as well as outcomes statistics of the R&I model. Sources and authors have been systematically referenced in APA style.

The targeted literature review mainly involved searches in public databases and journal search engines. The public databases used were PubMed, Scopus, Google Scholar and Research Gate containing abstracts and citations of academic journal articles. The PubMed database with more than 33 million citations and abstracts of medical literature is the most widely used database in the field of health science. With more than 36,000 titles, Scopus is a leading peer-reviewed database in life, social, physical and health sciences along with Web of Science, being the oldest European, easiest to navigate and owned by Elsevier, one of the main international publishers of scientific journals, allowing direct exports to the Mendeley reference manager also owned by Elsevier. Google Scholar allowed an easy way to search a wide range of academic literature, as well as snowball sampling with references and citations.

The search was done by article authors, title, abstract and keywords. The main keywords searched were in alphabetical order as follows: “access to medicine index”, “common good”, “drug prices”, “equity accreditation”, “ESG”, “global health innovation”, “health access”, “health equity”, “health innovation”, “health financing”, “impact investment”, “medical R&D/R&I model”, “one health”, “planetary health”, “public health policy”, “public health regulation”, “research gap”, “responsible equity”, “SDG”, “smart procurement”, “social innovation”, “value-based care”, “values in health”, among others. For the case studies, some keywords were “COVID-19 equity”, “compulsory/voluntary licensing”, “COVAX”, “Doha declaration”, “impact COVID-19 vaccines”, “orphan drugs”, “orphan drug policy”, “TRIPS agreement/amendment/waiver”, among others.

Searches were primarily from 2000 to 2023, and for some topics were restricted to 2020 onwards due to the relevance of the COVID-19 pandemic. They were in English and in indexed journal articles (including bioethics literature). In addition, the digital search helped identify grey literature, which comprises published reports, databases, website content, press articles, and opinion pieces. The literature review was conducted in three phases of the cHTA process:

- Before round 1, initial research work to generate discussion with cohort A.
- Before round 2, gather more information to redefine the points of disagreement of cohort A and stimulate new perceptions and attitudes in cohort B interviews.
- Before round 3, final check to assess the consistency of the final statements resulting from the cohort B interviews to be assessed by the full panel in the final round.

6.5.3 Data collection per objective

The five objectives relied on the participation of the different interest groups in the three rounds of the Delphi process. The process required first reconstructing the interpretive frames of each stakeholder (NP, PD, BT, and JS), then making the necessary adjustment to the PSM, to ultimately arrive at a final consensus construction of the PSM (Sekayi and Kennedy, 2017) and make policy recommendations.

As mentioned, the methodology comprises three primary data collection tools: an **initial survey** (R1), **in-depth interviews** (R1, R2) and the **Delphi scoring surveys** (R1-R3) complemented by secondary data collection with literature review (R1-R3). For all objectives, data collection implied a literature review and three main data collection tools, as follows:

O1. Health equity problem in the light of social values. Primary data collection through the preliminary survey, rounds of interviews and especially Delphi endorsement surveys with the selected actors on the NP and PD interpretive frames**.** The R3 Delphi survey had 8 statements to assess consensus on this objective.

O2. Main causes of the problem. Primary data collection with the three tools focused on the BT interpretive frame. The R3 Delphi survey had 44 statements to assess consensus on this objective, including a ranking question on the main causes.

O3. Co-created PSM. Primary data collection using all three tools, focused on co-creation of the proposed PSM. The R3 Delphi survey had 44 statements to assess consensus on this objective as an interpretive frame for JS. It included a ranking question on PSM governance and two checkbox questions on pull incentives (regulatory incentives and pricing models). Moreover, a benchmarking of main case studies identified a selection of successful experiences and best practices to address the main equity gaps in the current R&I model for certain health problems, as an inspiration for the new model. The stories selected comprised communicable and non-communicable diseases and included the identification of the factors that favour and hinder the success of the process. The benchmarking was based on case studies identified by experts in the preliminary survey (R1), in-depth interviews and scoring surveys (R1 and R2), supplemented with literature review.

O4. Barriers and Enablers. The identification of main barriers and facilitators was performed during the R1 and R2 interviews and Delphi surveys, and the ranking was completed in the R3 Delphi survey. The final survey had two ranking questions, one with a list of nine main barriers and another one with a list of nine main enablers identified during R1 and R2 surveys and interviews.

O5. Policy recommendations. Identified from the O1—O4 findings.

6.6 DATA ANALYSIS

Regarding qualitative analysis, semi-structured in-depth online interviews were video-recorded and transcribed (verbatim) for analytical treatment to elaborate qualitative statements to be scored by the panel. In terms of quantitative assessment, the preliminary and scoring digital surveys were conducted using a digital platform and a specific digital form that facilitate the collection of output data exported to excel spreadsheets. Content analysis applied the standard qualitative techniques (Miles and Huberman, 2014) in cHTA (Grin et al., 1997) and a modified Delphi consensus technique (Sekayi and Kennedy, 2017) as follows:

Identification of narrative statements

- **Coding the interview transcript** applying the **four categories** of the **interpretive frames** (NP, PD, BT and JS). Moreover, for BT and JS, the PSM 4S principles and governance scheme of the PSM policy brief were applied. This deductive method was useful to approach the data with a pre-established code list to show a sharp focus on insights as well as areas of convergence and divergence between groups of

participants (Fletcher and Marchildon, 2014). It was complemented with an inductive open coding when data generated did not fit the prior codes (Fletcher and Marchildon, 2014).

- **Identification of clear and inclusive statements to elaborate the Delphi surveys** from the coded transcripts keeping the original meaning of the point of view of all participants to be scored by the panel members with their level of agreement or disagreement, as well as with ranking and checkbox questions.
- **Incorporation of comments (open text box) from Delphi surveys.** After revision, R1 and R2 comments suggestions were incorporated into statement edits in subsequent rounds. The R3 final survey also allowed for an "other" option, as well as global feedback at the end of the survey, which were incorporated into the analysis of results, particularly in the areas of less agreement.

Scoring

- **Survey endorsement of statements** applying specific Likert scales (refer to Box 6.1).

Presentation of the findings

- **Delphi data analysis: Definition of consensus criteria.**

  i. The **R1 and R2 Delphi scoring surveys** (steps 1.3 and 2.1) were analysed considering panellists' neutral, moderate and strongly agree statements.

  > **R1 & R2 Consensus criteria:**
  > **≥ 80%** rated **strongly agree/agree/neutral** statements and, among them,
  > **≥ 50% agree/strongly agree.**

  Based on Diamond et al. (2014) systematic review, the most common definition is the percentatge agreement with 75% being the median threshold to define consensus. In R1, given this intermediate stage of reaching consensus, it is considered relevant to include a broader approach that includes neutral scores to enrich the discussion and then assess the final level of consensus with a more restricted criterion in R3 (see below). The consensus definition was defined a priori. Open-ended comments under "other" and disagreement statements were analysed to incorporate such feedback (including improvement of the statement description) in subsequent rounds.

  ii. The **R3 Delphi scoring survey** (step 3.2) applied a different Likert scale (Box 6.1) and defined criteria for supermajority consensus (level 1) and, at a lower level of agreement, simple majority consensus (level 2) (Diamond et al., 2014; Lazarus et al., 2022). Consensus criteria were decided a priori.

  > **R3 Consensus criteria:**
  > **LEVEL 1 Supermajority: >=67% agreement** (agree and somewhat agree).
  > **LEVEL 2 Simple majority**: **>=50% combined agreement**.
  > **LEVEL 3 No consensus: <50**% **combined agreement**.

Throughout the three rounds, the frequencies of all statements were calculated. In R3 the proportion who selected "not qualified to respond" was reported in the tables but not was included in the denominator to calculate the level of agreement (Lazarus et al., 2022). The comments made in the "other" option were analysed and reported especially for less consensus statements.

- **Delphi data analysis: Definition of non-consensus and areas of consensus with less agreement.**

  As stated, the criterion for non-consensus was decided a priori with less than 50% combined agreement. In addition, we specified criteria for consensus statements with lower level of agreement.

  R3
  LEVEL 3 No consensus <50% combined agreement.
  Consensus with less agreement >25% combined disagreement (somewhat disagree and disagree).

- **Selected quotes** from key informants from the one-hour in-depth interviews R1 and R2, as well as the analysis of open-ended text-box comments, were included in the results.

- **Result as a synthesis** between the different beliefs of the participants to create a consensus joint construction.

Evaluation criteria: completion of the Delphi process

The **evaluation endpoint** that defines the termination of the Delphi process (Diamond et al., 2014) was defined a priori as a balance between:

- **The number of Delphi rounds**: three rounds with two cohorts (two rounds per cohort) including three Delphi surveys was set as the expected number of rounds.
- **The achievement of consensus** as defined above comprising:
  i. **Degree of consensus statements:** The final findings reflecting consensus were a list of R3 Delphi survey combined agreement (agree and somewhat agree) statements based on supermajority consensus criteria (level 1) and simple majority consensus (level 2) (Diamond et al., 2014). A "**Minimum Consensus criteria**" was defined by identifiying the minimum cut-off key statements from the R3 Delphi survey that must reach consensus (level 1 or 2) to confirm a consensus PSM. The Minimum Consensus criteria resulted in a selection of 30 key statements from the R3 survey shown in Annex A.
  ii. **Checkbox questions** for the final finding of the PSM pull incentives was a table that reflected the panellists' choice of tophalf options.
  iii. **Ranking questions** (ordinal level of measurement)**.** For the four ranking questions (causes of the problem, PSM governance, barriers and enablers) the tophalf ranked selection was highlighted. Moreover, **Kendall's coefficient of concordance** (Kendall's W) was calculated for each of them

using the DescTools package in R version 4.1.2 (results shown in Annex D, Table D1) to determine the degree of agreement between experts when working with ranked data, especially inter-rater reliability (Habibi et al., 2014; Okoli and Pawlowski, 2004). Kendall's W is a nonparametric statistic for rank correlation. It indicates whether those who have ordered several categories according to their importance have used the same criteria to judge the importance of each category and agree on their ranking (Field, 2005; Habibi et al., 2014). Kendall's coefficient ranges from 0 to 1, indicating strong consensus for W>0.7; moderate consensus for W=0.5; weak consensus for W<0.3, and no consensus W=0 (Habibi et al., 2014). According to Okoli and Pawlowski (2004), consensus can be assessed by calculating Kendall's W, reiterate until panellists reach consensus or a consensus plateau. In our case, the W was calculated in R3 to assess the final level of consensus.

$$W = \frac{12S}{m^2(n^3 - n) - mT}$$

$$S = \sum_{i=1}^{n} (R_i - \bar{R})^2$$

Where m is the number of raters, n is the number of subjects in the ranking, and t is the number of tied ranks in each rater (zero in our case). The null hypothesis was Kendall's W equal 0 with a p-value of 0.05. Addititonally, Kendall's W was calculated for the four ranked questions for each expert segment to identify whether there was concordance in the rating preferences of each group.

- **The stability of judgements.** Delphi consensus normally implies that there are no significant endorsement changes in the final round with respect to the previous round. This measure was applied to a lesser extend, as the statements in each round changed as they revised and incorporated new ideas (see Box 6.1).

Quality reporting

- The quality of the Delphi reports followed the recommendations for conducting and presenting Delphi studies (CREDES) defined by Jünger et al. (2017).
- The presentation and communication of results follows the consolidated criteria standards for the presentation of qualitative research (COREQ) according to Tong, Sainsbury and Craig (2007).

Table 6.13 below shows the research matrix as a summary of the thesis objectives, research questions, hypotheses and methods.

Objectives	Research Questions	Hypotheses	Methods
1. Confirm, in the light of consensus social values, that the current biomedical R&I model has a health equity problem that needs to be addressed.	Which moral dilemma prevents health innovation from realising socially desirable goals?	There is a moral dilemma in health innovation that, when incentives are not aligned with public health priorities, efficiency (in terms of commercial rewards) takes preference over equity, resulting in a health equity problem.	cHTA based on literature review and three Delphi rounds with two cohorts of key informants, including a preliminary survey, two rounds of semi-structured in-depth interviews and three Delphi endorsement surveys, to reconstruct the interpretive frames identifying the normative preferences and the problem definition.
2. Identify the main consensus causes that hinder health innovation from fulfilling the desired equity goals.	Which are the agreed explanations by which health innovation is unable to fulfil the desired equity goals?	Consensus main causes that prevent equitable health innovation are related to the lack of sharing needs, results, risks and rewards, and outcomes, in addition to the lack of governance.	cHTA (as described above) to reconstruct key informants' interpretive frames identifying the background theory about the causes of the problem.
3. Validate the principles and conditions of a co-created consensus equitable health innovation model based on the Preferred Supplier model (PSM).	Which could be the underpinning characteristics of a co-created consensus PSM for health equity?	Governments, as major investors and buyers of biomedical innovation, are well positioned to drive industry toward environmental and health equity practices and get credit as Preferred Suppliers, by aligning incentives to public health priorities in accordance with the "4 Share" principles (sharing needs, results, risks and rewards, and outcomes) and adequate governance.	cHTA (as described above) to reconstruct key informants' interpretive frames to reach a joint construction (co-creation) of an equitable health innovation model based on the PSM. In case a moral dilemma is confirmed in O1, application of the Richardson method with the specification of norms to reach normative consensus.
4. Prioritise a set of barriers and enablers for the implementation of the co-created consensus PSM.	Which are the main ranked PSM barriers and drivers?	The key PSM barriers are related to the health systems capabilities, the pricing scheme and the dominant position of the industry in health policies. The key PSM enablers are related to expanding ESG practices.	cHTA (as described above) to reconstruct key informants' interpretive frames to identify and rank the main barriers and enablers to implement the PSM.
5. Make policy recommendations based on these findings.	Which policy recommendations arise from the consensus PSM?	Policy recommendations should consider appropriate incentives and regulation to promote the implementation of the consensus PSM.	Policy recommendations based on the previous findings.

15 **Table 6.13** Research matrix: from objectives to methods

6.7 BIOETHICAL CONSIDERATIONS

The present thesis has the necessary approval from the Bioethics Commission of the University of Barcelona (Institutional Review Board, IRB00003099). We consider the experts to have answered honestly and according to their perception of what the researcher expected (Keeney et al., 2001). As a disclaimer, the feedback provided by the expert panel solely reflects their individual opinion given their professional experience and not necessarily that of their institutions. Interviewees read and signed an informed consent and commitment of confidentiality form (Annex G) at the beginning of the process, including consent to:

- Voluntarily participate in the study.
- Accept the interview to be recorded and the content of the surveys used for the purpose of this research, always preserving the confidentiality of the information.
- Publish the name on the list of key informants as long as the content of the interview is not related in any way to the interviewee.

Additionally, the informed consent document notified about the personal data protection rights according to the EU regulation 2016/679 of April 27 and 3/2018 of December 5. Likewise, the experts were also informed that the principal investigator is responsible for the collected data and its custody. All data were stored electronically on a personal device with secure access keys to both the device (computer) and the files. All data were **anonymised** at the outset using alphanumeric codes assigned to each participant so that during the processing of the data at no time can the participation of an informant be associated with their name. The socio-demographic data collected from the selected informants comprised seven variables: full name, gender, age, country where they work, years of professional experience related to health R&I, professional sector and organization where they work.

The collection and protection of primary data was carried out electronically with surveys and interviews. The initial scoring survey was conducted virtually using a digital questionnaire. Responses were transferred to a Microsoft excel spreadsheet file and removed from the questionnaire design program. Answers were anonymised and assigned an alphanumeric code. The semi-structured interviews were performed with a telematic videoconference program (Gotomeeting) with image and sound recording. In all cases, the interviewees gave permission both in the signed informed consent and at the beginning of each of the interviews. The responses were transcribed into a Microsoft word file already coded with the alphanumeric code corresponding to each interviewee and the image and sound records will subsequently be removed. The following scoring surveys used the same online system described above. These surveys used the same data processing system as the initial scoring survey.

Moreover, the stakeholder's statements generated during this research study were disclosed to the rest of stakeholders in interviews and surveys in an anonymous format. That is, the participants did not know which informant the different statements belonged to. Finally, participants received the corresponding guidance information for conducting the surveys and interviews, as well as the next steps.

7 RESULTS

This chapter summarises the main results of the thesis. It is structured in five chapters, each of them referring to the five specific objectives outlined in section 3. Specifically, section 7.1 shows the consensus on the norms and the problem definition (O1) and the statements with no consensus or less agreement. Section 7.2 points out the consensus causes that prevent the current R&I model from meeting the health equity goals (O2). It also displays the ranking on the top five consensus causes of the problem, as well as the causes with no consensus or less agreement. Section 7.3 then shows the co-created consensus PSM R&I model for health equity (O3). As an introduction to this section, the three main case studies mentioned by the panel that inspire the new R&I model are described. Finally, the areas of the new model without consensus or with less agreements are shown. Section 7.4 indicates the resulting classification of the barriers and the enablers of the co-created PSM (O4). Ultimately, section 7.5 presents some policy actions to further develop and implement the PSM (O5).

Consensus results focus on the R3 final Delphi survey, that is, on agreement and disagreement statements, as well as ranking and checkbox questions reflected in Tables 7.1 —7.26. The R3 result tables show the variation (VAR) of each statement with respect to the R1 and R2 Delphi surveys, so if the statement was equal, revised or new. Revised and new statements include novel ideas generated by cohort B during the R2 interviews, incorporated into the R3 final Delphi survey. Results focus on R3 consensus statements, R3 consensus causes by expert segment (payer, performer, user and shaper), and R3-R2-R1 non-consensus and less agreement statements, including expert profile and open text comments. Finally, anonymised selected quotes from the interviews and surveys are included as examples of primary data that inspired and were converted into final statements evaluated by the panellists. The reader will appreciate the richness of the citations to get a better overall picture of what the statements refer to.

In the interest of transparency and rigor, the results tables for R1 and R2 are shown in Annex B and Annex C, respectively. R3 Kendall's W tables and additional results are shown in Annex D. A fourth round was not considered necessary nor appropriate to fulfil the primary objectives of the study as all statements that are part of the "**Minimum Consensus Criteria**" (see section 6.6) showed supermajority consensus (refer to Annex A, Table A1). Moreover, all R3 statements related to the co-created PSM showed simple or supermajority consensus.

7.1 THE HEALTH EQUITY POLICY PROBLEM IN THE LIGHT OF CONSENSUS SOCIAL VALUES (O1)

7.1.1 Consensus norms and problem definition

The first objective of this research was to confirm, in the light of consensus social values, that the current biomedical R&I model has a health equity problem that needs to be addressed. In this sense, the study sought to reach consensus on the type of norms that should guide healthcare innovation. In addition, it analysed whether the lack of or conflict with any of these consensus norms represented a major problem. This has been addressed primarily with the

Delphi technique, particularly in exploring agreement and disagreement regarding normative preferences (social values) and problem definition.

Normative Preferences

Health values show significant combined agreement among panel members of the R3 Delphi survey (level 1 range, with a range of combined agreement of 72-100%). This consensus on the normative preferences laid the foundations for the construction of a new R&I model. The two main rules that should guide the new R&I model are equity and efficiency. The desirability of the **health equity principle** in terms of ensuring equal access according to need was unanimously agreed by the panellists (combined agreement, 100%; agree, 91%) (Table 7.1, R3 STMT 1.1). The **efficiency principle**, meaning the "value for money" contribution of innovation to the well-being and sustainability of health systems (measured primarily by cost-efficiency), reaches a large supermajority (combined agreement, 86%; agree, 55%) (Table 7.1, R3 STMT 1.2). The panel agreed (combined agreement 77%; agree 50%) that there is an **ethical dilemma** between the two norms (Table 7.1, R3 STMT 1.3). That is, when incentives (risks and rewards) are not aligned with public health needs, the cost-efficient reward often prevents the principle of equity from being met.

In terms of industry decision-making, when the equity norm conflicts with the efficiency norm, the industry prioritises efficiency (rewards), resulting in an R&I system oriented toward benefits, rather than an equity-based approach to public health (combined agreement, 68%; agree 46%) (Table 7.1, R3 STMT 1.4). Mismanagement of risks and rewards throughout the R&I cycle leads to mutual **mistrust** between public and private actors (combined agreement 91%; agree, 55%) (Table 7.1, R3 STMT 1.5). The mutual uncertainty is motivated, among others, by the lack of transparency of the investment share in public-private R&I, as well as the difficulty of the private sector to predict the conditions of market access, giving rise to a profit-oriented R&I system.

Regarding the **desired R&I model**, the panel unanimously stated that **health equity** should be a **priority** principle of the model (combined agreement, 100%; agree, 82%) (Table 7.1, R3 STMT 1.6). However, panellists showed a slightly lower level of agreement (combined agreement, 86%; agree, 55%) that health equity is a priority in the decision-making of the organisations they work for (Table 7.1, R3 STMT 1.7).

Problem definition

Conflict with the **equity norm** and limited **speed** (as part of the efficiency norm) is considered the main consensus **problem** with the current system of medical R&I (combined agreement, 77%; agree, 46%). That is, innovative health solutions do not reach the world's population in an equitable, fast and sustainable manner (Table 7.1, R3 STMT 1.8).

16 **Table 7.1** R3 consensus Normative Preferences and Problem Definition

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
Normative Preferences (social values)										
STMT 1.1	**Norm 1: Equity** "Generally speaking, health systems should secure equal access to affordable, preventive, curative and good quality healthcare according to the need regardless of ethnicity, gender, age, social status or ability to pay".	Rev	1	100	91	9	0	0	0	0
STMT 1.2	**Norm 2: Efficiency / Cost-effectiveness** "Generally speaking, health systems should reward efficiency, normally quantified by cost-effectiveness analysis, so innovation really improving the patient journey for a certain cost (value for money), contributing to the health systems sustainability".	Rev	1	86	55	32	9	0	5	0
STMT 1.3	**Ethical dilemma.** In market economies, when incentives (risks & rewards) are not fully aligned with public health needs, these norms may imply an ethical dilemma because complying with rewarding efficiency frequently prevents from complying with equity.	New	1	77	50	27	5	5	14	0
STMT 1.4	**Efficiency dominates equity.** In industry decision-making, when the equity norm conflicts with the efficiency norm, efficiency (rewards) is superior to equity, resulting in a profit-oriented R&I model rather than public health equity-driven approach.	New	1	72	48	24	5	14	10	5
STMT 1.5	**Public-Private mistrust**. Mutual mistrust between public and private actors about the risk and reward management along the R&I cycle due to, among others, lack of transparency of public-private investments, but also unpredictability of market access conditions, keeping the R&D focus on most profitable diseases.	New	1	91	55	36	5	5	0	0
STMT 1.6	**Health equity as a R&D priority.** Improving health equity should be a priority for the biomedical R&D model.	New	1	91	55	36	5	5	0	0
STMT 1.7	**Health equity as a priority in decision-making in your organisation.** Improving health equity is a priority in the decision-making of your organization.	Equal	1	90	57	33	5	0	5	5
Problem Definition										
STMT 1.8	**Equity and speed as main problem.** The main problem with the biomedical R&I system is equity and speed, given that health innovation is not reaching citizens around the world fast enough in an equitable and sustainable manner.	New	1	81	48	33	5	10	5	5

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; NQ, participants who indicated that they were not qualified to respond; O, other responses (open text).

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of consensus.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Regarding the qualitative results, below are some selected quotes from the interviews and surveys. As mentioned, they illustrate the point of view of the key informants in their own words completing the analysis of results. The selected quotes were translated into final statements assessed by the panel members. In this case, the following quotes reflect the challenge of defining normative preferences and the problem with the current model as a result of an ethical dilemma.

Experts Quotes

Normative Preferences:

"How do we deal with the next pandemic. Do you think society would accept the same level of mortality and disruption in another pandemic? (…) That is why (…) ultimately these are societal questions" *– Shaper expert (E27)*

"Make clearer the value assessment framework. There are normative choices to be made. (…) I think that's the way forward, being more inclusive, have deliberation from the start, talk about what is the common goal. What are we trying to achieve? Why are we trying to achieve this?" *– Shaper expert (E13)*

Problem definition:

"We are in a period with great acceleration in understanding of disease biology and possible interventions, resulting in some amasing biomedical innovation (cell therapies, gene therapies, CGT, mRNA, immuno-oncology…). This innovation is not reaching people around the world fast enough in an equitable and sustainable manner" *– Shaper expert (E12)*

"We all know that we have to solve these problems *[lack of health access and equity].* ***I think nobody dares to disagree in public that we don't have a problem for instance around communicable diseases in developing countries... But no one is really doing anything about it"*** *– Payer expert (E03)*

"It depends who you talk to, really. This sort of more forward looking visionary, altruistic people in the industry, which there aren't many, would all agree with that. I think a lot of them quietly go back home and they just carry on keeping their shareholders happy. So, I think, to some extent, what they're saying is, we'd love to help you, but you have to make it worthwhile" *– Payer expert (E03)*

The analysis of consensus norms and problem definition was performed by expert segment (payer, performer, user and shaper) and the results showed that there was no significant differentiation between the actors due to the high level of panel consensus (Annex D, Table D6).

7.1.2 Norms and problem definition with no consensus or less agreement

This research considered of value to show in this chapter the statements without consensus or less agreement. In particular, the Delphi R3 survey showed no disagreement statements in terms of "no consensus" (combined agreement <50%) or "lower level of agreement" (combined disagreement > 25%) related to the value of equity in health (Table 7.1) [2].

Regarding R1 (preliminary survey and Delphi survey) and R2 (Delphi survey), that is, previous rounds of the Delphi methodology, they also did not show statements of disagreement on health equity values (Annex B, Table B1; Annex C, Table C1). However, in terms of problem definition, R1 cohort A did not reach consensus on abusive pricing as a problem for health equity (Annex B, Table B1, R1 (STMT 12)). The quote from dissenting statement was: "*The system of pharmaceutical innovation and access to medicines allows millions of people to die, in LMICs as well as in HICs, when the drug that would save their lives can be produced and sold at a price that would cover costs —including the R&D investment— and yield a reasonable, but not abusive, profit for the company*" (Canoy and Tichem, 2018; Maxmen, 2016; Moreno and Epstein, 2019). Therefore, R1 STMT 12 was not included in the R2 Delphi survey. As mentioned, R2 interviews contributed to clarify disagreements points and generated new ideas that were assessed in the R3 final survey round.

In brief, this chapter 7.1 confirms a significant consensus on the norms and the problem definition of health innovation that will facilitate consensus on identifiying the main causes of the problem (refer to section 7.2 below) and the co-creation of a more equitable and agile R&I model (detailed in section 7.3).

7.2 CONSENSUS CAUSES THAT PREVENT FROM FULFILLING HEALTH EQUITY GOALS (O2)

7.2.1 Consensus causes of the problem

This section aims to identify the main consensus causes (background theory, BT) that explain the equity and speed problem of the current R&I system claimed by the panel in the final Delphi survey (see section 7.1). For this, the present research applied five categories of causes corresponding to limitations in governance and the principles of "4 Share" (sharing needs, results, risks and rewards, and outcomes) that will define the PSM as a solution to the problem (refer to section 7.3).

Overall, a high level of agreement was found in the causes agreed upon between the panel (R3 Causes Tables 7.2-7.7, 95% statements with level 1 and 2 agreement). This broad agreement on the causes of the problem facilitated consensus on the co-design of an equitable and faster R&I model thereafter (see section 7.3). The consensus causes are described below according to the taxonomy of the five causes, namely governance, needs, results, risks and rewards and outcomes.

[2] Refer to the section 6.6 for the definition of no consensus and areas of consensus with less agreement.

1) Causes: lack of Governance

Lack of political will to **strengthen health systems in LMICs** is widely identified as the main governance constraint to consolidating UHC and fostering health innovation in these countries (Table 7.2 (R3 STMT 2.7)). The panel also states that current R&I model is not global but **governed** by **leading economies** prioritising their needs (Table 7.2 (R3 STMT 2.1)). Moreover, over the past 30 years, the medical market has seen a **concentration of supply** in a few large multinational companies (Table 7.2 (R3 STMT 2.5)). **WHO**'s role, as a multilateral actor is limited by a **lack of trust** (linked to financial accountability) and **power** vis-à-vis richer member states (Table 7.2 (R3 STMT 2.2)).

The system is very fragmented, asymmetrical in terms of resources and with different orientations, which leads to a **lack of private-public collaboration** that prevents responsible action in the face of unmet needs (Table 7.2 (R3 STMT 2.4)). Managers on both sides (healthcare providers and producers) often **lack** the appropiate **skills in health innovation** (Table 7.2 (R3 STMT 2.8)). This lack of unity in the health ecosystem is echoed in **insufficient coordination with other sectors** as health is considered different, justifying an isolated approach (Table 7.2 (R3 STMT 2.6)). In general, the current **social deal** is that government (mainly in HICs) should fund basic health research at universities and research institutions, so that industry can further develop, produce and commercialise these innovations incentivised by patent protection (Table 7.2 (R3 STMT 2.3)).

17 **Table 7.2** R3 consensus Causes: Governance

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
Causes - Governance										
STMT 2.1	**R&I governed by the main economies.** The current biomedical R&I system is not global as it is controlled by the main economies and compromised by vested interest.	New	1	86	55	32	5	0	9	0
STMT 2.2	**WHO limitations.** The difficulty with the World Health Organisation, as a multilateral organisation, is trust (i.e. absence of accountability of the non-designated funds) and the lack of real power in front of some member states.	New	1	71	59	12	12	6	12	23
STMT 2.3	**Social contract trap**. The current paradigm is that the government (particularly in high-income countries) funds basic R&D in universities and research institutions, and then the industry develops and manufactures new products incentivised by patent protection.	New	2	55	36	18	14	18	14	0
STMT 2.4	**Lack of private-public collaboration preventing "Responsible Capitalism".** Highly fragmented and misaligned R&I value chain due to different interests and resources, resulting in a lack of public-private collaboration to develop needed health products.	Rev	1	73	27	46	0	18	9	0
STMT 2.5	**Supply oligopoly.** Concentration on few huge biomedical multinational companies since the last 30 years.	New	2	62	43	19	10	24	5	5
STMT 2.6	**Lack of inter-sectorial coordination.** The healthcare sector is often reluctant to engage as fully and broadly as would be desirable with non-health actors because "health is different".	New	1	70	35	35	5	25	0	9

Table 7.2. R3 consensus Causes: Governance (cont.)

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
Causes - Governance										
STMT 2.7	**Lack of political will to strengthen health systems in LMIC** to implement first, the universal health coverage (UHC), and then, health innovations in low-and middle-income countries (LMIC).	Rev	1	94	47	47	5	0	0	14
STMT 2.8	**Poor health innovation management** among managers in both the provider and producer realms.	New	1	69	37	32	16	16	0	14

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; O, other responses (open text); NQ, participants who indicated that they were not qualified to respond.

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of agreement/disagreement.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Experts Quotes

Causes – Governance

Lack of political will to strengthen health systems in LMICs:
"95% of the WHO essential medicines list are generic medicines, so price is not a barrier for this. Some of these new medicines require diagnostics and infusion capabilities. So, the problem in South East Asia, Latin America and Africa is less about generating more data, it's more about strengthen health systems so that these therapies can be made available" *– Shaper expert (E12)*

R&I governed by the main economies:
"The current R&D model is largely driven by US VC *[venture capital**], a small country will change precisely nothing about that"*** *– User expert (E19)*

WHO limitations:
"***We have to be careful over-depending on any current governance structure, we can't rely too much. Because if you look at the WHO, the way WHO is funded, the way it's structured. It doesn't lend itself well. Because WHO receives so much from certain countries that have such, so many companies with very strong vested interest"*** *– Shaper expert (E17)*

Lack of public-private collaboration preventing "Responsible capitalism":
"I think companies do want to meet unmet health needs. They do want to be successful with regulators. They do want to partner with governments. They do want to treat more patients and improve outcomes for population but, you know, the clarity of those partnerships doesn't really exist" *– Performer expert (E11)*

2) Causes: lack of sharing Needs

Table 7.3 describes the main limitations of the current R&I system for sharing health needs, in terms of defining and focusing on priority challenges. The need for a paradigm shift, expanding the current **disease-based R&I model** to reward prevention and promotion solutions is a unanimous statement of the panel (Table 7.3 (R3 STMT 2.15)). Moreover, the R&I portfolio of health industry is strongly oriented towards serving the **US market**, with **high-profit** therapeutic areas (Table 7.3 (R3 STMT 2.11)). Moreover, there is a moderate consensus that industry prioritises R&I of alternative **me-too** treatments over unmet needs, as it involves less risk and investment, and significant returns (Table 7.3 (R3 STMT 2.12)).

On the other hand, global priorities are already defined in the UN **SDGs 2030 agenda**, but **lack** the necessary **incentives** to involve industry in achieving these ambitious goals (Table 7.3 (R3 STMT 2.10)). In this regard, there is a need to **expand** the **WHO Essential Medicine List** for **non-communicable diseases,** as the spectrum of diseases in LMICs is shifting towards diabetes, cardiovascular diseases and cancer, among others (Table 7.3 (R3 STMT 2.17)). Additionally, some LMICs (and some EU member states) still need to implement the basic benefit package of **UHC**, due to price and non-price constraints, before introducing innovative treatments (Table 7.3 (R3 STMT 2.16)).

At national level, there is a **lack** of a **value framework** of priority health challenges as a social choice. This frame should be adapted at the country or region level, considering epidemiology, income and health care model. As a result, negotiations between national health payers and producers are based on price rather than value based on chosen preferences (Table 7.3 (R3 STMT 2.9)). In terms of health policy, **pharmaceutical regulation** is heavily influenced by the private sector, with economic interests overshadowing public health guidance. This **industry lobby** results in a **technology-driven** R&I agenda that increases its return on investment (ROI) (Table 7.3 (R3 STMT 2.13)). Finally, the ecosystem shows a **lack of alignment** between the agendas of **developers, government** and **industry**. Research lines in academia and research centres are determined by principal investigators not always aligned with public health priorities and incentives (Table 7.3 (R3 STMT 2.14)).

18 **Table 7.3** R3 consensus Causes: Needs

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
Causes - Needs										
STMT 2.9	**Lack of a "Value frame" as a "social choice" of priority health challenges**, which is country-specific given the heterogeneous epidemiology, income and healthcare costs among countries/regions, resulting in price-based negotiations rather than value proposition-	Rev	1	82	41	41	9	9	0	0
STMT 2.10	**Lack of incentives to fulfill the UN SDG agenda**. Global priorities already set in the UN SDGs but not really impactful in engaging pharmaceutical organizations.	Equal	1	85	55	30	5	10	0	9
STMT 2.11	**US profit-driven R&I portfolio**. The biomedical corporates tend to target few high-profit therapeutic areas in selected markets, with the USA as the largest one.	New	1	95	63	32	0	5	0	14

Table 7.3 R3 consensus Causes: Needs (cont.)

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
Causes - Needs										
STMT 2.12	**Excess of "me-too" products.** R&D is mainly focused on alternative me-too treatments rather than unmet needs, because it implies less R&D risk and investment, and large markets (i.e. USA, EU).	New	2	52	33	19	14	19	14	5
STMT 2.13	**Pharmaceutical Policies predominantly ruled by private sector interests,** with the economic angle dominating the public health angle, resulting in a "technology push" R&D agenda that maximizes the industry return on investment (ROI).	Rev	1	68	36	32	14	14	5	0
STMT 2.14	**Lack of alignment between Academia–Government–Pharma**. Mismatch between academia research lines (determined by Principal Investigators) and the governments and big corporates agenda, because no one is clearly telling the academia what are the public health priorities and incentives.	Rev	2	64	41	23	14	14	9	0
STMT 2.15	**Disease-based R&I model.** The government should also reward health prevention and promotion rather than only disease-based solutions.	Rev	1	100	96	5	0	0	0	0
STMT 2.16	**UHC challenges.** The basic benefit package of the Universal Health Coverage (UHC) still needs to be implemented in some LMIC (and in some EU member states), overcoming price and non-price barriers before starting to introduce innovative medicines.	Rev	1	77	50	27	14	9	0	0
STMT 2.17	**Need to expand the WHO "Essential Medecine List" for NCD**. Disease spectrum is changing as non-communicable diseases (NCD, i.e. diabetes, cardiovascular, cancer) are now becoming more important in LMIC, so the WHO "Essential Medicine List" should include NCD drugs.	New	1	81	62	19	5	5	10	5

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; NQ, participants who indicated that they were not qualified to respond; O, other responses (open text).

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of consensus.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Expert Quotes

Causes – Needs

Disease-based R&D model:

"If the system changes the way it asks for products and services and, instead of devices and drugs, ask for prevention and promotion, the industry will follow the reward. (…) Solution-based rather than disease-based makes a lot of sense, but the payer has to drive it. But the problem is with fragmented markets like in the US… if all the payers are driving it in different ways" *– Performer expert (E11)*

US-profit driven R&I portfolio:

"The biomedical industry has become more consolidated and focused on bringing to market products that will sell well in the USA. (…) I think the problem is that we have the pharmaceutical industries that, over

the last 20 years, have become more and more consolidated, so fewer, fewer larger companies (…) even with European companies, the mindset of the business model for developing products is very much centred around the US thinking and the US market" *– Payer expert (E25)*

"The problem is mainly industry… they are orienting themselves towards the problems where they are sure to get the biggest profits and these are totally out of proportion to the relative benefit provided" *– Shaper expert (E17)*

Lack of incentives to fulfil the UN SDGs agenda:
"This *[statement]* ***makes it sound simple. Some national systems are of course more fragmented. I generally agree with the premise of better utilising monopsonic leverage to give a message of where the priorities are"*** *– Shaper expert (E17)*

Pharmaceutical policies predominantly ruled by private sector interest:
"Innovation is technology driven, profit driven. Innovation agendas are set, they are focused on technology push, not necessarily on the needs of the population" *– Shaper expert (E13)*

Lack of alignment between Academia-Government-Pharma:
"There's a clear mismatch of what the academia and the academic groups do and what the governments and big pharma are trying to address. So, finding ways to communicate and to make them educated in both sites and incentive them both, especially the academics here. I think that would be beneficial. (…) So, the academics, even the most brilliant ones, they need to understand that there's a responsibility on the research they do. But this is very difficult" *– Performer expert (E16)*

3) Causes: lack of sharing Results

Panellists substantially agreed on all aspects of data collection and sharing, indicating that the management of scientific and financial data is key to reach health equity. Particularly with regard to scientific data, the **lack of sharing real-world evidence** (RWE), its quality and integration with randomised control trials (RCTs) was widely accepted by the panel. This RCT-RWE data analysis gap reduces the potential for informed public health decisions (Table 7.4 (R3 STMT 2.22)).

Data regulation, notably the **insufficient development** of **ownership** of research **data**, is cited as one of the reasons for the data sharing gap. Some researchers and institutions take ownership of research data and choose not to publish them even for publicly funded projects (Table 7.4 (R3 STMT 2.20)). Moreover, there is a **gap** in the **publication** of R&D **results**. Researchers, institutions and countries are sometimes averse to publishing positive and negative (failure) results, incrementing research waste (outcomes not used) and delaying patient access to innovative solutions (Table 7.4 (R3 STMT 2.21)).

Regarding study design, **RCTs** are **time-intensive**, especially when aiming to intervene earlier in slowly evolving diseases (i.e. Alzheimer's disease) (Table 7.4 (R3 STMT 2.18)). Furthermore, RCTs are generally designed for selected patient segments showing the best prognosis. The result of

non-inclusive RCTs is that new drugs are initially approved only for patients without complications (Table 7.4 (R3 STMT 2.19)).

19 **Table 7.4** R3 consensus Causes: Results

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
Causes - Results										
STMT 2.18	**Time-consuming RCT.** Traditional randomised clinical trials (RCT) are too slow, in particular if we want to intervene earlier in slowly progressing diseases (i.e. Alzheimer's disease).	New	1	70	30	40	15	0	15	9
STMT 2.19	**Non-inclusive RCT**. Randomised clinical trials (RCT) design are mainly made for "beautified patients", highly-selected patient population with the best prognosis, so the drug is approved for patients without complications.	New	2	60	25	35	20	10	10	9
STMT 2.20	**Lack of R&D data sharing due to uncertain ownership**. Insufficient development of the research data ownership that prevents from being shared (i.e. some researchers may say "I don't share MY database" when, in fact, should be a public database because it has been financed by public authorities).	Rev	1	77	32	46	9	5	9	0
STMT 2.21	**Gap in publication of R&D results, including failure**. Reluctance of researchers, institutions and countries to publish all the significant results, including failure, causing excess research waste (outcomes cannot be used) and delays in patient access to innovative medical products.	New	1	68	41	27	23	0	9	0
STMT 2.22	**Lack of real-world evidence (RWE) data sharing**, data quality and integration with randomised control trials (RCT) and advanced analytics to make informed payment decisions.	Rev	1	95	43	52	5	0	0	5

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; NQ, participants who indicated that they were not qualified to respond; O, other responses (open text).

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of consensus.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Expert Quotes

Causes – Results

Lack of real-world evidence (RWE) data sharing:

"We are seeing the kind of acceleration of clinical knowledge. I mean that's what we have seen over the last years. We now have cell therapies, gene therapies, mRNA vaccines, immune oncology. These are all…amasing new technologies. We want to make them available to patients fast and there is a problem that, for these curative therapies, it takes a long time until we have the complete data, so I think we need new models that we say how do we strike a good balance between early access and maturity of the data" *– Shaper expert (E12)*

"The problem with real-world evidence is the quality of information, of data (…). The improvement should be in the public sector and for non-high-cost drugs, and to collect evidence for the whole population" – *Shaper expert (E15)*

"With old RCT *[randomized controlled trials]* ***you're punishing every single step and real-world evidence in a way can capture a lot of these. Our hope was that by using real-world evidence, you can have less burden of trials for patients (…) and hypothesis generation (…), what can we learn from the Super Responders?"*** – *User expert (E19)*

Lack of R&I data sharing because uncertain ownership:
"Some research centres or brilliant minds say: "I don't share MY database". Well (…) maybe it's not YOUR database. It's a public database because you are financed by your national authorities, by the European authorities" – *Shaper expert (E26)*

4) Causes: lack of sharing Risks & Rewards

The main consensus limitations of the current R&I system in terms of risks and rewards were differentiated in two categories: A) R&I gap (Table 7.5), and B) high price model supported by patents and value-based pricing as drivers of innovation (Table 7.6).

A. R&I Gap

Experts agreed on statements about the causes of the current R&I gap for certain public health challenges (Table 7.5). The R&I gap is mainly explained by the **lack of alignment** between **market incentives** and **public health needs** (Table 7.5 (R3 STMT 2.23)). On the one hand, for certain health challenges, there are no incentives for industry to assume the risks and costs of developing and marketing new technologies. On the other hand, the public sector has neither the mechanisms nor the financial resources to undertake the R&D cycle of innovative solutions for health equity. At the same time, experts identify the **modest R&I leadership** of the **Global South** (Table 7.5 (R3 STMT 2.32)). As a result, the international R&I agenda is driven by HICs, given their dominant contribution as payers (public and private) and performers (i.e. researchers, entrepreneurs, large corporations).

Insuficient innovation drive of academia as a developer is considered a limiting factor for the deployment of the collaborative **Open Innovation** model (Table 7.5 (R3 STMT 2.30)). Lack of researchers' business vision and skills, innovation-linked reward schemes, access to corporates and funding reduce the potential of open innovation deployment. Moreover, universities and research centres do not have enough flexibility or capacity to promote technology transfer (TT), especially through creation of spin-offs.

Innovation **developers** (academia, start-ups and SMEs) face a public and private **funding gap** for **early-stage projects**. Researchers and entrepreneurs do not develop promising discoveries due to a lack of public funding that could be used efficiently, in terms of high-quality evidence at a lower cost than companies (Table 7.5 (R3 STMT 2.26)). In addition, venture capital and private equity firms are often reluctant to fund early-stage projects for start-ups and SMEs due to high risk and long development cycles (Table 7.5 (R3 STMT 2.27)). Producers at the **SME** level are

constrained by the **lack of growth-stage investment**, mainly from venture capital funds and private equity funds (i.e. in the EU), which should enable these companies to grow and go public (initial public offering, IPO) (Table 7.5 (R3 STMT 2.28)).

As for payers, **public health purchasers fail to use** their **market power** to shape the R&I system with equitable goals (Table 7.5 (R3 STMT 2.25)). The public sector, as a major **investor** and **purchaser** of health innovation, is not using its market power to set the agenda, the incentives and the equity goals of public health priorities. In terms of incentives, there is a **dispersion** of public R&I **funding** that preventing substantial capital from being allocated to disruptive innovation (Table 7.5 (R3 STMT 2.29)). Besides, some R&I **incentives cause unintended consequences.** For example, regulatory incentives for rare diseases led industry to concentrate on some rare diseases with similar solutions or oncology for niche patients (Table 7.5 (R3 STMT 2.31). Finally, current R&I is led by **profit-maximising venture capital** (VC) through **high prices** of patent-protected products resulting in unmet health needs and access challenges of the end products (Table 7.5 (R3 STMT 2.24).

20 **Table 7.5** R3 consensus Causes: Risks and rewards (R&I gap)

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
Causes - Risks & Rewards										
A- R&I Gap										
STMT 2.23	**Mismatch between market incentives and Public Health needs**. For certain public health challenges there are no incentives for the private sector to take on the high risk and cost of development and market launch. On the other hand, the current public system is not designed nor capitalized to take on the level of risk to deliver health equity goals.	Rev	1	90	52	38	5	0	5	5
STMT 2.24	**Venture capital patent-driven R&I based on high prices.** The current biomedical R&I model is led by venture capital to maximise return on investment (ROI), mainly through high prices for patented products, leaving some health needs unattended and resulting in health access challenges of the end products.	Rev	1	71	52	19	14	10	5	5
STMT 2.25	**Public purchasers failing to use their market power.** Public sector, as significant investor and buyer in biomedical R&I, failing to use their market power to set the agenda, the incentives and the equity goals for public health priorities.	Rev	1	80	55	25	15	5	0	9
STMT 2.26	**Public funding gap in academia/start-ups/SMEs for early-stage projects**. Promising discoveries not developed due to lack of public funding for early-stage projects in academia, start-ups and SMEs that could be used efficiently (high-quality evidence at lower cost than corporates).	Rev	1	76	57	19	10	10	5	5

Table 7.5 R3 consensus Causes: Risks and rewards (R&D gap) (cont.)

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
Causes - Risks & Rewards										
A- R&I Gap										
STMT 2.27	**Private funding gap in start-ups/SMEs for early-stage projects.** Most of the venture capital and private equity firms do not target early-stage project companies due to the high risk and long development cycles.	New	2	58	32	26	5	21	16	14
STMT 2.28	**Lack of growth-stage investment for SMEs**, primarily from venture capital funds and private equity funds, for instance in the EU, which should offer firepower to SME companies to grow and investment for IPO (initial public offer) companies.	New	1	70	40	30	15	10	5	10
STMT 2.29	**Dispersion of public R&I funding** that prevents large budgets to be allocated to the best R&I projects in terms of disruptive innovation.	Rev	1	75	40	35	10	5	10	9
STMT 2.30	**Limited innovation "push" in academia**. Open innovation has increased the pressure for academia to do technology transfer (out-licenses and spinoffs), but researchers often lack the business vision and skills, rewards (i.e. academic career), access to corporates, funding and, on the other hand, academia is not flexible or empowered enough to create spin-offs.	Rev	1	82	50	32	9	0	9	0
STMT 2.31	**Unintended consequences of incentives.** For instance, regulatory incentives for rare diseases that make industry concentrate in few rare diseases with similar solutions or in oncology for niche patients.	New	1	74	37	37	16	11	0	14
STMT 2.32	**Lack of Global South R&I.** The majority of the funding (public and private) and the actors (researchers, entrepreneurs, industry, etc) are in developed countries, shaping the global R&I agenda.	New	1	96	59	36	5	0	0	0

N, total number of responses; RR, response rate.
Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; NQ, participants who indicated that they were not qualified to respond; O, other responses (open text).

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of consensus.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Expert Quotes

Causes – Risks and Results (R&I Gap)

Mismatch between market incentives and public health needs:
"The current VC-based incentive model works, but not in all areas of need, and does not lead to universal access of the end product… We have diseases for which there is no therapy, then we have diseases for which there is therapy that people cannot access because of price" *– User expert (E19)*

"The push incentives are useless if you don't have something to pull that product through into the hands of the patients. (…). Right now, there's too much money flowing into the R&D model from that perspective and not enough money flowing into the pull incentives" *– Payer expert (E18)*

Lack of Global South R&D:
"The 80% of the world that is struggling to get access, they are not investing into research and development for new medicines. I mean, the investment comes primarily from the US. (…). They need to organize their markets, they are investing significantly now into Universal Health Coverage" *– Shaper expert (E12)*

Limited innovation "push" in academia:
"That's an interesting dilemma here now about this push to the academics that has not been demanded by them to be pushed. I think (…) the academic career is not managed, it's not been measured by technology transfer. (…) But if you don't, not only patent, but license one of your patents, that means that the patent has to be good, you will not be a PI *[Principal Investigator]" (he laughs) – Performer expert (E16)*

Public funding gap in academia/start-ups/SMEs for early-stage projects:
"For the academic institutions (…), this early gap on tech transfer, requires much more money. If the private sector sees that there's an incentive from the public sector to do that, I think they will come and invest earlier" *– Performer expert (E16)*

Lack of growth-stage investment for SMEs:
"What an alternative to a VC *[venture capital]-****based system looks like? (…). This is a little bit what the European Union is working on. So, (…) the European Union is offering now VC, especially for this part of businesses, where we don't have so much… So,*** *[for]* ***the start-ups, the first phase seems to work, but then the scaling doesn't seem to work so well, and then we lose lots of start-ups to the US, where it's easier to get VC. So, I think that's a very interesting space to get our head around"*** *– User expert (E19)*

Public purchasers failing to use their market power:
"Offer incentives proportional to the investment made by different parties. A significant proportion, if not a majority, of the money put into the R&D process is actually coming from public institutions. Then much better, frankly, (…) to adequately fund the public institutions and then you incentivize the private sector for the very small amount that is required of them in terms of late stage manufacturing scale" *– User expert (E06)*

"We recognize that you're not going to make as much profit on this malaria drug as you would on this drug for male pattern baldness, but we will give you sort of an injection of funding in order to facilitate that collaboration" *– User expert (E06)*

"From that perspective *[health equity],* ***the challenges are incentives and risk. And the fact that they are either lacking or not enough incentives to take on the risk, and the risk is not distributed across (…) the network of players in this space"*** *– Payer expert (E18)*

B. High Prices based on Patents and Value-based Pricing (VBP) as main innovation drivers

The agreed-upon causes of the health innovation equity problem related to high prices are shown in Table 7.6. The need to **redefine value-based pricing** (VBP) was widely accepted by the panel (Table 7.6 (R3 STMT 2.33). The price of a medical product should consider the value (to the patient and the healthcare system), but also other variables such as the R&I **risk** assumed, the **ability to pay** and the **purchase volume.** Furthermore, the experts claimed **abusive patent** practices by the dominan pharma and biotech companies expanding the scope or the term of a patent (patent evergreening) prolonging the high prices (Table 7.6 (R3 STMT 2.37). On the other hand, the panel significantly pointed out the **lack of systemic thinking** in national reimbursement models. That is, the price of a new health product should consider the **savings** for the healthcare system and the increase in **productivity**, that are normally overlooked, instead of focusing on the immediate increase in health costs (Table 7.6 (R3 STMT 2.41).

There is a **gap in which regulatory-cleared products reach the market** or are launched with significant delay because the industry prioritises high price negotiations. This happens because confidential price trading occurs first in higher-income countries and then in others (Table 7.6 (R3 STMT 2.34). Importantly, there is a **lack of transparency** about the **investment mix** in R&I (private and public), which is usually not reported, and which should modulate the price of the product (Table 7.6 (R3 STMT 2.36).

The lowest level of agreement in this domain is related to the **price-value paradox** (Table 7.6 (R3 STMT 2.35) and the **US R&I funding model** (Table 7.6 (R3 STMT 2.38). There is no consensus on VBP that means low net benefit for the public system (Table 7.6 (R3 STMT 2.39) nor on risk-sharing practices that incentivise high prices (Table 7.6 (R3 STMT 2.40). Refer to section 7.2.3 for more details.

21 **Table 7.6** R3 consensus Causes: Risks and rewards (Pricing)

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
Causes - Risks & Rewards										
B- High prices based on Patents and Value-based Pricing (VBP) as main innovation drivers										
STMT 2.33	**De-constructing Value-Based Pricing (VBP).** Value cannot be the only product pricing criteria, but other parameters, such as the R&D risk assumed as well as the ability to pay and volume, should be considered.	New	1	91	67	24	10	0	0	5
STMT 2.34	**Gap in regulatory authorised products reaching the market.** Biomedical firms prioritise the highest price resulting in regulatory authorised products not reaching the market or with considerable delay (i.e. in some EU member states), since confidential price negotiation first happens in countries with the highest income.	Rev	1	79	42	37	11	11	0	14

Table 7.6 R3 consensus Causes: Risks and rewards (Pricing) (cont.)

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
Causes - Risks & Rewards										
B- High prices based on Patents and Value-based Pricing (VBP) as main innovation drivers										
STMT 2.35	**Price-Value paradox.** Low expected profits from medications that provide the most health benefit and converse. (i.e. generic antibiotics can still treat the majority of infections versus innovative cancer treatments with low impact on survival).	Rev	2	57	24	33	19	19	5	5
STMT 2.36	**Lack of transparency about the R&D investment mix** as it normally involves public R&D co-funding that is not reported and that should modulate the price.	New	1	67	38	29	10	10	14	5
STMT 2.37	**Abusive patent practices** by dominating biomedical companies to expand the scope or the term of a patent (i.e. patent evergreening) prolonging the high prices.	Rev	1	80	45	35	10	10	0	9
STMT 2.38	**High price US-driven business model as investment in public health.** The global pharmaceutical development is largely funded by American patients who accept to overpay for pharmaceuticals, recognizing that the removal or relaxing of price controls is an investment in public health.	New	2	52	26	26	16	21	10	14
STMT 2.39	**VBP means low net benefit for the public system.** Value-based pricing (VBP, as cost per QALY gained) allows health payers to pay more for a technology that either generates more clinical benefit or saves costs to the system. Payers have a maximum price per QALY gained as a threshold. In practice, companies price their products an amount that sits close to that threshold. The net benefit for the public sector is close to zero, because much of that benefit is company profit.	Rev	3	42	10	32	16	26	16	16
STMT 2.40	**Risk-sharing practices incentivise high prices.** Risk-sharing agreements such as the Managed Access Funds in the UK is a conditional approval and reimbursement after clinical trial phase II. By paying industry before completing the trials, the health payer should have a lower price because it is de-risking pharma. In reality, the company ask a high price upfront and, if the evidence is finally not worth that value, they commit to give a rebate, which is not normally done. This happens because health systems have pressure to get the product to patients.	New	3	47	18	29	18	24	12	23
STMT 2.41	**Lack of systemic thinking in national reimbursement models.** When assessing the cost of a drug (i.e. Alzheimer), the savings for the healthcare system and the increase in productivity are not normally considered, only the impact of the drug price in the health budget	Rev	1	79	63	16	16	0	5	14

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; NQ, participants who indicated that they were not qualified to respond; O, other responses (open text).

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of consensus.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Expert Quotes

Causes – Risks & Rewards (High prices)

De-constructing value-based pricing (VBP):
"The value is a starting point, and then we negotiate from there. (…) I strongly advocate against value being the only criteria, because we've got to be realistic about your ability to pay and volumes, and I have said this very strongly, that continuing to restrict to subgroups of patients based on cost-effective is not a strategy that is sustainable for (…) public health" *– Shaper expert (E24)*

Abusive patent practices:
"Products that seek to improve health and wellbeing should be framed as global public goods, and not as profit-making products. We need to have an R&D system that is not led by the pharma companies, such as the Drugs for Neglected Diseases Initiative (DNDi) with MSF *[Médecins sans Frontières]* ***with a much smaller role of pharma industry, so the profit motivation is reduced. Your entire R&D mindset is that we want to get the products to people. You sell the product at the cost of manufacture and allow a very narrow window of patent protection in order that industry can recoup the R&D costs"*** *– User expert (E06)*

Lack of systemic thinking:
"If you look at the proportion of drugs over health budget, it's a small proportion. It's just for the system the easy part to squeeze (…). So, (…) if you look, for example, at Alzheimer, how much new neurodegenerative drugs and the care for these people costs to the system, that's huge! (…) My grand-mother has Alzheimer's, what it costs for care for these years? if you put that into a therapy that would be a lot of money for a therapy. But we don't calculate it that way" *– User expert (E19)*

Gap in regulatory authorised products reaching the market:
"Yes, there are several, too many products approved by regulators like the EMA which are not reaching the market. And the reason is not the conditions of the HTA, but are the prices claimed by the industry" *– Shaper expert (E21)*

Lack of transparency about the R&I investment mix:
"The funding should be much more visible everywhere because, you know, I have a real problem when I hear about the billions, billions of dollars profit for Pfizer yesterday. When you consider how much of that was driven by COVID and how much of borrowed money was given by the US Government (…) to the development. It's an emergency situation yes, but there should be some come back on that, maybe some tax or something" *– Performer expert (E10)*

5) Causes: lack of sharing Outcomes

The experts agreed on the causes of the problem related to health outcomes as shown in Table 7.7. Many countries have **not implemented HTA** assessment based on value outcomes to vindicate the choice of an innovative technology (Table 7.7 (R3 STMT 2.42). Notably, companies **complying** with **environmental and health equity** outcomes do **not** receive a **distinctive reward** for it (Table 7.7 (R3 STMT 2.43).

22 **Table 7.7** R3 consensus Causes: Outcomes

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
Causes - Outcomes										
STMT 2.42	**Lack of HTA assessment.** Lack of Health Technology Assessment (HTA) of value-based outcomes in many countries that justify the choice of innovative technologies.	New	1	85	50	35	5	10	0	9
STMT 2.43	**Lack of a differential reward for companies fulfilling environmental and health equity practices** (they don't get credit for it).	New	1	100	65	35	0	0	0	9

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; NQ, participants who indicated that they were not qualified to respond; O, other responses (open text).

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of consensus.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Expert Quotes

Lack of HTA Assessment:
"HTA, in my opinion, was also a potential tool for identifying knowledge gap" *– Performer expert (E02)*

Lack of differential reward for companies fulfilling environmental and health equity practices:
"So, everyone's hands are tied. So, who is, who can be a market shaper? The public sector as a monopsony and as an investor, so that's a little bit the idea" *– Shaper expert (E27)*

7.2.2 Main consensus causes ranking and by expert segment

Main Causes Ranking

In accordance with the scheme of the methods section (section 6.5.1), I hereby convey the results of the ranking of the main causes of the problem with the current health innovation model grouped into five cross-cutting themes (Table 7.8). This synthesis of the study's findings on these five transversal topics was informed by the results of the R2 survey and interviews results and the principles that define the PSM.

The top ranked consensus cause is the **mismatch between incentives and public health needs**. It is followed by the **mismanagement of risks and rewards** during the R&I cycle. Third, the lack of **developer funds** and **alignment with priority health challenges**. Fourth, the **aberrant patent protection practices** and **value-based pricing** applied by the industry. Finally, the **lack of data sharing**, both scientific and financial records.

23 **Table 7.8** R3 consensus Causes rank

R3 Delphi survey (n=27, RR= 81%)

STMT 2.44	**Ranked** main **CAUSES** that prevent the current R&I system from fulfilling health equity goals in order of importance (with 1 being 'Most important' and 5 being 'Least important').	
Rank	**Statement**	**Value**
1	Lack of alignment between incentives and public health needs	38
2	Unequal distribution of Risks & Rewards	67
3	Developers lack of funds and alignment with priority health challenges	73
4	Perverse use of patents and value-based pricing	74
5	Lack of transparency in scientific and financial data	78

Value indicates the aggregated rank value assigned by the panellists to each statement, meaning that the lowest the value the higher the rank postition.
Developers refers to academia, startups and SMEs.

Kendall's W[3] coefficient of concordance for the ranked five main causes of the problem wih the current R&I model was calculated to assess the level of agreement accross the panel. Kendall's W was 0.2153 (chi-squared 18.9455, degrees of freedom 4, p-value 0.0008, see Annex D, Table D1) reflecting a weak level of agreement between the experts. This result means that the panellists have applied different criteria to judge the importance of each root cause, so their rankings were significantly different (Habibi et al., 2014; Okoli and Pawlowski, 2004). Statistically, raters were concordant with a low Kendall's W in the evaluation of causes at the 0.05 significance level, as the null hypothesis (Kendall's W equal to 0) was rejected with p=0.0008 (Grande, 2017; Habibi et al., 2014; Okoli & Pawlowski, 2004).

Furthermore, Kendall's W for the main causes was calculated for each expert segment to identify whether there was concordance in the rating choices of each group, as they might be expected to share a similar viewpoint (Annex D, Table D2). The results showed a Kendall's W of 0.6444 for payers, 0.1633 for performers, 0.5556 for users, and 0.2543 for shapers. That is, there appeared to be a moderate agreement between the rating preferences of payers and users and a weak agreement between performers and shapers. However, there was no evidence that raters were concordant in prioritising causes, as p-values were greater than 0.05, so the null hypothesis could not be rejected at the significance level of 0.05 (Habibi et al., 2014; Okoli and Pawlowski, 2004). Overall, there was no concordance on ranking priorities between each expert segment.

Main Causes by expert segment

Although Kendall's W is low, the ranking of the main causes of the problem by expert segment (payer, performer, user and shaper) was analised to identify differences in preferences between groups (Table 7.9). More importantly, some quotes from experts are also provided to get a qualitative insight of each segment's point of view.

[3] *Refer to the section 6.6 for further details of Kendall's W non-parametric test.*

24 **Table 7.9** R3 consensus Causes rank by expert segment

R3 Delphi survey (n=27, RR= 81%)

STMT 2.44	**Ranked** main **CAUSES** that prevent the current R&I system from fulfilling health equity goals in order of importance (with 1 being 'Most important' and 5 being 'Least important').				
Statement	**Value**	**Payer**	**Performer**	**User**	**Shaper**
Lack of alignment between incentives and public health needs	38	●●	●	●●	●●
Unequal distribution of Risks & Rewards	67	●	●	●	●
Developers lack of funds and alignment for priority health challenges	73		●	●	●
Perverse use of patents and value-based pricing	74	●	●	●	●
Lack of transparency in scientific and financial data	78		●		●

(●●) Ranked as priority 1-1.9, (●) ranked as priority 2-3.9, (empty) ranked as priority 4-5.

Developers refers to academia, startups and SMEs.

Payers (NHS, public banks, private VC) focused primarily on incentive misaligment as a key cause of the health equity problem. Inadequate distribution of risk and rewards and irregular use of patents were other prominent causes.

Expert Quotes

Unequal distribution of risks and rewards:
"The challenges are incentives and risk. And the fact that they're either lacking or not enough incentives to take on the risk, and the risk is not distributed across (…) the network of players in this space (…). There are no incentives for the real drivers of medicine and vaccine innovations to take on the cost of development (and the inherent risk associated with that) and the risks of launch (delays, diversion, lack of delivery and treatment infrastructure) are high" *– Shaper expert (E18)*

Developers lack of funds:
"Does the government have to promote**? [Venture capital public-private matching fund] **(…) Depending on how it's structured, it may or may not work (…). The two things go hand in hand, you know, what comes first the entrepreneurs or the capital? If they just both, they have to kind of spontaneously combust at the same time. So, it's always been the case that if there's talent and really good ideas, capital emerges and finds a way. And then it's a question of just how quickly it organizes. So, you know, my feeling is the technology and the management have to emerge first and then the capital will follow" *– Funder expert (E22)*

Performers (start-ups and SME developers and large corporate developers and suppliers) balanced their ranking among the five cross-cutting causes. In particular, start-ups and SME developers claimed the lack of transparency in scientific and financial data as the main cause of the equity problem, as well as lack of funds and alignment for priority challenges. Big pharmaceutical and biotech companies emphasises the lack of incentives for public health needs.

Expert Quotes

Lack of alignment between incentives and public health needs:
"There should be incentives for the breakthrough because otherwise you just won't get breakthrough, you won't get technology if there's no payment for it" *– Performer expert (E11)*

Public funding gap in academia/start-ups/ SMEs for early-stage projects:
"There is not enough funding for early stage R&D projects. So, the challenge will be to develop this vehicle, early stage investment, vehicle, public and private, so increase this funding from both sites" *– Performer expert (E16)*

Users (prescribers and users, beneficiary representatives) pointed out the importance of incentives for top health priorities, followed by the inappropiate distribution of risk and rewards, and the perverse use of patents. The lack of alignment and funding of academia and small-scale developers was also highlighted by this segment.

Expert Quotes

Unequal distribution of risks and rewards:
"We believe that transparency should be a key feature of any R&D system. So, when there is public investment, there should be more transparency and conditions attached. So those receiving support from public entities should not (…) have all this freedom to set the prices they want and then, you know, negotiate, whatever they want. They should follow some ethical and some access commitments when they launch the products in the markets" *– User expert (E14)*

"Offer incentives proportional to the investment made by the different parties. (…) A significant proportion, if not a majority, of the money put into the R&D process is actually coming from public institutions. Then much better, frankly, (…) to adequately fund the public institutions and then you incentivize the private sector for the very small amount that is required of them in terms of late stage manufacturing, scale up, and so on. (…) It's a prelude to incentivization which is kind of transparency and then you incentivize proportional to how much people actually paid into the process in the first place" *– User expert (E06)*

Shapers (evaluators, regulators, policy makers) agreed that lack of incentives is a key cause of current health inequity. As performers, shapers scored the remaining four cross-cutting causes in a balanced manner. That is, considering the importance of unbalanced distribution of risks and rewards, the perverse use of patents, the lack of aligment and funds of developers, as well as the lack of scientific and financial data sharing.

Expert Quotes

Lack of alignment between incentives and public health needs:
"We have to put incentives that are really interesting and out competing. We have to find something that is so attractive that will outcompete the current model, because people have choice!" *– Shaper expert (E17)*

Unequal distribution of risks and rewards:
"The current public system is not designed nor capitalized to take on the level of risk needed to deliver health equity goals, and the private system is not incentivised to" *– Shaper expert (E18)*

7.2.3 Causes with no consensus or less agreement

In the R3 final survey, there were 2 cause statements with no consensus (combined agreement <50%) and 12 cause statements with a lower level of agreement (combined disagreement > 25%) related to the causes of the problem (Annex D, Table D7). See section 6.6 for definition of non-consensus and areas of consensus with less agreement.

In R3, the panel did not reach consensus on 2 causes on high prices for medical products.

- **Causes risks and rewards - High prices (no consensus):** Value-based pricing (VBP) was not considered by experts to produce a low net benefit to the public system when applying cost-effectiveness analysis with a threshold (Annex D, Table D7 (R3 STMT 2.39) (Littlejohns et al., 2019). The panel, especially performers and shapers, was not convinced by this explanation: *"VBP (cost per QALY gained) allows health payers to pay more for a technology that either generates more clinical benefit or saves costs to the system. Payers have a maximum price per QALY gained as a threshold. In practice, companies price their products an amount that sits close to that threshold. The net benefit for the public sector is close to zero, because much of that benefit is company profit".* Risk-sharing practices that incentivise high prices was the second statement without consensus, particularly among performers (Annex D, Table D7 (R3 STMT 2.40). Experts did not agree on this rational: *"Risk-sharing agreements, such as the Managed Access Funds in the UK, is a conditional approval and reimbursement after clinical trial phase II. By paying industry before completing the trials, the health payer should have a lower price because it is de-risking pharma. In reality, the company ask a high price upfront and, if the evidence is finally not worth that value, they commit to give a rebate, which is not normally done. This happens because health systems have pressure to get the product to patients".*

Moreover, there were 12 consensus causes with less agreement (Annex D, Table D7) as follows, including discrepancy by segment and open-ended comments:

- **Causes Governance (less agreement)**: Significant disagreement, mainly among performers and shapers, that medical supply has been concentrated in few large multinational companies for the last 30 years (Annex D, Table D7 (R3 STMT 2.5)). Some experts, mainly performers, disagreed with the fact that the current R&I paradigm is that the government (particularly in HICs) funds basic R&D in universities and research institutions, and then the industry develops and manufactures new products incentivised by patent protection (Annex D, Table D7 (R3 STMT 2.3)). One user panellist noted that countries also benefit from the industry's commercial success, with attractive jobs and taxes, but this benefit is often not seen in the places where the research originated. Other statements with less agreement were the lack of intersectorial coordination (public sector reluctant to engage with non-health actors) claimed by shapers (Annex D, Table D7 (R3 STMT 2.6)) and the poor innovation skills of health managers (Annex D, Table D7 (R3 STMT 2.8)).
- **Causes Needs (less agreement)**: Less agreement, especially among shapers and performers, on the excess of me-too drugs (Annex D, Table D7 (R3 STMT 2.12)) which implies less risk and investment in R&D, and targeting large markets (i.e. USA, EU). One expert specified that although the industry opts for low-risk investments in large markets, these are not me-too. Another informant mentioned that there is innovation

and not just me-too products, linked to guaranteed high returns. Pharmaceutical policies dominated by private sector interest (Annex D, Table D7 (R3 STMT 2.13) and lack of alignment between academia, government and the pharmaceutical sector led to a higher level of disagreement (Annex D, Table D7 (R3 STMT 2.14).

- **Causes Data (less agreement)**: Non-inclusive randomized-controlled trials (RCTs) designed for uncomplicated patients showed greater disagreement among performers and shaper panellists (Annex D, Table D7 (R3 STMT 2.19).
- **Causes risk and rewards – R&I gap (less agreement):** The private financing gap in start-ups and SMEs for early-stage projects (Annex D, Table D7 (R3 STMT 2.27)) generated a higher level of disagreement. In the open text response, one panellist mentioned that this pattern began to change 5 to 10 years ago, with the rise of venture capital funds investing in early-stage projects trading long-short stocks. Unintended consequences of incentives (i.e. rare diseases) generated larger disagreement (Annex D, Table D7 (R3 STMT 2.31)).
- **Causes risk and rewards – High prices (less agreement):** Less agreement on two price statements. The first, the price-value paradox (Annex D, Table D7 (R3 STMT 2.35) stating low expected profits of drugs that provide the greater health benefit and vice versa (i.e. generic antibiotics can still treat the majority of infections versus innovative cancer treatments with low impact on survival). The second, stating that, in the US R&I funding model, citizens accept to pay a high price for medical products as a way to finance public health (Annex D, Table D7 (R3 STMT 2.38), was opposed especially by big pharmaceutical performers and shapers.

Regarding previous rounds, in Delphi R1 survey, 15 causes statements did not show consensus, and in Delphi R2 survey, 3 statements did not showed consensus (Annex B, Tables B2 and B3; Annex C, Table C2). Consensus statements with less agreement (combined disagreement > 25%) were those that indicated no consensus, so they are included above.

- **Causes governance (no consensus)**: Low association between actors due to the industry's profit-driven R&I system that overlooks the global burden of disease (Annex B, Table B2 (R1 STMT 3).
- **Causes needs (no consensus):** The main problem is in LMICs to implement UHC and develop effective treatments for neglected diseases (Annex B, Table B2 (R1 STMT 4). How to reboot the agenda in HICs dominated by the industry lobby through patient groups, resulting in smaller pool of patients oon increasingly expensive drugs (i.e. cancer drugs), was another non-consensus statement (Annex B, Table B2 (R1 STMT 6).
- **Causes results (no consensus**): Industry does not share enough R&D data (Annex B, Table B2 (R1 STMT 8).
- **Causes risks and rewards – R&I gap (no consensus**): Cohort A disagreed with the existance of a significant public and private funding gap for start-ups and SMEs (Annex B, Table B3 (R1 STMT 12)). Lack of focus of public funding on the best R&I projects (Annex B, Table B3 (R1 STMT 13)). It also disagreed with the low tolerance for R&D failure and the pressure to make profit along the value chain. In other words, the public sector finances universities and industry that have the challenged of doing TT and being profitable (Annex B, Table B3 (R1 STMT 14)). Cohort B disagreed (high percentage of "other" answers) that public purchasers fail to use their market power to set the priority

agenda and provide incentives, including smart procurement (Annex B, Table B3 (R2 STMT 2)).

- **Causes risks and rewards – High prices (no consensus):** Cohort A differed on several statements. First, for public payers to reimburse some drugs not adding significant value to patients and healthcare systems (Annex B, Table B3 (R1 STMT 11)). Second, the patent system is unsuccessful because it drives R&D to maximize industry profit while neglecting global health needs (Annex B, Table B3 (R1 STMT 15)). Third, patients are often overlooked when applying the "fee-for-service" or "fee-for-drug", as the solution does not always address the root of the problem (Annex B, Table B3 (R1 STMT 16). Fourth, price negotiations at the country level (i.e. EU) are not transparent as producers and payersusually do not disclose the price (Annex B, Table B3 (R1 STMT 17)). Fifth, the procurement system in the EU could be improved, even though its strong regulation and evaluation (Annex B, Table B3 (R1 STMT 18)). Sixth, the VBP allows industry to set a high price for new medical products without any equity concern (Annex B, Table B3 (R1 STMT 23)). Seventh, the VBP model discouragements R&I investment in areas with reasonably good generic drugs, as new products will be priced relative to the generic base. For instance, cancer drugs rarely reach the generic stage, as each new drug is compared to its expensive predecessor, keeping prices high (Annex B, Table B3 (R1 STMT 24)). Eighth, products that seek to improve health and wellbeing should be framed as "global public goods" that allow a very narrow window of patent protection for industry to recoup R&D costs (Annex B, Table B3 (R1 STMT 25)). In contrast, cohort B disagreed that VBHC pricing should reflect a high ROI as a result of high-impact disruptive innovation that truly changes the patient journey, delivers healthcare savings, and increases productivity (Annex B, Table B3 (R2 STMT 8)). Moreover, there is controversy over the pharmaceutical industry's focus on solutions "beyond the pill" (Annex B, Table B3 (R2 STMT 9)).

These non-consensus R1 and R2 statements were analysed and revised for inclusion in the R3 interview discussion with cohort B and the final Delphi survey.

7.3 Co-created consensus Preferred Supplier R&I model for health equity (O3)

7.3.1 Case studies inspiring the new R&I model

As part of the research process, some key case studies were identified by the elite interviewees as success stories and lessons learned that addressed the main gaps of the current model of medical R&I for certain challenges. These reference experiences have contributed to the co-revision of the PSM. The benchmarking shows the three most mentioned case studies by the experts in the preliminary survey (R1), the interviews and the scoring surveys (R1 and R2), suplemented by the literature review.

- **Case study 1**. **Incentives for niche markets of drug development for rare diseases**, as a measure to bridge an R&I gap.
- **Case study 2. IPR flexibility for affordable drugs against HIV/AIDS pandemic**, as an example of the application of compulsory patent licensing for equitable access.

- **Case study 3. Accelerated response to the COVID-19 pandemic**, as a new paradigm of massive incentives to overcome the R&I and speed gaps, including production and procurement strategies for health equity.

There were some additional success stories that were not developed into full case studies as they were less frequently referenced by the key informants. Specifically, in terms of push incentives (R&I funding), experts mentioned the cooperation of the Venture Centre of Excellence (VCoE) between EIF and EIT Health, and the EIC Accelerator and EIF dilutive funds for early stage start-ups in Europe. In terms of regulatory pull incentives, they pointed out the paediatric legislation in the EU and the US (including Priority Review Vouchers). Regarding pricing pull incentives, experts cited the potential impact of the recently introduced de-link subscription or the Netflix pricing model for new antibiotics against multidrug resistant bacteria and Hepatitis C; Managed Access Funds for cancer and non-cancer drugs that have successfully completed phase II clinical trials; the Voluntary Scheme for Pricing and Access to Medicines in the UK; the access to CAR-T therapies in the US and Western Europe following regulatory approval; the US New Tech Add-On Payment Program (NTAP), as well as the Health Impact Fund (HIF). In terms of process innovation, one expert mentioned the GRAIL study on cancer diagnostic in the UK as a process innovation.

The three main case studies are described below.

→ CASE STUDY 1: Incentives for niche markets of drug development for rare diseases

Challenge: R&I gap for rare diseases as a small market without commercial incentives.
Measure: Orphan Drug legislation providing R&I regulatory and economic incentives for new rare disease products, including regulatory market exclusivity.
Governance: Country or region level.
Year:
1983 US Orphan Drug Act (ODA)
1993 Japan
1997 Australia
1999 EU
2000 Taiwan
2003 South Corea, etc.

There are more than 7,000 known rare diseases (RD) (FDA, 2022a), affecting 4% of the world population, estimated at 300 million people worldwide (Nguengang Wakap et al., 2020). Among them, between 25 and 30 million Americans and 26 million people living in the EU (EMA, 2023a). RD is a condition that affects a small percentage of the population. In the EU, a RD is defined as a life-threatening or chronically debilitating disease with low prevalence of less than 1 per 2,000 (Moliner and Waligora, 2017). In the US, about 1 in 1,500 people or less than 200,000 people in the country (US Government, 2002). Several factors can lead to a diagnosis of RD, however around 80% of those diagnosed are caused by genetic factors with a high percentage from early childhood (Endocrinology, 2019; IQVIA, 2023). A RD diagnosis carries a lifelong sentence as these diseases are rarely curable and more than 30% of children with a RD die before their fifth birthday (UK Government, 2022).

An orphan drug (OD) is a drug for a RD or condition. The specificities of RDs, with a broad range of conditions, limited number of patients and scarcity of relevant knowledge and expertise

(Moliner and Waligora, 2017), imply extremely limited individual markets, reducing the incentives for R&I investment (Govindaraj et al., 2018). In response, **orphan drug legislation** has been introduced in a number of countries to **stimulate R&I** in RD treatments by providing **incentives** to companies to pursue their development (Hall and Carlson, 2014). The important precedent was in the US with the **Orphan Drug Act (ODA)** enacted by the Food and Drug Administration (FDA) in 1983 (US Government, 1983), followed by Japan in 1993, Australia in 1997, the EU in 1999 (EU, 1999), Taiwan in 2000, and South Korea in 2003.

Drug developers must receive orphan drug designation from regulatory agencies (i.e. FDA in the US; European Medicines Agency, EMA, in the EU) in order to receive the incentives (Miller, Fermaglich and Maynard, 2021). Regulatory and economic incentives have been successful in attracting industry, which was previously unwilling to invest in RD therapeutic development due to low return on investment (Dawkins et al., 2018). **Regulatory market exclusivity** is considered the most important incentive, whereby orphan-designated drugs have a period of time (i.e. 7 years in the US and 10 years in the EU) of market exclusivity until a new drug receives regulatory approval (Hall and Carlson, 2014).

Additional incentives in both countries are protocol assistance and monitoring, and reduced or waived regulatory fees. In the US, RD sponsors also benefit from tax credit and specific grants for clinical trials (Hall and Carlson, 2014). In the EU, incorporating information derived from the pediatric investigation plan into the product information of any OD results in an additional 2 years of market exclusivity (Thakur, 2022).

The main strengths and weaknesses of the incentives offered by OD legislations are summarized below, complemented by quotes from the expert panel.

Scope

> **Pro:** RDs remain a challenge with 300 million people affected worldwide (Nguengang Wakap et al., 2020). This includes LMICs, such as India, with 70 million people affected by RDs (Thakur, 2022). Of the approximately 7,000 known RDs, **less than 10%** have an FDA-approved treatment available (FDA, 2022b). Current challenges in developing new treatments for RDs may deter the investment in this area without the incentives of OD regulations (Lore, 2023). These challenges are: 1) Shortage of medical knowledge given the complexity of RDs and uncertainty about underlying causes; 2) Affected populations are small and spread around the world; 3) Physicians may not be familiar with the diseases; and 4) There may be many subtypes of the same disease, each with its own complexities.
>
> **Cons**: Regulation and incentives are **limited** to RDs, with low prevalence worldwide. Moreover, according to Simoens et al. (2012), there is a no social preference for treating RDs. Although society places a higher value on the severity of the disease, this criterion is equally relevant for many common diseases. Besides, the criterion of equity in access to treatment, which underpins the OD legislation, places more value on improving health in RDs than in common diseases, which implies that population health is not maximized (Simoens et al., 2012).

Legal framework

Pro: Globally, the number of countries with **OD policies** and **regulations** has grown rapidly since 2013 (Chan et al.,2020). There is a total of 92 countries with legislation, regulations or policies that facilitate access to ODs (Chan et al.,2020). Europe has the highest OD policy establishment rate (42 out of 54, 78%), while Africa has the lowest (6 of 47, 13%). Between 2013 and 2019, OD policies increased gradually in LMICs, although countries with OD policies were wealthier.

Cons: Need to **extend** the OD policies to more countries, especially **LMICs**, such as India (Gahilod, Veeranna and Thakre, 2023; Thakur, 2022). Disparities in geographical distribution and income levels affect the establishment of OD policies (Chan et al., 2020). OD policies were established in only 19.4% of the 31 low-income countries or areas (Chan et al., 2020). Moreover, there is a policy gap in price regulation (i.e. managed entry agreements, MEAs) and incentives to encourage R&I (i.e. market exclusivity, clinical trial funding) and market availability (i.e. payer subsidies, reimbursement, fee waivers) (Chan et al., 2020). Therefore, policies should be developed or refined to optimize patient access to available and affordable ODs (Chan et al., 2020).

Impact

Pro: Before the introduction of ODA in the US in 1983, only 10 orphan drugs were approved in a decade, compared to 247 drugs for more than 200 RDs in the 25 years after the legislation (Dawkins et al., 2018). In Europe, after the adoption of the EC Regulation 141/2000 in 1999, 63 orphan drugs received marketing authorization by 2010, a decade after its implementation (Dawkins et al., 2018). In 2010, there were around 400 orphan medicinal products available for less than 300 RDs (Dawkins et al., 2018). **OD designation** has **accelerated** significantly in recent years, with half of the OD indication approvals since the 1983 occurring in the past seven years (IQVIA, 2020). In 2022, **54%** of **FDA new drug approvals** (20 out of 37) were approved to treat **RD**s (FDA, 2023a). The IQVIA (2020) report on RDs in the US highlights: 1) Total orphan indications approved since ODA approval reached 838 by the end of 2019 and were awarded to 564 different groups; 2) The significant increase in new OD indications has focused on **rare cancer** treatments, with 45% of approvals since 2015; and 3) Innovations for RD patients have become available in 2019, including **gene therapy** for children with spinal muscular atrophy and cutting-edge nucleotide therapy for acute hepatic porphyria). In terms of research, the creation of the **International Rare Disease Consortium** (IRDiRC) for international collaboration, in R&D of a standard set of clinical outcomes assessment (COAs) adapted to the specific disease indication, which is expected to be publicly available at minimal or no cost (Thakur, 2022). Different initiatives around genomics and other omics are also being developed in different countries, including India, with a large number of RDs attributed to genetic diversity (Thakur, 2022). Regarding market access, the specialised pathways have proven to accelerate time to market in some countries (Fontrier, 2022). Drug repurpose is considered in the field of ODs to be faster and less expensive than traditional new drug development for industry, despite the challenge of demonstrating the benefit-harm balance and regulatory issues (Sherman and Fetron, 2020) (Fetro and Sherman, 2020).

Cons: As mentioned, more than **90%** of **RDs** have no approved treatment, being an **unmet need**. Even when the treatment is available, patients continue to face challenges in being treated (IQVIA, 2020). Currently, the causative gene is still unknown for about half of all RDs and only 15% of rare genetic diseases have a single-gene diagnostic test readily available in the 40 countries of the Orphanet consortium (Dawkins et al., 2018; Orphanet, 2023). A patient survey reported that it took 7.6 years on average in the USA and 5.6 years in the UK to obtain a proper diagnosis, during which patients typically visited eight physicians (four primary care and four specialists) and received two to three wrong diagnoses (Endocrinology, 2019). Furthermore, in all RDs there is a disproportionate level of R&I and market launches concentrated towards high prevalence diseases, such as cancer, endocrine and metabolomic disorder, cardiovascular and infectious diseases (EURORDIS, 2021). Nearly all R&D activity and market launches of designated orphan products occur in the US followed by Europe (EU Rare2030, 2023). According to IQVIA (2020), most drugs with orphan indications treat only one RD, specifically 343 out of 564 drugs with orphan approval in the US since 2019. Billing spending on drugs with orphan indications reached $58 billion in the US in 2019. This is 11% of total bill spending in 2019 ($518 billion), growing at a rate of 14% over the past five years. Affordability of OD treatments is a challenge, with an average **annual cost of $32,000**, and more than a third of drugs with orphan indications costing more than $100,000 annually. However, high-cost therapies are usually prescribed for a small proportion of patients (only 23% patients received a drug with an annual cost of more than $100,000). Estimates of the cost of OD development are difficult to come by (Jayasundara et al., 2019). OD reimbursement does not always correspond with HTA recommendation (Kawalec, Sagan and Pilc, 2016). Finally, under current policies, between 675 and 807 orphan-designated products, and between 2,485 and 3,088 non-orphan products, can be expected to be launched between 2020 and 2030. Based on these estimates, we will be 200 to 400 **therapies short** of meeting the IRDiRC target of 1,000 new therapies for RDs by 2027 (Austin et al., 2018), so **policy changes** are needed in the short term (EU Rare2030, 2023).

Table 7.10 Case study 1: Incentives for Rare Diseases strengths and weaknesses

CS 1. Rare Diseases	Pro	Cons
Scope	○ RD affect 300 million people worldwide, including LMICs such as India. ○ Treatment available for <10% of RDs. ○ Challenges persist.	○ Restricted to RDs. ○ Low prevalence. ○ Without social preference.
Legal	○ Global growth in OD regulations and policies. ○ The EU leads the OD legislation and the rate of establishing policies.	○ Lack of OD legislation and policies, especially in LMIC. ○ Policy gap regarding price regulation and incentives for market availability and R&I. ○ Need to develop or refine OD polices to optimize patient access to available and affordable ODs.
Impact	○ Notable increase in the number of OD indications.	○ 90% of RD without treatment. ○ Insufficient treatment availability.

	○ Rise in treatments against rare cancer. ○ Innovations in gene therapy. ○ International research collaboration (i.e. IRDiRC). ○ Shorter time to market. ○ Drug repurpose as faster and cheaper opportunity.	○ Lack/delay in diagnostic. ○ Equity gap for less prevalent RDs. ○ R&I focused on the US and EU. ○ Exorbitant treatment cost. ○ Reimbursement not aligned with HTA. ○ Policy changes to achieve the IRDiRC goal.

Expert Quotes

"The pediatric voucher *[FDA priority review voucher for rare pediatric diseases]* ***is kind of acceleration of the regulatory and (…) you can sell your pediatric voucher to a company that, if you analyze that deal, you will see how that has been an incentive for the development of pediatric drugs, (…) because now they have something to sell. (…) So, for example, if you create an "early-stage voucher", meaning that, if you invest into something that is really, really early stage, you get some incentives"*** *– Performer expert (E16)*

"20 years ago, the orphans. At that time, the FDA was the first one to issue an Orphan legislation followed by EMA back in 1999. And then what, which was the reason? The reason was rare disease, low prevalence, few patients, no revenue for the company. Fine. Let's give incentives for the companies to develop products for orphan diseases. Fine. And the system was not a voucher. Was decreasing some agency fees during the development of the product, and second, increase the (…) market exclusivity (…). If they get an orphan product approved, they get 10 years market exclusivity. This has created a tremendous amount of products for treating orphan diseases. We come today, after… 20 years, I would say, I don't remember now exactly (…), but it's more than 100 medicines for more than 100 rare diseases approved over this time, which probably would not be developed and approved without this legislation and (…) you have not entered into the (…) trading issue of the vouchers" *– Shaper expert (E21)*

"The creation of these type of platforms, which is something that will be more or less oriented for certain areas, or certain diseases, could be extremely positive. The *[European]* ***Commission is also contributing with the creation of the European Platform of Rare Diseases Registration (…) which tries to put together (…) approximately 628, if my memory is good, registries of rare diseases that exist in the European Union, (…) private, public, from academia, from patients' organizations, from pharma companies, etc are together in this European platform of rare diseases registration in order to facilitate to the research community or to the companies interested in doing a clinical trial, not only (…) the epidemiological results about certain diseases, but also to permit the co-operation public-private and patients…researchers. All these things are absolutely necessary"*** *– Shaper expert (E26)*

***"In the case of rare diseases, it is the existence of the European Reference Networks** [ERNs] **at the moment 24 at the European level, created, by a decision of the** [European] **Commission. (…) Approximately 900 hospitals and clinical providers are participating in the ERNs for facilitating the sharing of the knowledge are also platforms in 24 defined areas that permit (…) to share, not only experiences, diagnoses, data, etc, but also (…) failures, particularly in the fields of diagnosis"** – Shaper expert (E26)*

→ **CASE STUDY 2: IPR flexibility for affordable drugs against HIV/AIDS pandemic**

Challenge: Prohibitive prices of new patented antiretroviral drugs for LMICs affected by HIV/AIDS pandemic in 2000.
Measure: The WTO Doha Declaration in November 2001 confirmed TRIPS intellectual property rights (IPR) flexibilities, such as allowing governments to grant compulsory licenses of patented medical products to low-cost generic producers, for instance, in the event of a national emergency.
Governance: World Trade Organisation (WTO) and 164-member states.
Year:
1994 TRIPs Agreement.
2001 Doha Declaration confirming TRIPS flexibilities.
2017 TRIPS Amendment including imports/exports.

In 2000, 36.1 million people worldwide were living with HIV/AIDS, around two-thirds in Africa (UNAIDS, 2000). A large majority, especially in LMICs, lacked access to effective anti-HIV/AIDS drugs, such as the **highly active antiretroviral therapy** (HAART) due to the unaffordable price (Hoen et al., 2018). On 14 November 2001**,** the 4th Ministerial Conference of the **World Trade Organisation** (WTO) in Qatar adopted the **Doha Declaration** (WTO, 2001) on the **TRIPS Agreement** (Trade-Related Aspects on Intellectual Property Rights) and Public Health (WTO, 1994). The TRIPS agreement, signed in 1994 by 153 countries, protected the IPR by establishing 20 years of patent protection as an industry incentive, as well as patent exceptions and compulsory licensing rights from governments.

The **Doha Declaration** reaffirmed the right of WTO member states to apply legal flexibilities still in place today, such as **compulsory patent licensing.** For instance, in the event of a national emergency, governments can extend a non-exclusive license of a patented medical innovation (medicines, vaccines and diagnostics) to generic producers without the patent holder's permission. This measure enabled the production of **generic** products before the original patent expired (Qunaj, Kaltenboeck and Bach, 2022). Another flexibility was that least-developed country members were granted an initial ten-year transition period to comply with TRIPS and were eligible for further extensions of transition periods with appropiate motivation (UNAIDS, 2013; UNDP, 2011; WTO, 2013). The patent holder still has rights to the patent, including the right to receive compensation for copies of the products made under the compulsory licence (WTO, 2023). The price of the license is defined by the authorities of the country concerned (WTO, 2023).

In response to a proposal from African WTO members, on 23 January 2017, the TRIPS agreement was amended to resolve the problem of member states with insufficient or no pharmaceutical manufacturing capacity to implement compulsory licensing. The **amendment** to the **TRIPS**

agreement allowed **exports** to these less developed countries (Abbas and Riaz, 2017; Solovy, 2021). The new article 31bis replaced a temporary waiver giving effect to paragraph 6 (WTO, 2023) of the Doha Declaration (Abbas and Riaz, 2017). The TRIP flexibilities were intended to **accelerate** the production or import of generic antiretrovirals and considerably **reduce** the **price** per treatment in many LMICs, which has ocurred in several cases (Fanjul and Villanueva, 2016; Hoen et al., 2018; Vawda, 2022). For instance, flexibilities in the TRIPS allowed Brazilian governments to issue compulsory licenses for the production of generic HAART in 2001 (Fanjul and Villanueva, 2016).

Compulsory licensing regulation has also promoted **voluntary licensing** by industry in reaction to the mandatory threat. In voluntary licensing, the pharmaceutical corporation holding the patent licenses the IPR to generic manufacturers to produce affordable versions for a broader population. For example, in South Africa in 2002, the South African Competition Commission singled out GlaxoSmithKline and Boehringer Ingelheim for abusing their dominant position by charging excessive prices for their antiretroviral drugs (Cullinan, 2022). This was in application of competition law (UNCTAD, 2002), as reported by activist Hazel Tau, member of the Treatment Action Campaign (Cullinan, 2022). The two pharmaceutical companies finally agreed to grant voluntary licenses to generic HAART drug producers in exchange for a 5% royalty to avoid compulsory licenses (Fanjul and Villanueva, 2016). Voluntary licenses can be channeled through the **Medicines Patent Pool (MPP)**, an organization created by UNITAID in 2010, which first licenses the product to the innovator and then sub-licenses to generic producers (MPP, 2023a). In 2011, Gilead was the first company to out-license patented antiretroviral drugs to the MPP for sublicensing to generic drug manufacturers in developing countries (Gilead Sciences, 2016).

Between 2002 and 2014, the number of people receiving antiretroviral therapy increased from 300,000 to 13.5 million (Gilead Sciences, 2016; UNAIDS, 2015). The HIV measure was also a mirror of other diseases such as cancer (Friedman, Gu and Klausner, 2019) and hepatitis C (Pedrana et al., 2020). HIV/AIDS remains a major global public threat wih 40.4 million people affected (WHO, 2023c). There is no cure for HIV infection, however with access to effective HIV prevention, diagnosis and treatment methods, the infection has become a chronic health condition, with longer and healthier lives (WHO, 2023c).

The main strengths and weaknesses of the TRIPS agreement's flexibility on compulsory licensing are summarized below:

Scope

Pro: The Doha Declaration recognised the **gravity** of the public health problems that afflict many LMICs, especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics, but not limited to certain diseases (WHO, 2002). The Declaration stated that governments can announce public health crises in the event of "**national emergency** or other circumstances of extreme urgency" (Hoen, 2016, cited in Pedrana et al., 2020). The national emergency can be a short- or long-term situation (WHO, 2002), although the scope and duration of the licence must be limited to the purpose for which it was granted. If a medical product is not patented in a least developed country, the government does not need to issue the compulsory license. Only the supplying country, if the medicine is patented in that country, has to issue the compulsory license (WTO, 2023).

Cons: Focus on national emergencies in LMICs versus more systemic change.

Legal framework

Pro: The Doha Declaration was a strong **political statement** involving a ministerial decision with legal effects for WTO members and bodies to facilitate access to medicines for LMICs without becoming involved in legal battles (WHO, 2002). The TRIPS Agreement regulated **compulsory licenses** mainly to supply the domestic market. The amendment of the TRIPS agreement is a formal decision adopted by the WTO in line with the Doha Declaration that allows the granting of compulsory licenses for exports to countries with insufficient pharmaceutical industrial capacity (Solovy, 2021). TRIPS regulation acknowledges the role of IPRs for the development of new medicines and their effects on prices, so that health-related patents may be treated differently than other patents (WHO, 2002). According to Hoen et al. (2018), with the increasing trend of patenting pharmaceutical products, the use of TRIPS flexibilities is becoming more relevant and urgent to ensure access to essential medicines (Wirzt et al., 2017). Parallel imports (products marketed in one country that are imported to another country without the approval of the patent owner) are regulated by the legal principle of "exhaustion" (once the product in placed on a market the patents rights are exhaust for the patent holder) managed by the corresponding national authorities (WTO, 2006). **Competition laws** at national or regional level (i.e. EU) also favour compulsory and voluntary licenses (OECD, 2019).

Cons: The Doha Declaration is a **non-binding** statement of intent (WHO 2002). **Lack** of **national legislation** allowing **compulsory licensing** (Wong, Cole and Kohler, 2022; Vawda, 2022). Compulsory licensing procedures, specially in LMICs, should be made user-friendly by promoting expedited administrative procedures rather than more time-consuming and costly judicial procedures (Vawda, 2022).

Impact

Pro: The use of TRIPs flexibilities has been more **frequent** than commonly assumed, with 176 cases of TRIP flexibilities between 2001 and 2016 by 89 countries (56.8% of compulsory licenses or non-commercial public use of licenses and 22.7% of pharmaceutical transition measures for least-developed countries, 20.5% other issues) (Hoen et al., 2018). Of the 176 instances, 152 (86,4%) were implemented. Therefore, the practical and legal path offered by TRIPS flexibilities to access lower-costs generic equivalents is increasingly important (Hoen et al., 2018). According to Vawda (2022), the effect of licenses issued between 2006 and 2007 on **price reduction** has been significant. For example, the price of the antiretroviral efavirenz was reduced by more than 7 times, that of lopinavir/ritonavir by 3 times, and that of the anti-cancer drugs docetaxel and letrazole by 24 and 70 times respectively (Vawda, 2022). Progressive application of TRIPS flexibility measures to others diseases such as hepatitis C and cancer (Pedrana et al., 2020) as well as voluntary licenses by industry (Gilead Sciences, 2016). For instance, despite the significant reduction in the cost of hepatitis C treatment in recent years (Pedrana et al., 2020; Global Fund, 2020), since 2014 Gilead and Bristol-Myers Squibb have issued non-exclusive voluntary licenses for key hepatitis C drugs to 112 LMICs (where 65% of the people live with hepatitis C) (Pedrana et al., 2020). Moreover, generic manufacturers holding voluntary licenses could also sell to countries outside the list of 112 if no granted patent is infringed. Voluntary licensing may be a better way than compulsory licensing to

increase access afforfable drugs in developing countries (Solovy, 2021). On the other hand, industrialized countries decided not to use compulsory licenses for imports (WTO, 2023). As a result, compulsory licenses are rarely used in HIC outside the US as a way to get discounts on pharmaceuticals, but are more commonly used to improve access to medicines in LMICs (Qunaj et al., 2022).

Cons: The concentration of compulsory licenses for HIV/AIDS and related diseases accounted for 77,8% of the TRIPS flexibility cases between 2001-2016, according to Hoen et al. (2018). Controversy over pricing, with some authors pointing out that compulsory licensing has resulted in higher prices relative to the median procurement price (Beall et al., 2015, cited in Solovy, 2021). Beall and Kuhn (2012) state that, despite the significant occurrence of compulsory licenses, their activity has decreased since 2006. Wong et al. (2022) point out the **lack** of **domestic manufacturing** capacity, added to an **unviable import process** according to article 31bis. Furthermore, LMICs are under considerable political pressure from other WTO members to refrain from issuing compulsory licenses (Wong et al., 2022), requiring a more detailed assessment of health governance worldwide (Beall and Kuhn, 2012). Compulsory licensing can reduce incentives for innovation in new technologies that could improve public health, so WTO members should carefully evaluate the costs and benefits (short and long term) before exercising that option (Solovy, 2021). Finally, there are abusive practices in voluntary licenses as private contracts that should be regulated, such as lack of transparency or lack of regulation (MSF, 2020). Moreover, middle-income countries are often not included in voluntary licensing agreements (MSF, 2020).

Table 7.11 Case study 2: IPR flexibility for HIV/AIDS strengths and weaknesses

CS 2. IPR flexibility	**Pro**	**Cons**
Scope	○ Access to patented innovations for national emergencies in low-resource settings. ○ Governments leadership in national emergencies. ○ No time limitation (short-term and long-lasting emergencies).	○ Primmariliy targeted at public health crises in LMICs (versus a more systemic measure).
Legal	○ Doha Declaration strong political commitment with legal effect. ○ IPR TRIPS agreement on compulsory licenses for local markets. ○ Amendment of the IPR TRIPS agreement on compulsory licenses for exports to countries without pharmaceutical production capacity. ○ Differentiation of health-related patents. ○ Relevant use of compulsory licensing in a context of	○ The Doha Declaration is a non-binding statement of intent. ○ Lack of national TRIPS-aligned compulsory licensing legislation in some LMICs and HICs (to export). ○ Expensive and time-consuming court proceedings.

	widespread pharmaceutical patents. ○ Parallel imports regulated through an international exhaustion regime managed by national authorities. ○ Competition laws favour licensing.	
Impact	○ Significant number of TRIPS flexibility instances. ○ Price reduction for LMICs that apply compulsory licenses. ○ Extension to other diseases (i.e. hepatitis C, cancer). ○ Increasing voluntary licenses by industry. ○ Fair use of compulsory licensing by HICs.	○ Concentration of TRIPS flexibilities on HIV/AIDS. ○ Controversy over the effective price reduction for LMIC by applying compulsory licensing. ○ Downward trend in compulsory licensing. ○ Lack of manufacturing capacity in some LMICs and ineffective imports when applying compulsory licenses. ○ Pressure on LMICs to refrain from issuing compulsory licenses. ○ Innovation incentives can be reduced by compulsory licensing. ○ Voluntary license lack price transparency and exclude middle-income countries.

Expert Quotes

"HIV/AIDS dual market (HICs and LMICs)" *– Shaper expert (E17)*

"HIV, though heavily driven by activism and a disruption to the existing R&D model" *– User expert (E06)*

"How you would come to an agreement about licensing to others? Say the compulsory license route was being considered in the past, particularly by South Africa for HIV drugs some years ago, and that started a trade war in the US. What it did do was highlight the issue and created an environment by the American pharmaceutical companies entered into a voluntary arrangement …I think you need that threat of doing something compulsory to get the voluntary arrangement in place" *– Payer expert (E25)*

→ CASE STUDY 3: Accelerated COVID-19 pandemic response

Challenge: Rapid development, production and global distribution of safe, effective and affordable vaccines, diagnostics, therapies and personal protective equipment to address the COVID-19 pandemic.
Measure: Massive global public-private collaboration, including financing and market access measures to boost COVID-19 R&I with initiatives such as the ACT-Accelerator and the Operation Ward Speed.

Governance: Governments (especially the US and Germany), medical industry, multilateral organisations (i.e. WHO, UNICEF), public-private partnerships (i.e. GAVI, CEPI, Global Fund, FIND), philanthropists (i.e. BMGF, Wellcome Trust).
Year:
2007 International Health Regulation (IHR).
2019 December Cluster of pneumonia cases in Wuhan (China).
2020 January 11 Publication of SARS-CoV-2 virus' genome.
2020 January 30 Declaration of COVID-19 as PHEIC by WHO in application of IHR.
2020 March 11 Declaration of COVID-19 as a Pandemic by the WHO.
2020 April 24 Launch of the ACT-Accelerator.
2020 May 15 Launch of Operation Ward Speed.
2020 December 2 First authorised COVID-19 vaccine.
2022 June 17 TRIPS waiver for patented COVID-19 vaccines approved by the WTO.
2023 November 13.6 billion COVID-19 vaccine doses administered; 1.96 billion delivered by COVAX, a pillar of the ACT-Accelerator for global access to COVID-19 vaccines.

The set of vaccines against **COVID-19 vaccines** represents the most remarkable success in the recent response to the pandemic and probably the most significant medical advance in recent decades in terms of impact on public health and the global economy. Strong collaboration and funding between governments and industry, especially in the US (Baker and Koons, 2020; WHO, 2023d), along with unprecedented real-time data sharing between the international scientific community and public-private partnerships (Druedahl, Minssen and Price, 2021), have greatly speed up the availability of safe and highly effective vaccines between 12 and 18 months after the declaration of a pandemic, instead of the average 10 years. Globally, around **13.6 billion doses** of COVID-19 vaccines have been administered, of which **5.6 billion people** have been **vaccinated** with at least one dose and 5.2 billion people vaccinated with a complete primary series (WHO, 2023e). However, while some countries have fully vaccinated large portions of their populations, many others have only just begun or are still waiting for their first doses to arrive (Watson et al., 2022). Inadequate access to vaccines in LMICs has limited impact in these settings, reinforcing the need for global vaccine coverage and equity (Watson et al., 2022).

On December 31st 2019, China reported a cluster of pneumonia cases in Wuhan (Hubei Province), identifying a new coronavirus (WHO, 2020b). On January 11th 2020, China publicly shared the genetic sequence of COVID-19 (Rahimi, Mirzazadeh and Tavakolpour, 2021). The 30 January 2020, the Director-General of WHO declared the nooutbreak of the novel coronavirus (2019-nCoV) a **Public Health Emergency of International Concern** (PHEIC) (WHO, 2020c) in application of the **International Health Regulations** (IHR). This was the sixth time that the WHO declared a PHEIC since the IHR came into force in 2005. Furthermore, on March 11th 2020, the WHO characterized the COVID-19 outbreak as a **pandemic** (WHO, 2020c). The reaction to the PHEIC was the deployment of massive public-private funding and international partnerships, such as the creation of the global Access to COVID-19 Tools Accelerator (ACT-Accelerator) framework and Operation Ward Speed in the US.

The main strengths and weaknesses of the COVID-19 pandemic response are summarized as follows:

Scope

Pro:

- **COVID-19 Pandemic due to high transmission of the virus**. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has caused an unprecedented pandemic of coronavirus disease 2019 (COVID-19) in a very short time due to its high transmissibility (Liu and Lou, 2022). Safe and effective vaccines against COVID-19 were urgently needed to help build herd immunity and end the pandemic (Fontanet and Cauchemez, 2020). The updated balance (30 November 2023) is more than 772 million confirmed cases of COVID-19, including around 7 million deaths, reported to WHO (WHO, 2023e). Following a predominantly global downward trend in COVID-19 cases and deaths from April to December 2022, both began to rise in late 2022 due a surge in cases in China, which peaked in December 2022. Cases and deaths have been falling rapidly since January 2023 (WHO, 2023f).
- **Risks of new variants**. The Omicron SARS-CoV-2 variant (first reported to the WHO in November 2021 (CDC, 2021)) has been the only variant detected between October 2022 and March 2023. It is important to highlight that COVID-19 vaccines, tests and existing treatments remain largely effective in reducing severe morbidity and death (WHO, 2023e). Nonetheless, the fight against SARS-CoV-2 is not over, as the virus continues to evolve rapidly (Rubin et al., 2022), for instance with the new EG.5 strain (known as Eris) (Katella, 2023), and still causes substantial number of infections, hospitalizations, and deaths. The most affected populations are older people and individuals with pre-existing health conditions and underlying comorbidities. This emphasises the importance of ensuring that all high-risk and high-priority populations are fully vaccinated and boosted, and that COVID-19 diagnostics and antivirals are available for those most at risk. The challenge is to ensure long-term support for the management of COVID-19 as part of routine public health programmes (WHO, 2023f).
- **Preparation for new "Disease X" pandemics**. ACT-Accelerator partner agencies are also preparing for the next pandemic, with initiatives such as the "**100 Days Mission**", which explores how to respond to the next "Disease X" by compressing the development of safe, effective and accessible vaccines to within 100 days of the disclosure of the genetic sequence of a pandemic pathogen (WHO, 2023f). WHO is working on a framework to strengthen pandemic prevention, preparedness and response (refer to Pandemic Treaty in the legal section below).

Cons:

- **Efforts focused on pandemics** caused by emerging or re-emerging infectious diseases, leaving other public health challenges unattended and underfunded in terms of R&I and healthcare (Bill and Melinda Gates Foundation, 2020).

Legal

Pro:

- **Legally binding International Health Regulations (IHR).** The COVID-19 pandemic was declared a **Public Health Emergency of International Concern** (PHEIC) by the WHO Director General on March 11th 2020 and was declared over on May 5th 2023 (WHO,

2023g). That was the result of the implementation of the **International Health Regulations** (IHR) (2005), an international law in response to the increase in international travel and trade and the emergence and resurgence of international disease threats (WHO, 2008). This binding instrument of international law was introduced 54 years ago, and the latest revision came into force on June 15th 2007, following the outbreak of SARS-CoV-2, and has the commitment of 196 countries. The IHR agreement requires countries to improve their core capacities, including legislation, coordination and surveillance, to detect and respond to national health emergencies (Hannon et al., 2022; WHO, 2008; WHO, 2015). The IHR also defines the procedure for reporting disease outbreaks to WHO and disease control measures.

- **ACT-Accelerator global partnership framework.** The **Access to COVID-19 Tools Accelerator** (**ACT-Accelerator**) was launched in April 2020 as a **global** (non-binding) **partnership** to accelerate the development, production and equitable access to COVID-19 tests, treatments and vaccines (WHO, 2021c). ACT-Accelerator seeks **equity** and **scale** in the delivery of essential tools for COVID-19 emerging virus risks. It has four pillars, COVAX is the COVID-19 vaccine pillar, and the other pillars are diagnostics, therapeutics and health systems and the response connector. The ACT-Accelerator (WHO, 2023h) brings together governments, academia, businesses, civil society, philanthropists and global health organisations (the Bill and Melinda Gates Foundation, CEPI, FIND, Gavi, The Global Fund, Unitaid, Wellcome Trust, WHO, and the World Bank) under the motto ***"no one is safe, until everyone is safe",*** cited by the director general of WHO. Its contributors have committed **$24.2 billion** (WHO, 2023d) since the start of the pandemic (budget from April 2020 to March 2023 budget, as reported by WHO on June 1st 2023), with the US (31.3%), Germany (16.3%), Japan (7.5%), Canada (7.4%), UK (5.0%) and the EC (5.0%) as main donors.
- The **Operation Ward Speed (OWS) partnership in the US** (US Government, 2020a) was a public-private partnership launched in May 2020 by the Trump administration. OWS' goal was to produce and deliver 300 million doses (prioritising the American people) of safe and effective SARS-CoV-2 vaccine in less than one year. That is, initial doses available by January 2021 and deployed by mid-2021. This was part of a broader strategy to accelerate the development, manufacturing, and distribution of COVID-19 vaccines, therapeutics, and diagnostics (Slaoui and Hepburn, 2020; US Government, 2020a). The initiative was an interagency program that mainly comprised the Department of Health and Human Services (HHS) - including the Centers for Disease Control and Prevention (CDC), the FDA, the National Institutes of Health (NIH) and the Biomedical Advanced Research and Development Agency (BARDA) -, the Department of Defense (DOD), and the industry (US Government, 2020a). The companies executed the development process and manufacturing and the government leveraged its capacity to facilitate technical, logistic and financial enablers (Slaoui and Hepburn, 2020). The OWS, initially focused on 8 vaccine candidates, judged to be the most promising based on four criteria: strong preclinical data or early-stage clinical data, potential to enter in Phase III efficacy trials in July-November 2020, be based on different vaccine platform technologies that enable rapid and effective **manufacturing** and demonstrate industrial **scalability** (Slaoui and Hepburn, 2020). In October 2020, OWS received $18 billion from the US government for the industry (Baker and Koons, 2020). In February 2021, OWS was transferred to the White House COVID-19 Response Team (Zraick, 2021) and was active until February 2021, with a commitment to donate any surplus vacciness to less developed regions, such as Africa. The US government

decided not to involve OWS in partnerships with the Chinese vaccine, the WHO Solidarity trial, CEPI or the EC, which coordinated and funded international vaccine development (Cohen, 2020).

- **Compressed R&I timeline.** The main difference from a non-pandemic environment was the compacted timelines. OWS and vaccine companies adopted different strategies to accelerate vaccine development and mitigate risk (US Government, 2021). First, OWS selected vaccine candidates using a variety of mechanisms to stimulate immune response, applying four **vaccine platform technologies**: messenger RNA (mRNA), replication-defective live-vector, and recombinant-subunit-adjuvanted protein and the attenuated replication live-vector platforms (US Government, 2021). Second, **adaptations** to the traditional **R&I process** have implied relying on **data** from other companies using the same platform, as well as **overlapping clinical trial phases** with each other and with animal studies to accelerate development (US Government, 2021). Vaccine firms also initiated large-scale manufacturing during clinical trials (US Government, 2021).
- **Market access: Regulatory Fast Track.** The application of **conditional marketing approval** by regulatory agencies contributes to **fast track** the use of vaccines and medicines in the COVID-19 emergency situation declared by governments (Cubanski et al., 2023b) as soon as available sufficient data to proof that the benefits overweigh the risks (EMA, 2023b). For instance, the **emergency use authorisation** (EUA) by the FDA in the US (FDA, 2023b) (i.e. for Pfizer-BioNTech, Moderna and Novavax vaccines) and the EMA **emerging health threats plan** in the EU supported by the EMA's pandemic Task Force (EMA, 2020).
- **Market access: Advanced Market Agreements** performed by both HICs (i.e. USA, EU) (EC, 2023d), and ACT-A COVAX pillar to secure COVID-19 vaccine doses for 92 LMICs (GAVI, 2023; Towse et al., 2021).
- **Market access: TRIPS IPR Waiver for COVID-19 vaccines.** On June 17th, the temporary waiver of TRIPS IPR on patented COVID-19 vaccines was approved by WTO Ministerial Decision (WTO, 2022a). It allowed WTO members to go beyond the requirements of articles 31 and 31bis of the TRIPS Agreement on compulsory licenses for vaccines (to manufacture and export/import COVID-19 vaccines without authorisation from the patent holder) and, if subsequently approved, also for other COVID-19 health products (Yu, 2023). The decision was far away from the waiver proposal presented by India and South Africa in October 2020. These two countries proposed to partially suspend the TRIPS agreement, which targets copyrights, patents, industrial designs and undisclosed information of health products (not only vaccines) (Yu, 2023), with partial support from the US (only in vaccines) (Kohler, Wong and Tailor, 2022). The EU initially opposed the IP waiver and recommended clarifying the use of compulsory licenses to facilitate implementation, although data protection and market exclusivity for medical products in the EU's regulations (which prohibits the registration of generic equivalents for a defined period) could hinder this effort (MSF, 2021). Moreover, compulsory licenses can only be granted on a country-by-country and product-by-product basis, and the process of exportating the product has proven prohibitively complex, undermining expedite implementation (MSF, 2021). Finally, in June 2021 the EU changed the position (European Parliament, 2021) and India, South Africa, the EU and the US (together with the WTO Secretariat) initiated a high-level quadrilateral consultation (Quad proposal (WTO, 2022b)) providing the basis for negotiating the Ministerial Decision on the waiver focused on COVID-19 vaccines (Yu, 2023).

- **Market access: Voluntary licensing of COVID-19 therapeutics** has ocurred between industry and initiatives such as the MPP. In October and November 2021, MPP signed licensing agreements with Merck and Pfizer for their antiretroviral COVID-19 pills (MPP, 2022). These were the first voluntary licensing agreements for COVID-19 and have covered the retail sale of the treatments in 105 LMICs. In March 2022, the MPP entered into sublicensing agreements with 36 generic companies for the production of Pfizer's oral treatment for COVID-19 (MPP, 2021). Pfizer agreed not to receive royalties on sales in low-income countries and to further waive royalties on sales in all countries covered by the agreement while COVID-19 remains classified as a PHEIC by the WHO.
- **Market access: Compulsory license and government use of COVID-19 therapeutics.** During the pandemic some governments (such as Israel, Hungary, Russia, Ecuador) implemented mandatory licensing and government use of COVID-19 therapeutics (South Centre, 2021).
- **Increase in health data collected** during the COVID-19 pandemic from primary data collection in electronic health records (EHR) and administrative claims to AI-based analysis on the web that influencces research and routine health care (Dron et al., 2022; Gupta et al., 2021; Zhou et al., 2020).

Cons:

- **Regulation: IDH limitations and the need for a Global Pandemic Treaty.** When the COVID-19 hit, the limitations of the IHR reporting system became clear (Hannon et al., 2022). IHR is governed by member states ministries of health, which normally do not have the power to commit resources to improve IHR capacities (Hannon et al., 2022). The IHR mainly addresses capacities at national level, which does not affect global coordination (Hannon et al., 2022). On the other hand, the response to the COVID-19 pandemic showed wide inequities in terms of morbidity, mortality, and access to medicines (Phelan, 2023). It has clearly underlined the shortcomings of our current R&I system and the **lack** of a **global health governance** to ensure timely and equitable access to medicines and health technologies for all (Perehudoff et al., 2022). A new **global social contract** is needed to align individual state interests and incentives for the pharmaceutical industry with the global goal of public health and health security (Perehudoff et al., 2022). As a reaction, in March 2021 a group of world leaders announced an initiative that was taken to the WHO (Butchard and Balogun, 2022). The new accord for Pandemic Prevention, Preparedness and Response, referred as **WHO Pandemic Preparedness Treaty,** is a work in progress that can create the conditions for an effective social contract aimed at ensuring **equity** in access to the tools needed to prevent pandemics, as well as access to health care for all people (Perehudoff et al., 2022; WHO, 2023i). The World Health Assembly (WHA) established an Intergovernmental Negotiation Body (INB), representing all regions of the world, to draft and negotiate this new WHO regulation (WHO, 2023i; WHO, WIPO and WTO, 2023). The INB is expected to submit a draft pandemic agreement for consideration by the WHA 2024 (WHO, 2023i). The INB agreed that the instrument should be legally binding, with some non-binding elements (WHO, WIPO and WTO, 2023). Some voices propose that governance of the pandemic must be elevated from the WHO to the **UN General Assembly**, in which countries are represented by their **heads of state**, placing public health in a broader context of international law, security, trade, and human rights (Hannon et al., 2022; Saxena et al., 2023).
- **Governance: ACT-A partnership not legally binding.** ACT-Accelerator is a collaborative framework, not legally binding (WHO, 2023j). COVAX hoped that high-

and middle-income countries would buy into it, while poorer countries would receive vaccines almost free of charge for 20% of their population, which did not materialise (Daems and Maes, 2022; Storeng, de Bengy Puyvallée and Stein, 2021). Currently, COVAX focuses only on the poorerest countries (Daems and Maes, 2022).

- **Market access: Priority access for HICs.** The US Trump administration expedited an executive order on September 8th 2021 requiring priority access to US-developed COVID-19 vaccines (The White House, 2021).
- **Market access: Inconsistent support for "health as a human right" and "equal access to scientific progress" according to the ICESCR**. During the 20-month negotiation of the TRIPS waiver of the IPR at the WHO, most stakeholders (mainly in HIC) declined to contextualize the waiver within the human right to health and to the equal enjoyment of the benefits of scientific progress, according to article 12 and article 15 of the International Covenant on Economic, Social and Cultural Rights of 1966 (ICESCR). Their positions on IPR seemed virtually unchanged from those of the HIV/AIDS crisis of the early 2000s before the Doha Declaration. This underscores the unreliability of the international trade system as a way to tackle public health challenges and improve access to life-saving products (Kohler et al., 2022). Supporters (some WTO members, specially form LMICs; civil society; experts) considered the TRIP waiver as a necessary first step in removing access barriers related to IPR, while opponents (initially the EU, UK, Switzerland and to some extent the US) claimed that IPRs were not a barrier to access but trade restrictions, distribution bottlenecks and raw material shortages (Bourla, 2021; Kohler et al., 2022; Yu, 2023). Other arguments were that the waiver would threaten innovation to develop technologies for new variants of COVID-19 and undermine existing voluntary licensing partnerships (Kohler et al., 2022).
- **Market access: Lack of national compulsory licensing legislation** aligned with the TRIPS agreement that facilitates the implementation of the IPR flexibility measures during health emergencies in LMICs, but also in HICs such as some EU member states (Davies, 2023; MSF, 2021; Perehudoff, Hoen and Boulet, 2021; Vawda, 2022; Wong, Cole and Kohler, 2022).
- **Market access: Lack of industry voluntary licensing and technology transfer (TT) for global solidarity** (Geiger and Gross, 2023). The global community is urgently calling for additional voluntary licensing by industry, such as through the COVID-19 Technology Access Pool (C-TAP) with MPP and UNITAID as implementing partners, among others (WHO, WIPO and WTO, 2023). Moreover, key technological innovations, such as mRNA, were invented in academic labs and biotech SMEs and then licensed to larger corporations to complete clinical trials and manufacturing. Despite this success, patents, trade secrets and know-how owned by large companies may impede future R&I of mRNA technology due to legal barriers (Gaviria and Kilic, 2021). Collaborations for vaccine development against COVID-19 have focused primarily on **material transfer** rather than active TT exchange (Druedahl et al., 2021). Additionally, it seems reasonable that scientists and institutions that contributed to generate the initial IPR, benefit as **co-inventors** and **co-owners** of **patents,** and receive **royalties** from commercialisation earnings (which can be reinvested in future developments). This was shown in the dispute between Moderna and NIH in the US over the IPR of the COVID-19 vaccine (Moch, Arabi and Pre, 2021; Mueller, 2023). The US government is increasingly assertive with IPRs, especially if doing so can influence the price of prescription drugs (Moch, Arabi and Pre, 2021). Even IPR flexibility measures, such as compulsory licenses or waivers for patented technologies, must be complemented by

access to TT, such as manufacturing processes and techniques owned by pharmaceutical companies in the form of **compulsory trade secrets licensing** aligned with the TRIPS agreement (Gurgula, 2021a; Gurgula, 2021b). The **mRNA TT Programme**, launched by WHO and MPP in June 2021, aims to establish locally owned mRNA capacity in LMICs (MPP, 2023b). The core of the programme is the Afrigen TT Hub, opened in April 2023 in South Africa, with the aim of providing training and technology elsewhere for the production and marketing of health products (WHO, 2023k).

- **Data: Lack of regulation of R&I data exchange.** The COVID-19 pandemic has demonstrated the importance of ensuring timely access to personal EHR for health threat preparedness and response, research, innovation, regulation and policy making (European Parliament, 2022). Healthcare systems are using new processes (i.e. telehealth screening, remote testing, etc) that make current **data protection regulations** (i.e. HIPAA in the US and GDPR in the EU) on data flows for clinical care and research **not** fully **appropriate** for the effective exchange of health information (Lenert and McSwain, 2020). The new context requires a **pooled** and **publicly available datanset** (Cosgriff, Ebner and Celi, 2020; Dron et al., 2022). In response, the EC presented a regulation proposal for the **European Health Data Space** (EHDS) in May 2022 to be approved by the European Parliament and the Council (EC, 2023e). The EU EHDS will promote the secure sharing of patient data, citizen control over their data, support research into treatments, medicines and medical devices and encourage access to and use of health data for research.
- **Data: Lack of transparency in R&I funding reports.** For instance, the Oxford-AstraZeneca COVID-19 vaccine, in which public and philanthropy funding accounted for 97-99% of identifiable funding related to this vaccine at the University of Oxford as of fall 2020 (Cross et al., 2021).
- **Data: Increased risk of fraudulent medical studies with the preprint rise** during the COVID-19 pandemic influencing public health policies (Watson, 2022).

Impact

Pro:

- **Faster vaccine development**. In less than a year after the pandemic was declared, some pharmaceutical companies successfully developed several types of vaccines against COVID-19 (Liu and Lou, 2022). Under **OWS**, the first COVID-19 vaccine, the Pfizer-BioNTech vaccine with 95% efficacy, was authorised for emergency use in the UK on December 2nd 2020 (BioNTech, 2020; US Government, 2020b). It was the first mRNA vaccine ever authorised. A few days later, the vaccine received emergency approval in the US, Canada, Switzerland and the EU. Two years later, as of December 2nd 2022, according to the **COVID-19 vaccine tracker** (2022)**,** there were 242 vaccine candidates, including **50 vaccines approved** by at least one country, among which 11 had WHO emergency use authorisation, and 201 countries had approved vaccines. According to the G20 report (WHO, 2022), by April 2022 the world had a complete COVID-19 toolkit of vaccines, tests, treatments and personal protective equipment to mitigate risk. COVID-19 vaccines acted as the first line of defence and remain highly effective in reducing severe illness and death, even as the virus has continued to **mutate**.

- **Increased coverage of COVID-19 vaccines**. Globally, around **13.5 billion doses** of COVID-19 vaccines have been administered, with **70%** of the world's population receiveing **primary vaccination** (WHO, 2023e). Between them, the **ACT-Accelerator** has helped deliver **1.96 billion** doses of the COVID-19 vaccine to date through **COVAX** (Act-Accelerator, 2023). Moreover, ACT-Accelerator has delivered 176 million tests to 184 countries, allocated 313,558 therapeutics to countries, and delivered 736 million personal protective equipment (Act-Accelerator, 2023). Overall, according to Watson et al. (2022), the vaccinations **prevented 14.4 million deaths** from COVID-19 in 185 countries and territories between December 8th 2020 and December 8th 2021. The estimate rose to 19.8 million deaths when using excess deaths (number of "all-cause" deaths measured during a crisis, above what could be observed under normal conditions). It represents a 63% reduction in total deaths (19.8 million from 31.4 million) during the first year of COVID-19 vaccination. Among **COVAX Advance Market Commitment** countries, the authors estimated that **41%** of **excess mortality** was **averted.** Nonetheless, in LMICs, an additional 45% of deaths could have been avoided if the 20% vaccination coverage target set by COVAX had been achieved by each country. An additional 111% of deaths could have been averted if each country has reached the 40% target set by the WHO by the end of 2021.
- **Improved delivery of COVID-19 vaccines in countries with less coverage.** While some trade bottlenecks were being tackled, the main challenges were the delivery of COVID-19 vaccines (getting the shots done) and prioritising high-risks populations (healthcare workers, the elderly and people with co-morbidities, including immunocompromised people) (WHO, 2022). The **COVID-19 Vaccine Delivery Partnership (CoVDP)** (WHO, 2023l) was created in January 2022 by WHO, UNICEF, and GAVI with partners such as the World Bank, to support **in-country delivery** in the **92** countries with Advanced Market Commitments, focusing on the 34 countries with the lowest coverage. The CoVDP has resulted in 378 million does administered since January 2022 and 28 countries increased their vaccination coverage above 10%, among them, 22 countries coverage increased above 20%, 6 of these countries above 40% and 2 of these countries above 50% (WHO, 2023l).
- **Advancing mRNA vaccine technology for COVID-19 and other diseases.** COVID-19 messenger RNA (mRNA) vaccines have gained global recognition due to their unprecedented **success rate** in protecting against a deadly virus (Huff, Jaffee and Zaidi, 2022). Although mRNA vaccines have been studied in preclinical models and cancer patients for nearly three decades, development has been slow. Technological advances in COVID-19 may potentially lead to successful adaptation of the mRNA vaccine platform for cancer therapeutics (Huff et al., 2022), among others.
- **R&I expansion with "Project Next-Gen".** The goal of the next generation of vaccines and treatments is to be effective regardless of the evolution of SARS-CoV-2 and to better prepare for the next pandemic (Becerra and Jha, 2023). The US Biden administration announced the **Project Next-Gen**, which will coordinate **whole-of-government** effort to advance innovations from laboratories through clinical trials and safely deliver to the public (Becerra and Jha, 2023). The $5 billion investment will focus on 3 areas: vaccines with broader immunity both against SARS-CoV-2 variants and the entire family of epidemic-prone sarbecoviruses, vaccines that generate effective mucosal immunity to block infection and transmission, and monoclonal antibodies against viral evolution and new threats from betacoronaviruses (Becerra and Jha, 2023).

Cons:

- **Great loss of human life, social disruption and economic contraction.** 6.9 million deaths (WHO, 2023e), disruption of households and societies at large, and impact on development are the main consequences of the COVID-19 cited by governments (WHO, 2023i). The virus reduced global economic growth in 2020 to -3.2% and global trade fell by 5.3% in 2020 (Jackson et al., 2020).
- **Disproportional impact on vulnerable populations**, increasing inequalities by income, age, race, sex and geographic location (WHO, WIPO and WTO, 2023). According the trilateral study, *"an additional 71 to 100 million people are being pushed into extreme powerty as a result of the pandemic"* (WHO, WIPO and WTO, 2023).
- **Inequity in the COVID-19 vaccination**. Globally, the COVID-19 vaccine inequity gap still persists. In 2021, although 58% of the world's population had **primary vaccination**, only **11%** of the population in LICs was vaccinated, compared to **73%** in HICs (WHO, 2022).
- **Low delivery of the COVID-19 vaccine in LMICs.** The main current constraint has been the delivery of the COVID-19 vaccine to LMICs (WHO, 2022). In 2021, WHO set the target of **vaccinating 70%** of the **population** in all countries, to end and recover from the pandemic. The target has only been met by 52 countries, while the interim target of 40% coverage has yet to be achieved by 69 countries, 21 have not yet reached even 10% coverage (WHO, 2022). Moreover, more than 50% of the deaths that occurred in some LMICs analysed could have been prevented (Gozzi et al., 2023). Additional non-pharmaceutical interventions to reduce transmissibility would have been necessary to compensate for the lack of vaccines (Gozzi et al., 2023).
- **COVID-19 vaccine global shortage** was a binding constraint in 2021, despite some progressive improvements in trade blockages in 2022 (WHO, 2022).
- **Lack of vaccine production,** especially in **LMICs**, which urgently requires expanding and diversifing manufacturing, building local infrastructure and conducting TT training to break the cycle of dependence on a highly concentrated vaccine market (Feinmann, 2021; WHO PAHO, 2021; WHO, WIPO and WTO; 2023).
- **Lack of shared multinational EHR.** Despite digital progress, a unified multinational COVID-19 EHR does not exist (Cosgriff et al., 2020).
- **Whole-of-society and whole-of-government approaches recommended** to ending COVID-19 pandemic while maintaining proven prevention measures through a vaccines-plus approach that deploys public health and financial measures to complement vaccination (Lazarus et al., 2022). OWS should be followed by support to optimise vaccination practice and acceptance worldwide to counter misinformation and vaccine hesitancy (Kim et al., 2021).
- **Non-COVID-19 diseases unattended**. The COVID-19 pandemic has overwhelmed healthcare systems around the world, having an undesirable impact on the prevention, diagnosis and treatment of other diseases. For instance, childhood vaccination rates fell during the pandemic due to postponed vaccination campaigns, which delayed immunizations to 13.5 million people in LICs (Asundi, O'Leary and Bhadelia, 2021; US Global Leadership Coalition, 2021). Moreover, the 2022 Access to Medicine Index noted that only five companies of the twenty companies analysed were targeting **emerging infectious diseases** other than COVID-19, and for most of them, the pipeline was empty (Access to Medicine Foundation, 2022).

27 **Table 7.12** Case study 3: COVID-19 response strengths and weaknesses

CS 3. COVID-19	Pro	Cons
Scope	○ **COVID-19 pandemic** due to **high transmission** of the virus requiring herd immunity. ○ **Risks** of **new variants.** ○ **Preparation for new "Disease X" pandemics**, including the development of a safe and effective vaccine within 100 days.	○ **Focus on pandemics** caused by emerging or re-emerging infectious diseases.
Legal	○ **Regulation:** the **IHR** legally **binds** 196 countries. ○ **Partnership: ACT-Accelerator global partnership** to accelerate the development of COVID-19 tools and ensure equitable access. ○ **Partnership: OWS public-private partnership** in the US. ○ **Compressed R&I timeline** with overlapping phases and manufacturing. ○ **Market Access** (MA): **regulatory Fast Track** with emergency authorisations. ○ **MA: Advanced Market Commitments** in HICs and LMICs (i.e. ACT-Accelerator COVAX pillar). ○ **MA: TRIPS IPR waiver** for COVID-19 **patented vaccines** approved by the WTO in June 2022. ○ **MA: Voluntary licensing** of COVID-19 treatments (i.e. through Medicines Patent Pool). ○ **MA: Compulsory licensing** of COVID-19 treatments by some governments. ○ **Data: Increase** in **digital health data** collected.	○ **Regulation: IHR limitations** and need for a **new global social contract** such as the **WHO Global Pandemic Treaty** (in preparation). ○ **Governance: ACT-Accelerator not** legally **binding.** ○ **MA: Priority access for HICs** (i.e. US executive order for priority access to COVID-19 vaccines developed in the country). ○ **MA: Inconsistent support for "health as a human right"** and **"equal enjoyment of scientific progress"** (ICESCR) for TRIPS waiver on COVID-19 vaccines. ○ **MA: Lack of compulsory license legislation,** especially in LMICs, aligned with TRIPS to facilitate implementation. ○ **MA: Lack of industry voluntary licensing and TT for global solidarity** (lack of sharing patents, trade secrets, and know-how). ○ **Data: Lack of regulation on R&I data sharing** (i.e. European Health Data Space regulation to be approved). ○ **Data: Lack of transparency in R&I funding reporting.** ○ **Data: Higher risk of fraudulent publicatitons** due to increase in **preprinting.**
Impact	○ **Rapid development of COVID-19 vaccines:** First authorised COVID-19 vaccine by December 2020 (9 months after the pandemic declaration) and 50 vaccines approved by at least one country by December 2022.	○ **Great loss of human life, social disruption** and world **economic contraction** of -3.2% in 2020. ○ **Disproportional impact on vulnerable populations,** increasing inequalities by income, age, race, sex and geography.

	○ **Increassed coverage of the COVID-19 vaccine** with 13.5 billion doses, 70% of the global population with the first dose (including 1.96 billion doses delivered by ACT-Accelerator). ○ **Improved delivery of COVID-19 vaccines** in countries with least coverage through the **CoVDP partnership.** ○ **Advancing m-RNA vaccine technology** for other diseases (i.e. cancer). ○ **Expansion of R&I** with the **Project Next-Gen**.	○ **Inequity in COVID-19 vaccination**: 11% of the population of LICs is vaccinated against 73% in HICs. ○ **Low delivery of COVID-19 vaccine in LMICs.** ○ **COVID-19 vaccine shortage** in 2021 with some improvements in 2022. ○ **Lack of vaccine production capacity in LMICs.** ○ **Lack of shared multinational EHR.** ○ **Whole-of-society and whole-of-government approaches recommended** in addition to the vaccine-plus strategies most needed to end COVID-19 as a public health threat. ○ **Non-COVID-19 diseases unattended** (i.e. childhood vaccination or small pipelines for other emerging infectious diseases).

Expert Quotes

"**[COVID-19 response shows]* ***the collaboration between academia, industry and governments to solve a global health crisis" *– Shaper expert (E12)*

"COVID-19 provides many success stories as well as highlights the difficulties and challenges of such a "better" way of working" *– Shaper expert (E27)*

"Of course, COVAX is well funded, you know, all of these things are funded, yes, but that's because people know what it's going to be spent on" *– Shaper expert (E27)*

"COVID generated a commonality on the need for investment that is unparalleled. But will that last? with other pressures on public finances, and the relatively short-term perspective of most political bodies" *– Shaper expert (E27)*

"EU centralised procurement of COVID-19 vaccines and personal protective equipment that made available at different prices for different countries. Apply this price segmentation to different geographies" *– Shaper expert (E12)*

"I guess they** [EU, UK]* ***entered into Preferred Supplier status for the development of the COVID-19 vaccines. So, I guess that what they offered there was just guaranteed volumes that they would purchase if the product was successful, so they put all the risk of development on the Company. (…) it works for that scene, because we know that we wanted to buy large volumes that covers the whole population. I'm just trying to think, if you're trying to do it for areas where there is market

failure, that companies are not doing the development for those conditions at the moment, you just need to think through why is it that they are not happening and if you offer those guarantees to purchase it… whether that will really overcome what the problem is. At the moment, we sort of guarantee that we will buy pretty much any medicine that comes to the market if the company develops" *– Payer expert (E25)*

"Why don't we incentivize this type of project like the platforms ready to go when a new pandemic comes? Then it makes sense, right? So, and I think that Spain, Europe and many countries should be now asking themselves (…), why don't we have the European vaccine? (…) BioNTech was a German company, right? But why don't we have it? right? Why BioNTech wasn't kept as a European company? and that's because there was no money to make it a really successful growing company. So, it was acquired by Pfizer at that point… Why don't we, don't have the Spanish vaccine? So, we don't have the Spanish vaccine because no one invested in that, full stop. That's it. So, I think we should be asking ourselves what do we want to do and just put the efforts there" *– Payer expert (E08)*

7.3.2 Co-created consensus Preferred Supplier Model (PSM)

This section aims to confirm the consensus norms, principles and characteristics (target, indicators, incentives, governance) of the new co-created equitable health innovation model based on the PSM. The results are grounded on the final R3 Delphi survey and are organized into the following categories:

- **A.** Introduction: Transversal 3x3 principles of the R&I model.
- **B.** Specified Normative Preferences of the new R&I model to reach consensus.
- **C.** PSM co-created definition.
- **D.** PSM "4 Share" (4S) Principles: sharing needs, results, risks and rewards, and outcomes.
- **E.** PSM 4 Accreditation criteria and Regulation: ESG, Access to Medicine Index-like and disclosure of scientific and financial data.
- **F.** PSM Incentives: push and pull incentives.
- **G.** PSM Governance: reformulated WHO, public-private consortium, EU lead or US lead.

The R3 results showed a high level of agreement among the panel on the statements defining the new PSM (R3 PSM Tables 7.13-7.24, 100% statements with level 1 and 2 consensus). The significant consensus on the **co-created PSM**, obtained through the co-revision of the initial PSM proposed, points out the direction to follow in further developing and piloting the model.

A. Introduction: Transversal 3x3 principles of the R&I model

The panel widely agreed that the new R&I model should be guided by a 3X3 matrix of transversal principles (Table 7.13 (R3 STMT 3.1)) namely, three R&D principles and three of market access as follows:

R&D principles

1. **Open Innovation** process.
2. **Collaborative**: moon-shot missions, multi-stakeholder, and data sharing.
3. **Expansive**: expanding the solution space to other applications.

Market access principles

1. **Inclusive**: health equity and One Health / Planetary Health approach.
2. **Fast access to patients.**
3. **Balanced rewards**: hybrid revenue model balancing risk and impact (outcomes).

28 **Table 7.13** R3 consensus co-created PSM: Intro and specified Normative Preferences

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
A- INTRO										
STMT 3.1	Transversal 3X3 principles that should guide biomedical R&I: **R&D principles** 1) Open Innovation 2) Collaborative (moon-shot missions, multi-stakeholder, sharing data) 3) Expansive (expanding the solution space to other applications) **Market access principles** 1) Inclusive (health equity, One Health approach) 2) Fast access to patients 3) Balanced rewards (hybrid revenue model balancing risk & impact)	Rev	1	86	48	38	10	0	5	5
B- SPECIFIED NORMATIVE PREFERENCES										
STMT 3.2	To solve the moral dilemma, the efficiency norm could be re-specified as follows: **Norm 2 specified:** Efficiency "Generally speaking, health systems should reward risk-taking and efficiency, quantified by cost-effectiveness analysis, so effective innovation really improving the patient journey for a certain cost (value for money), contributing to the sustainability of the health systems AND, in case this reward doesn't happen naturally, preventing from fulfilling health equity, for instance when difficult to show results (i.e. mental health), small populations (i.e. rare diseases), low availability to pay (i.e. LMIC, disregarded socio-economic groups), restricted use (i.e. new antibiotics), and for public health emergencies (i.e. new epidemics), that reward should necessarily be incentivised conditioned to a global access	Rev	1	80	30	50	10	10	0	9

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; O, other responses (open text); NQ, participants who indicated that they were not qualified to respond.

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of agreement/disagreement.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Expert Quotes

Transversal 3x3 R&I principles

Open innovation process:
"Traditionally, pharmaceutical companies were doing R&D in-house. (…). No one was making push in us to do that. They were reading our papers, obviously, they were inviting us, sometimes to a congress and to getting ideas. (…) But, with all this open innovation, all this movement in the last 20 years, where pharma has been reducing a lot the in-house development, especially on early stage and accelerating all this external innovation, creating corporate venture capital, investing into biotechs (…). At the end of the of the day, introduces a lot of pressure to the academics because now they have to kind of be the first step of the factory" *– Performer expert (E16)*

Expansive - expanding the solution space to other applications:
"By developing one solution, we can actually apply it for many other solutions that would eliminate the additional cost, that would allow to have much more, much greater, let's say, applicability of what we already developed" *– Performer expert (E01)*

Fast access to patients:
"We are seeing the kind of acceleration of clinical knowledge (…) over the last years. We now have cell therapies, gene therapies, mRNA vaccines, immune oncology. These are all…amasing new technologies. We want to make them available to patients fast"– Shaper expert (E12)

B. Specified Normative Preferences of the new R&I model to reach consensus

To solve the moral dilemma identified above (see section 7.1.1), there is wide consensus (Table 7.13 (R3 STMT 3.2)) to specify (underlined text) the efficiency norm as follows:

Norm 2 specified: Efficiency *"Generally speaking, health systems should reward* ***risk-taking*** *and efficiency, quantified by cost-effectiveness analysis, so effective innovation really improving the patient journey for a certain cost (value for money), contributing to the sustainability of the health systems* ***AND, in case this reward doesn't happen naturally, preventing from fulfilling health equity*** *for instance, when* ***difficult to show results*** *(i.e. mental health),* ***small populations*** *(i.e. rare diseases),* ***low availability to pay*** *(i.e. LMICs, disregarded socio-economic groups), restricted use (i.e. new antibiotics), and for* ***public health emergencies*** *(i.e. new epidemics),* ***this reward should necessarily be incentivised conditional on the commitment of global access".***

As mentioned in the methods (see section 6.2.2), an adaptation of the Richardson's model was applied specifying a norm for the resolution of an ethical dilemma to achieve normative consensus.

Expert Quotes

Norm 2 specified:
"I fully accept that, you know, why should companies have to disclose things immediately? They are commercial operators, that is

legitimate. But if you are in the situation of a Public Health Emergency of Global Concern, whatever the fancy term is from the WHO, maybe in those circumstances there should be some alternative parameters that can apply. (…) Then, for example, is such a situation, I would certainly sort of say that, if that sort of provision is triggered clearly, then you need to make sure that you are providing appropriate incentives to the companies that will be affected. Absolutely" *– Shaper expert (E27).*

C. PSM co-created definition

The panel showed broad consensus on the definition of the PSM. They generally agreed that the PSM **gives credit** to medical companies engaged with environmental and social practices (equity and data sharing) as **preferred providers** of the public sector for priority health challenges (Table 7.14 (R3 STMT 3.3)). They stated that **incentives** for these health priority challenges should be **conditional** on a commitment to **global access** and **data sharing** practices that lead to more equitable and faster outcomes (Table 7.14 (R3 STMT 3.6)). At the same time, by doing so, providers would improve their Preferred Supplier accreditation level.

Experts perceived the model as a "**social safety net"** mechanism for priority health challenges to be activated by governments and multilateral organizations (i.e. WHO) and with the support of other stakeholders (i.e. investors, philanthropists, civil society organizations) (Table 7.14 (R3 STMT 3.7)). The PSM also represents an assurance to health payers and funders that social and environmental requirements are met, as a baseline condition (Table 7.14 (R3 STMT 3.4)).

As a tradeoff for companies complying with socially desired environmental and equity standards, the public sector will offer substantial **push incentives** (mainly for academia, start-ups and SMEs that will transfer the asset or be adquired by large corporates or going public through an IPO) and **pull incentives** (for large accredited firms) for priority health challenges identified by governments and **referenced** to the **UN SDGs** (Table 7.14 (R3 STMT 3.5)). For large corporations, only those accredited as Preferred Suppliers who develop effective and affordable innovative solutions can benefit from the incentives (that is, no binding condition for the goverment).

PSM accreditation could initially apply to listed and large pharmaceutical and biotech companies (i.e. > 500 employees or > €500 million turnover) and gradually incorporate SMEs (Table 7.14 (R3 STMT 3.9)). Push incentives would primarily target academia, startups and SMEs in discovery and early development phases; and pull incentives would mainly benefit large accredited Preferred Supplier corporates, and progressively include SMEs.

As a final reflection, the experts considered that the PSM promotes public funding for priority R&D, as it could be efficiently used by academia, startups and SMEs (assuming professional competence and impact-oriented R&D), involving less private investment, so translating into lower prices (Table 7.14 (R3 STMT 3.8).

29 **Table 7.14** R3 consensus PSM: Definition

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
C- CO-CREATED PREFERRED SUPPLIER MODEL DEFINITION										
STMT 3.3	**Get credit for health equity practices.** In the Preferred Supplier model, biomedical companies engaged with environmental and social practices (equity and data sharing) get credit as preferred providers of the public sector for priority health challenges.	New	1	81	48	33	10	5	5	5
STMT 3.4	**Accreditation as a guarantee.** The Preferred Supplier model proposes an accreditation of the biomedical corporates for health payers and funders to have a level of guarantee that the social and environmental requirements are met, as a baseline.	New	1	70	35	35	15	10	5	9
STMT 3.5	**Incentives as a trade-off**. In exchange the public sector provides significant push incentives (mainly for academia/SMEs) and pull incentives (for accredited corporates) for the priority health challenges identified by governments and referenced to the UN SDGs. For large corporates, only those accredited as Preferred Suppliers developing effective innovative solutions can benefit from the	New	1	75	25	50	5	10	10	9
STMT 3.6	**Incentives conditioned to equity & data sharing**. The incentives for the health priority challenges should be conditioned to a global access commitment and data sharing practices that lead to equitable and quicker outcomes. By doing so, providers would improve their Preferred Supplier accreditation	New	1	85	40	45	0	10	5	9
STMT 3.7	**Social safety mechanism**. The model can act as a "social safety" mechanism for health priority challenges to be activated by governments and multilateral organizations (i.e. WHO) and supported by other stakeholders (i.e. investors, philanthropists,	New	1	80	35	45	5	10	5	9
STMT 3.8	**De-risk role of public sector by increasing the R&I funding.** The more public funding dedicated to priority R&I, the more efficiently it could be used by academia, startups and SMEs (assuming professional competence and impact-oriented R&I), requiring less private investment, and resulting in lower prices.	New	2	64	18	46	23	5	9	0

Table 7.14 R3 consensus PSM: Definition (cont.)

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
C- CO-CREATED PREFERRED SUPPLIER MODEL DEFINITION										
STMT 3.9	**Target companies.** Preferred Supplier accreditation could initially apply to listed and large pharma and biotech companies (i.e. >500 employees or >500m€ turnover) and progressively incorporate SMEs. Push incentives would mainly benefit academia/startups/SMEs discovering potential solutions, and pull incentives would mainly benefit accredited Preferred Supplier large corporates and progressively incorporate	New	1	70	20	50	5	15	10	9

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; O, other responses (open text); NQ, participants who indicated that they were not qualified to respond.

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of agreement/disagreement.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Expert Quotes

Get credit for health equity practices:
"Absolutely. Absolutely. And I think that's the way to talk about it *[regulation to reward companies fulfilling environmental and health equity practices]* ***(…) This will be a new approach, a new paradigm that valorizes the fundamental role that these industries play"*** *– Performer expert (E10)*

Incentives conditional on equity and data sharing:
"It's an interesting approach, and I really would like to congratulate you, because I think it's really hard to have this really pragmatic approach of also listening to what industry has, you know, as a claim, in terms of incentives, and trying to find the balance" *– User expert (E14)*

Social safety net mechanism:
"Almost a "social safety net" mechanism (…). Something that can be triggered by governments, public authorities in such a situation. (…) What I'm saying is that the decision then would be for public authorities. At the moment, the decision is for private entities… the extent to which they share" – Shaper expert (E27)

D. PSM "4 Share" (4S) Principles

The PSM proposes a public health investment and procurement system that prioritises business with companies fulfilling the criteria of the "4 Share" (4S) principle: sharing Needs, Results, Risks and Rewards, and Outcomes that guarantee equitable access to innovative solutions in exchange for incentives for priority health challenges.

1) PSM: sharing Needs

The panel focused primarily on ensuring an R&I portfolio that responds to priority health challenges. That is, a substantial part of the Preferred Supplier's R&I portfolio should be on priority needs (Table 7.15 (R3 STMT 3.10)).

Health priorities should be defined by each government value framework (Table 7.15 (R3 STMT 3.11)) based on:

- **Epidemiology** (i.e. burden of disease).
- **Market failure** where impact is not naturally rewarded, such as when it is difficult to show results (i.e. mental health), small populations (i.e. rare diseases), low ability to pay (i.e. LMICs), restricted use (i.e. new antibiotics), among others.
- **Public health emergencies** (i.e. new epidemics).

30 **Table 7.15** R3 consensus PSM: Principles - sharing Needs and Results

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
D- ACCREDITATION REQUIREMENTS: 4 "SHARE" PRINCIPLES										
STMT 3.10	**Share NEEDS. Balanced R&I portfolio in health priority challenges**. Preferred Suppliers should invest a tangible part of their R&D portfolio in meeting the priority needs.	Rev	1	91	55	36	5	5	0	0
STMT 3.11	**Share NEEDS. Priorities** should be defined by governments, according to their value frameworks, mainly considering 1) epidemiology (i.e. burden of disease), 2) market failure in which impact is not rewarded naturally, such as when difficult to show results (i.e. mental health), small populations (i.e. rare diseases), low ability to pay (i.e. LMIC), restricted use (i.e. new antibiotics), etc as well as 3) public health emergencies (i.e. new epidemics).	Rev	1	95	41	55	5	0	0	0
STMT 3.12	**Share RESULTS. Contribute to open "Health Data Spaces"**. Preferred Suppliers should share scientific data, from R&I project pipeline and raw data to results (clinical trials, real-world evidence), including failure, as projects co-financed with public funds.	Rev	1	95	62	33	0	5	0	5
STMT 3.13	**SHARE RESULTS. Patient-centred and Adaptive evidence generation.** Preferred Suppliers should promote clinical trials with patient-centered design including "Medicine Adaptive Pathway to Patients" (MAPPs), in which the target population is adjusted as the evidence	Rev	1	100	65	35	0	0	0	23

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; O, other responses (open text); NQ, participants who indicated that they were not qualified to respond.

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of agreement/disagreement.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Expert Quotes

Shared needs - Priorities:

"You should start with "what are the guiding values?" What are the underlying values that guide our investment decisions? It could be (…) effectiveness, or cost-effectiveness, or whatever. I mean, it could also be equality or solidarity in a system. I don't know. But I think the discussion about these values is implicit. Because we start with, oh, we need to have cost-effectiveness data. Well, we, therefore, we need to have a QALY. But (…) if you choose to use the QALY, it means that you (…) use a normative framework that maximizes health for the population" *– Shaper expert (E13)*

"It must be a combination of (…) classical epidemiological elements (…) but there are also the neglected diseases, the rare diseases, although epidemiologically, probably they would not be a priority, but then it's a moral and ethical thing that mature or more advanced societies don't want to leave behind"– Performer expert (E02)

"If you are talking about open innovation and we are talking about in the ecosystem we can open the eyes and see how we can do it better (…) What is called Horizon Scanning. (…) If Horizon Scanning needs was applied we were better prepared for the pandemic, because the data was there and we were not using this data to plan. (…) We were not able to use this knowledge for planning, you know, scenarios. This is lack of policy, not a lack of knowledge or lack of evidence"– Performer expert (E02)

2) PSM: sharing Results

Open "**Health Data Spaces**" should be nurtured by the scientific evidence generated by Preferred Suppliers as projects co-financed with public funds. Scientific data comprises the R&I project portfolio, raw data, clinical trial results and real-world evidence (RWE), including failure (Table 7.15 (R3 STMT 3.12)). The experts unanimously recommended adaptive and patient-centred evidence generation (Table 7.15 (R3 STMT 3.13)). That is, clinical trials conducted by Preferred Suppliers should have a patient-centered design, including "Medicine Adaptive Pathway to Patients" (MAPPs), in which the target population evolves as evidence is generated.

Expert Quotes

Share results – Contribute to open "Health Data Spaces":

"I fully agree with transparency, I fully agree in sharing results would work (…) so that at least we can optimize public spending. I really believe that the suppliers, so the innovators, the enablers, and the suppliers should work more together. So, when I talk about the innovators I talk about, you know, companies with therapeutics, medtech, digital tech, internet of things, AI, that work more with the enablers, with the medical suppliers, with the distribution of medical supplies, on vaccinations, with the training centers, with the CROs" *– Funder expert (E20)*

***"We need a better integrated evidence paradigm connecting RCT** [randomized controlled trials], **RWD** [real-world data] **and advanced analytics and modeling"** – Shaper expert (E12)*

"Inside the countries, sometimes we have more functional or less functional systems by regulatory agencies that do market surveillance after the product is reaching people (…). This is basically the phase IV (…). It's where you are really looking at the large-scale use. So yeah, it's very important to integrate more this information coming from different sources and relating that to the data of approval (…) to inform decisions like (…) changes in treatment guidelines, and, you know, how to deal with side effects that can create a lot of important health policy discussions if we have more integrated data" – User expert (E14)

Share results – Patient-centred and Adaptive evidence generation:
"[Given the current scientific acceleration] ***We need new models (…) [with] a good balance between early access and maturity of the data"*** – Shaper expert (E12)

"We will switch from one-time decisions to iteration. So, we continue to learn and improve, and then, you know, improve continuously instead of nothing before, and then without control afterwards, as we are currently working. It's going to take this to this adaptive process, you learn over time and, so, you have to adjust over time. Because, if you wait until you have that evidence, you know, you've lost a decade, and that's not how this works. So, I think (…) we are already rethinking how we now generate evidence, and that's why this real-world evidence is so important" – User expert (E19)

"So, the only things that, in my view, have worked really well for certain diseases or therapeutic areas are this type of, I think it's working well also in Europe, is this type of early launches so that you can start using the drug for severe use, easiest for certain patients in a very controlled matter. So that the drug gets to the patient as early as possible, which is also, should be also a driver. And then (…) you end generating the full package of evidence that could at the end of the day have an impact on how much you are reimbursed for that, once you are already in the market. (…) You cannot do that in all therapeutic areas because it's about the balance in risk and benefit, right? so, you cannot do that for non-severe diseases" – Payer expert (E08)

3) PSM: sharing Risks & Rewards

The panel unanimously agreed that to **de-risk** market access, Preferred Suppliers should **work earlier** with health regulators and payers and obtain input from **multi-stakeholders** (i.e. patient feedback) (Table 7.16 (R3 STMT 3.23)). Moreover, to assess the R&I risk assumed, Preferred Suppliers should **declare** the **public funding** received during the development cycle (Table 7.16 (R3 STMT 3.15)). Nonetheless, private investment in R&I could be voluntary disclosed by companies, as they would certainly be incentivised to do so, especially if the share of private investment is large (Table 7.16 (R3 STMT 3.16)).

The **price** of medical products negotiated between public payers and Preferred Suppliers should be **modulated** by **disclosing public** (and private) **R&I funding received** along the value chain in exchange for favorable market access for products with positive evidence (Table 7.16 (R3 STMT 3.17)). Importantly, the panel agreed on a **hybrid pricing** model that balances **risk and impact**. The price for innovative products should balance impact (results), in terms of **health outcomes** in value-based model, modulated by the risk (investment) assumed along the development pipeline, defined by the **public-private R&I funding mix** (Table 7.16 (R3 STMT 3.14)). The **impact** would be rewarded with **new pricing models** such as the "**Netflix" model**, with an annual subscription and rewards de-coupled from sales volume and linked to value (health outcomes). For instance, Netflix pricing has already been applied to the development of new antibiotics (i.e. in the UK) based on the population health gain. These new pricing models should apply price modulation (i.e. segmentation) for health access (Table 7.16 (R3 STMT 3.18)).

Moreover, a general agreement on **price segmentation** of innovative based on **countries' ability to pay** (i.e. GDP per capita) could be considered (Table 7.16 (R3 STMT 3.19)). **Price-volume** agreements with a **budget cap** (more volume implies a lower price per patient) could also be considered by Preferred Suppliers (Table 7.16 (R3 STMT 3.20)). **Voluntary licensing** is another pricing strategy for global access in which corporates holding a patented innovation license it to low-cost generic manufacturers (i.e. India, China, Brazil, South Africa) to sell products to LMICs. This voluntary external license would include knowledge sharing for effective TT (Table 7.16 (R3 STMT 3.21)).

Finally, the panel mostly agreed to create **investment consortia** between Preferred Suppliers and global development players (i.e. World Bank, philanthropists, impact investors) to boost medical R&I infrastructure, distribution and negotiation skills in LMICs (Table 7.16 (R3 STMT 3.22)). Governments, in turn, would facilitate market access with regional HTA Agencies (i.e. in West and East Africa), among other measures.

31 **Table 7.16** R3 consensus PSM: Principles - sharing Risks and Rewards

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
D- ACCREDITATION REQUIREMENTS: 4 "SHARE" PRINCIPLES										
STMT 3.14	**Share RISK & REWARDS. Risk-Impact hybrid pricing model.** Rewards for innovative products should balance Impact (outcomes/value-based) modulated by the Risk assumed along the development pipeline defined by the R&I public-private funding mix.	Rev	1	85	33	52	5	10	0	5
STMT 3.15	**Share RISKS& REWARDS. Disclosure of Public R&I funding to assess the risk assumed.** To assess the R&I risk assumed, Preferred Suppliers should declare the public funding received during the cycle.	Rev	1	100	82	18	0	0	0	0
STMT 3.16	**Share RISK & REWARDS. Voluntary disclosure of the private R&I investment**. Companies could decide to voluntary disclose the R&I private investment, as they will be naturally incentivized to do so, especially if the private investment share is large.	New	**2**	55	36	18	9	27	9	0

Table 7.16 R3 consensus PSM: Principles – share Risks and Rewards (cont.)

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
D- ACCREDITATION REQUIREMENTS: 4 "SHARE" PRINCIPLES										
STMT 3.17	**Share RISK & REWARDS. Public R&I funding should modulate price.** Disclosure of public (and private) R&I funding should affect the price negotiation between the Preferred Supplier and the public payer in exchange for favorable market access for products with positive evidence.	Rev	1	81	48	33	5	10	5	5
STMT 3.18	**Share RISK & REWARDS. New pricing models such as "Netflix" model**. Impact would be rewarded with new value-based prices for some priority products, such as the de-linked Netflix/subscription model for new antibiotics (based on the population health gain), applying price modulation for health access.	Rev	1	78	33	44	11	6	6	18
STMT 3.19	**Share RISK & REWARDS. Price Segmentation agreement.** Price modulation for global access could consider a general agreement on price segmentation for innovative products according to the countries' ability to pay (i.e. GDP per capita).	New	1	84	68	16	11	5	0	14
STMT 3.20	**Share RISK & REWARDS. Price-Volume negotiations.** Price modulation for global access could consider Price-Volume agreements with countries with a budget cap (more volume implies lower price per patient).	New	1	74	42	32	21	5	0	14
STMT 3.21	**Share RISK & REWARDS. Voluntary licenses to low-costs manufacturers.** Price modulation for global access could consider Voluntary Licenses to low-cost manufacturers (i.e. India, China, Brazil, South Africa) to sell in LMIC, with the know-how sharing for technology transfer.	New	1	82	36	46	9	9	0	0
STMT 3.22	**Share RISKS & REWARDS. Promote R&I investment in LMIC.** Support consortiums between Preferred Suppliers and global development players (i.e. World Bank, philanthropists, impact investors) to invest in biomedical R&I infrastructure, distribution and negotiation skills in LMIC. In exchange, governments facilitate market access with, for instance, regional HTA Agencies (i.e. in West and East Africa).	New	1	90	65	25	5	0	5	9
STMT 3.23	**Share RISK & REWARDS. De-risk R&I through early collaboration.** To de-risk market access, Preferred Suppliers should work earlier with health regulators and payers, and get multi-stakeholder input (i.e. patients).	New	1	100	71	29	0	0	0	5

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; O, other responses (open text); NQ, participants who indicated that they were not qualified to respond.

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of agreement/disagreement.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Expert Quotes

Shared risks & rewards – De-risk R&I through early collaboration:
"We like to work early with payers, we do that more in the US too, we have early meetings before even getting regulatory approval... So that we have an idea of what the payer questions will be, the points that payers will be looking for in the clinical studies (…) I think that's (…) primarily the way that we're reducing risk, it's just trying to, sort of a partnership" *– Performer expert (E11)*

Shared risks & rewards – Disclosure of public R&I funding:
"Tracking the *[R&I]* ***cost is really doable"*** *– Funder expert (E08)*

Shared risks & rewards – Public R&I funding should modulate price:
"Preferred Supplier conditions are linked to the conditions of receiving public funding, in that case, I think that there is more room for intervention, and it's much more feasible" *– Payer expert (E20)*

Shared risks & rewards – Risk-Impact hybrid pricing model:
"It is something which is necessary, the transparency, in terms of the determination of the price because, well, it's very difficult to understand how a price is attributed to a certain medication. (…) I'm much more in favor of the hybrid formula. I think that, two aspects should be taken into account, results and certainly cost of production (…). But, the position of the pharma companies is not very in favor of this formula of the hybrid, but they will be forced to accept, in general is the trend" *– Shaper expert (E26)*

Shared risks & rewards – Price segmentation agreement:
"It is absolutely correct that the price for this medicine in the US and Europe is different from the price in Southeast Asia and Africa. And to a principle that we agree I mean, WHO has said that it can be linked to GDP per capita and some people agree with that, other people don't agree with that, but if you just use it as a starting point, you could then say "if a country like Egypt has a GDP per capita, which is 10% of what it is in the US, that the prices of medicines and probably salaries for physicians and others are also kind of much, much lower at 10% or 20% of what they could be in other parts of the world" *– Shaper expert (E12)*

Shared risks & rewards – Promote R&I investment in LMICs:
"It's absolutely sinful that there's virtually no vaccine production capacity in Africa. (…) One of the things Pfizer can do is, maybe with other pharmaceutical companies, is a pharma consortium for investing in pharmaceutical production and distribution in Africa. And basically, even though it's going to take 10, 15 years to develop that appropriately, you know, you gotta, gotta start now. And then make that conditional with the regional economic zones in Africa. Well, we'll build a plant, we'll train people, we'll produce (…). But what we don't want to do is have to deal with 54 different patent laws and 54 different regulatory laws. We can deal with, you know, 6 or 7, but not 54. (…) There needs to be an East Africa regulatory agency, there needs to be an Eastern Africa Patent and Trademark Office (…). And you

figure out how you're gonna regulate for your 7- or 8-member countries and then we'll provide pharmaceuticals" *– Payer expert (E22)*

4) PSM: sharing Outcomes

Health innovation assessment should normally involve a **Health Technology Assessment** (HTA) with a **cost-effectiveness** and/or **population health gain** analysis (Table 7.17 (R3 STMT 3.24)). **Ethical, legal** and **social** aspects (ELSA) should also be considered when necesssary. A **systemic evaluation** that measures patient health improvement with clinical data, patient-reported outcome measures (**PROMs**) and experience measures (**PREMs**) is recommended, as well as **cost reduction** for the health care system (Table 7.17 (R3 STMT 3.25)).

Finally, the PSM is considered a **"Responsible Capitalism" accreditation** of businesses with best corporate practices: environmental (i.e. in R&D, manufacturing and distribution), social (i.e. health equity, data sharing), and financial (i.e. reduce share buybacks and reinvest some in R&D) (Table 7.17 (R3 STMT 3.26)).

32 **Table 7.17** R3 consensus PSM: Principles - sharing Outcomes

R3 Delphi survey (n=27, RR= 81%)

D- ACCREDITATION REQUIREMENTS: 4 "SHARE" PRINCIPLES										
Statement		**VAR**	**CON**	**CA (%)**	**A (%)**	**SA (%)**	**SD (%)**	**D (%)**	**O (%)**	**NQ (%)**
STMT 3.24	**Share OUTCOMES. HTA evaluation.** Outcomes resulting from health innovation should be generally evaluated with Health Technology Assessment (HTA), applying cost-effectiveness and/or population health gain measures, incorporating Social, Legal and Ethical aspects when needed.	Rev	1	90	71	19	5	5	0	5
STMT 3.25	**Share OUTCOMES. Systemic approach.** Progressively apply a systemic healthcare approach measuring the improvement in patient's health with clinical data, patient-reported outcome measures (PROMS) and experience (PREMS), and savings for the system.	Rev	1	90	75	15	0	5	5	9
STMT 3.26	**Share OUTCOMES. Preferred Supplier as "Responsible Capitalism" accreditation.** Incentives should be given to companies with best corporate practices: environmental (i.e. in R&D, manufacturing and distribution), social (i.e. health equity, sharing data), and finance practices (i.e. reduce share buybacks and reinvest part of the profit in R&D) that determine the Preferred Supplier accreditation.	Rev	1	89	47	42	0	11	0	14

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; O, other responses (open text); NQ, participants who indicated that they were not qualified to respond.

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of agreement/disagreement.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Expert Quotes

Shared outcomes – HTA evaluation:

"If you really would like to drastically speed off access (…), can HTA bodies and payers deal with more immature evidence and already provide patient access? (…). The trade-off is (…) how early in the development process can you be reasonably assured that there is clinical benefit of something? And also, be reasonably assured of what the added value of that new treatment is over existing treatment options. And, therefore, how that translate into the right price" – *Shaper expert (E23)*

"HTA bodies and payers might decide that the product doesn't offer value for money. And that, I mean, in my view, that, as a problem, (…) *[is]* ***more caused by unrealistic price setting by pharmaceutical companies"*** *– Shaper expert (E23)*

Shared outcomes – Preferred *Supplier as "Responsible Capitalism" accreditation:*

"Giving, if you like, a sort of a marker, some print, a sticker, or something for delivering things is a very good idea because it's incentivised. I take the, you know, the environmental, sustainable, etc requirements as being baseline and, you know, non-debatable. The one question that I would ask (…) would be the extent to which that such a model, once you've got it going, would become THE model or an optional question (…). Because (…) there'll be the big question for (…) big operators, whether to stay outside and try to play their own game or whether to join" *– Shaper expert (E27)*

E. PSM 4 Accreditation criteria and Regulation

Accreditation criteria

Substantial consensus that the Preferred Supplier accreditation criteria could be defined by these two pillars and the four related indicators:

Pillar 1. Corporate Impact: Environmental, Social and Governance (ESG) and Access to Medicine Index-like.

1. **ESG:** Disclosure by the industry of ESG KPIs (key performance indicators), along with financial statements. This measure is already **required** in some countries (i.e. EU, USA) for large and public companies to address their **externalities** and deliver meaningful long-term impact (Table 7.18 (R3 STMT 3.27)).
2. **Access to Medicine Index-like** KPI. Specifically, for the **healthcare** sector, an "Access to Medicine Index" (ATMi) like could spur industry to improve global access by getting credit as Preferred Suppliers. ATMi ranks the world's largest 20 pharmaceutical firms according to their ability to **expand access in LMICs**, assessing **governance** (strategy), **R&D portfolio** and **implementation** (price and delivery). Since 2008, the biennial index has been published by the Access to Medicine Foundation in the Netherlands, an international non-profit organization. An **ATMi**-based index could be adopted considering the Preferred Supplier "**4 Share**" principles and converted into a **KPI** to be

measured and audited (Table 7.18 (R3 STMT 3.29)). It is worth mentioning that the ATMi index was known by 46% of the panellists (Table 7.19 (R3 STMT 3.28)).

Pillar 2. Data Disclosure: Scientific and funding disclosure as a general condition for all projects that receive public R&I funding.

3. **Disclosure of Scientific Data** in **Open Health Data Spaces** for **ALL** projects receiving **public R&I funding** (not just Preferred Suppliers). Disclosure should be made at three levels: R&I project pipeline, raw data and results, including failure. Regarding results, a specified time period and/or license could be given, except in the event of a Global Public Health Emergency (Table 7.18 (R3 STMT 3.30)).
4. **Disclosure of public R&I Funding** for **ALL** projects receiving **goverment funding** (not just Preferred Suppliers). Public R&I funding could be tracked through the development cycle linked to the **commercial asset** (i.e. patent, registered software) by applying blockchain technology to store transactional records (Table 7.18 (R3 STMT 3.31)).

Regulation

The experts agreed on the **transparency obligation** of the Preferred Suppliers to present **annually audited indicators** at the moment of the submission of the dossier to the **regulatory agencies**. Table 7.18 (R3 STMT 3.33 to 3.36) shows the results as follows:

- **Indicator 1: ESG** (Environmental, Social and Governance): already mandatory in some countries along with financial reports. Required for Preferred Suppliers.
- **Indicator 2: ACCESS TO MEDICINE INDEX-like** proposed as voluntary. Required for Preferred Suppliers.
- **Indicator 3: Disclosure of SCIENTIFIC Data** proposed as mandatory for all projects financed with public funds. Required for Preferred Suppliers.
- **Indicator 4: Disclosure of PUBLIC R&I FINANCING Data** proposed as mandatory for all projects financed with public funds. Required for Preferred Suppliers.

As mentioned, all thirty R3 **"Minimum Consensus criteria"** statements (see section 6.6) showed supermajority consensus to confirm the overall panel consensus on the PSM (see Annex A, Table A1).

33 **Table 7.18** R3 consensus PSM: Accreditation criteria and Regulation

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
E- ACCREDITATION CRITERIA & REGULATION										
ACCREDITATION										
The Preferred Supplier accreditation criteria could be defined by these 2 pillars and their corresponding indicators:										
Pillar 1. Corporate Impact (ESG & Access to Medecine Index)										
STMT 3.27	**ESG KPI.** Disclosure by industry of Environmental, Social and Governance (ESG), alongside the financial information. Already mandatory In some countries (i.e. EU, USA) for large and public companies to address their externalities and deliver meaningful impact over the long term.	New	1	90	65	25	0	5	5	9

Table 7.18 R3 consensus PSM: Accreditation criteria and Regulation (cont.)

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
E- ACCREDITATION CRITERIA & REGULATION										
ACCREDITATION										
The Preferred Supplier accreditation criteria could be defined by these 2 pillars and their corresponding indicators:										
Pillar 1. Corporate Impat (ESG & Access to Medecine Index)										
STMT 3.29	**Access to Medicines Index KPI.** For the biomedical sector, an "Access to Medicines Index (ATMi) like" could stimulate industry to improve global access by getting credit as Preferred Suppliers. The ATMi ranks the world's largest 20 pharma firms according to their ability to expand access in LMIC, assessing Governance (strategy), R&D portfolio and Implementation (pricing and delivery). Since 2008, the biennial index is published by the Access to Medicine Foundation in Netherlands, an international not-for-profit organization. An index similar to ATMi could be adopted considering the Preferred Supplier "4 SHARE" principles and turned into a KPI to be measured and audited.	New	1	83	22	61	0	6	11	18
Pillar 2. Data Disclosure (scientific and financial data)										
STMT 3.30	**Disclosure of Scientific Data in "Open Data Spaces" for ALL the projects receiving public R&I funding (not only for Preferred Suppliers)**. Share at 3 levels: R&D project pipeline, raw data and results, including failure. For results, it could be given a certain period of time and/or a license, except in case of a Global Public Health Emergency.	Rev	1	82	55	27	9	5	5	0
STMT 3.31	**Disclosure of R&D public Funding for ALL the projects receiving public funding (not only for Preferred Suppliers).** The R&I public funding could be tracked during the R&D cycle and linked, for instance, to the commercial asset (i.e. patents, software) applying blockchain technology.	Rev	1	80	50	30	0	10	10	9
REGULATION										
STMT 3.32	**Preferred Supplier regulation.** For all the priority products submitted by the Preferred Suppliers to the Regulatory Agencies (i.e. EMA, FDA) for marketing approval, there should be the transparency obligation, at the moment of the submission of the dossier, to present annually audited indicators.	New	1	83	56	28	0	6	11	18
The annually audited indicators could be these 4:										
STMT 3.33	**Indicator 1: ESG KPI** (Environmental, Social and Governance): already mandatory in some countries along with the financial reports. Required for Preferred Suppliers.	New	1	89	53	37	0	6	6	14
STMT 3.34	**Indicator 2: ACCESS TO MEDICINE INDEX-like KPI**: proposed as voluntary. Required for Preferred Suppliers.	New	1	71	35	35	12	12	6	23

Table 7.18 R3 consensus PSM: Accreditation criteria and Regulation (cont.)

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
E- ACCREDITATION CRITERIA & REGULATION										
REGULATION										
STMT 3.35	**Indicator 3: Disclosure of SCIENTIFIC Data**: proposed as mandatory for all public-funded projects. Required for Preferred Suppliers.	Rev	1	90	65	25	0	10	0	9
STMT 3.36	**Indicator 4: Disclosure of R&I PUBLIC FUNDING Data:** proposed as mandatory for all public-funded projects. Required for Preferred Suppliers.	Rev	1	95	85	10	0	5	0	9

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; O, other responses (open text); NQ, participants who indicated that they were not qualified to respond.

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of agreement/disagreement.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

34 **Table 7.19** R3 consensus PSM: Awareness of Access to Medicine Index

R3 Delphi survey (n=27, RR= 81%)

E- ACCREDITATION CRITERIA & REGULATION			
ACCREDITATION			
Statement		**YES (%)**	**NO (%)**
STMT 3.28	**Access to Medicines Index.** Did you know about the existence of the Access to Medicines Index?	46	55

Expert Quotes

Regulation – Annual audited indicators:
"I would definitely agree that there have to be mechanisms to audit that the companies are also following some principles" *– Shaper expert (E12)*

Accreditation & Regulation – Access to Medicine Index-like and Disclosure of public R&I funding:
"To use an organization such as similar to Access to Medicines *[Foundation]* ***which is… does some sort of ranking system on companies (…) It could be a stronger review and a stronger recommendation, and it could bring in some of those elements that you mentioned. For example, make it absolutely clear about the level of public funding that's been involved in the development of the product. Yeah, I think there are ways of doing that and I completely agree with the point that it should be more visible"*** *– Performer expert (E10)*

Accreditation & Regulation – Disclosure of scientific data:
"If you're getting money from the public purse, (…) whatever the results, the data (…) from that, whether it is good, bad, or indifferent becomes a matter of public knowledge" *– Shaper expert (E27)*

"We need clear regulations around data security and data privacy, and these are two separate things. Data security is that we can be sure that when people have a legitimate need to use the data they can get access to this. And then there's data privacy that I have complete control of my data. I think in Europe we're very much focused on the data privacy and that has made it difficult for the data actually then to be used for population health purposes or for improving healthcare. I think we also need to kind of provide that trade-off between data security, we all want absolute security, I can see that the data is protected, (…) that it's encrypted, that we know exactly who is going to use this data" *– Shaper expert (E12)*

Regulation - Disclosure of public R&I funding data:
"The disclosure of R&D, I think, this could be, for example in Brazil, there is a new legislation in discussion that brings that idea (…) When a company is registering the drug to the regulatory agency, this is one of the information they need to file, you know, that R&D costs. So, maybe having some of those things that you expect companies to comply voluntarily under a mandatory framework would work best. Of course, you know, decisions on areas to invest that's up to the company. *[Disclosure of]* ***R&D investments and costs when applying for registration (…), I think disclosure could be, you know, part of a mandatory package"*** *– User expert (E14)*

"[Tracking R&I investment] ***So, that is saying that you have a transparency obligation at the moment of the submission of the dossier, for example, to EMA (…) or to FDA. (…) Or why can't we have an obligation on transparency as public funding anyway? (…) independent of whether or not you're making an application to EMA (…) that it is known that X amount is going into that piece of research"*** *– Shaper expert (E27)*

F. PSM Incentives

PSM accreditation is a recognition of good practices, **not** a **binding** condition, so there is no initial contract with Preferred Suppliers, who compete to develop the best possible solutions in terms of cost-effectiveness and health equity. Preferred Supplier rewards are based on significant push incentives (funding, encourages upstream R&I) and pull incentives (market access, encourages commercialisation for priority health challenges) as described below.

PUSH Incentives

Strong consensus on push incentives based on **early-stage R&I funding**, mainly with donations and public-private investment in academia, research centers, start-ups and SMEs engaged in preliminary development and TT of the asset (Table 7.20 (R3 STMT 3.37)). Equally agreed was the push incentive about **growth-stage R&I investment** with a long-term public-private venture capital matching fund to complete phase II-III clinical trials, especially for SMEs (Table 7.20 (R3 STMT 3.38)). Finally, the promotion of **long-term "social impact investment"** and supportive **"corporate holding investment"** presented a significant consensus. In the first, rewards are based on social outcomes. In the latter, investors support the company as board members and

the focus is on achieving the social mission and long-term sustainability, based on organic growth rather than selling as exit strategy (Table 7.20 (R3 STMT 3.39)).

35 **Table 7.20** R3 consensus co-created PSM: Push incentives

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
F-INCENTIVES										
The Preferred Supplier accreditation is a recognition of good practices (not a binding condition), so there is no initial contract with the Preferred Suppliers. Preferred Supplier rewards are based on significant PUSH (funding) and PULL (market access) incentives for priority health challenges such as:										
STMT 3.37	**PUSH Incentives.** Intensify **early-stage R&I funding,** especially with grants and public-private investment vehicles to academia/research centers and start-ups/SMEs with development and tech transfer commitments.	New	1	91	59	32	0	5	5	0
STMT 3.38	**PUSH Incentives.** Intensify **growth-stage R&I investment** for clinical trials phase II-III with long-term public-private venture capital matching fund, especially for SMEs.	New	1	91	50	41	0	5	5	0
STMT 3.39	**PUSH Incentives.** Promote **long-term "Social Impact Investment"** (rewards based on social outcomes) and supportive **"Corporate Holding Investment"** (investors supporting the CEO of the company as members of the board of directors) oriented to accomplish the company long-term mission with benefits based on organic growth rather than selling.	New	1	85	50	35	0	10	5	9

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; O, other responses (open text); NQ, participants who indicated that they were not qualified to respond.

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of agreement/disagreement.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Expert Quotes

Intensify early-stage R&I funding:

"To increase and to support massively the small and medium environment, and not the big pharma (…). Incentivise SME because they are creating the most of our new medicine. What they do is finally to license or be acquired by a big pharma. The big pharma will add the muscle, the capacity to do things, to market, to get all the regulatory issues done. But if you look at the creativity is clearly in favour of the small (…) No need to incentivize pharma because the industry is very well incentivized by marketing the product at prices that are incredibly high" *– Shaper expert (E21)*

Intensify growth-stage R&I Investment:

"We should not underestimate the power of the investment community. The value of working towards that community that will organically, sustainably invest in biomedical life science. Grants play a very important role, right? But grants have certain limitations in the value that they offer (…) But grants might not be that valuable if you talk about small companies or biotech companies or start-ups, entrepreneurs who have (…) biomedical ideas, (…) projects in their hands. I think that here, you really need also investors. You need people from the scientific community that have the network, that are scientists themselves, or were former scientists (…), have a business

mindset that kind of give them access to hospitals or patient communities, that can give them a platform" *– Payer expert (E20)*

PULL Incentives

As shown in the methodology (see section 6.5), R3 included two checkbox questions on different pull incentives options, one for **regulatory pull incentives** and the other for **pricing pull incentives** (Tables 7.21 and 7.22). In each of them, the panellists could select a maximum of four items. The statements were nominated based on R2 survey and interviews results.

Table 7.21 below shows the best **regulatory pull incentives** to be offered to Preferred Suppliers with proven innovative solutions. The top half pull incentives related to regulatory actions were five. First, **alignment** between **regulatory** (risk-benefit analysis) and **HTA agencies** (i.e. cost-effectiveness and population net gain analysis). Second, **alignment** between **US (FDA)** and **EU (EMA)** regulatory bodies for product approval. The following three items shared the same frequency. **Fast track approval** of priority products for public health challenges. **Regulatory exclusivity extension** (EE) which provides exclusive marketing rights for a priority pharmaceutical product for a certain period of time. And finally, the creation of **regional regulatory agencies** in LMICs to simplify and standardise procedures.

36 **Table 7.21** R3 consensus PSM: Pull incentives (Regulatory)

R3 Delphi survey (n=27, RR= 81%)

F-INCENTIVES			
STMT 3.40	**PULL Incentives.** PSM best **regulatory incentives** (panellists could select a maximum of 4 items)**.**		
Top position	**Pull incentive**	**Frequency (#)**	**Frequency (%)**
1	Regulatory agency – HTA agency alignment	13	59
2	Regulatory FDA – EMA alignment	11	50
3	Regulatory Fast Track	10	46
4	Regulatory "Exclusivity Extension" (EE)	10	46
5	Regional Regulatory Agencies in LMIC	10	46
6	Managed Access Funds	8	36
7	Regulatory Transferable Exclusivity Extension (TEE)	6	27
8	Transferable Regulatory Fast Track (Priority Review Voucher)	2	9
9	Not qualified	2	9
10	Other	1	5

Frequency (#) refers to the number of panellists who have selected the item and Frequency (%) refers to the corresponding percentage of the total number of panel respondants.

Regulatory "Exclusivity Extension" (EE) means to market exclusivity for the priority product for a certain time.

Managed Access Funds provide conditional approval Clinical Trial phase II committed to perform phase III in a certain period of time.

Regulatory Transferable Exclusivity Extension (TEE) or Transferable Exclusivity Voucher (TEV).

Expert Quotes

Regulatory agency – HTA agency alignment:

"They are reinforcing the link (…) with the EUnetHTA (…). The assessment carried out by the EMA can be useful for the Health Technology Assessment body (…). In this direction, yes, they have to continue reinforcing this relationship. (…) But the main scope of the assessment of the EMA is not reimbursement, so they have to take decisions from a regulatory point of view in terms of safety, efficacy and quality of the products independently of the reimbursement conditions" *– Shaper expert (E21)*

Regulatory Fast Track:
"If you have to increase the review period and give a priority review to a product, it should not be based on vouchers, it should be based on needs...Personal view" *– Shaper expert (E21)*

Regional Regulatory Agencies in LMICs:
Refer to quote by Funder expert (E22) in 7.3.2. Section D. PSM 4S Principles: share Risks & Rewards.

Regarding **pull incentives** linked to **pricing**, the panel choice is illustrated in Table 7.22. As before, experts could select a up to four items with tophalf incentives on the next five. First, **outcome-based risk-sharing agreements** (i.e. conditional coverage of a certain population), such as managed entry agreements (MEAs). Second, **pooled procurement** to increase purchasing power, especially in LMICs. Third, **"Netflix" value-based pricing model**: annual subscription fee de-linked from volume for a given population over a period of time, as a managed entry agreement (MEA). Fourth, mentioned in equal manner as the previous one, the **risk-sharing agreements** based on **financial measures**, such as price-volume and budget cap, as a managed entry agreement (MEA). Lastly, **"beyond the pill"** valuing **prevention** and **promotion** initiatives.

37 **Table 7.22** R3 consensus PSM: Pull incentives (Pricing)

R3 Delphi survey (n=27, RR= 81%)

F-INCENTIVES			
STMT 3.41	**PULL Incentives.** PSM best new **Pricing model incentives** (panellists could select a maximum of 4 items).		
Top position	**Pull incentive**	**Frequency (#)**	**Frequency (%)**
1	Outcome-based Risk-sharing agreements (i.e. conditional coverage)	12	55
2	Pooled/Centralized purchasing specially for LMIC	11	50
3	Netflix pricing model	10	46
4	Financial-based Risk-sharing agreements (i.e. price-volume, budget cap)	10	46
5	"Beyond the pill" embracing Prevention and Promotion	8	36
6	Advanced Market Commitment	7	32
7	Bundle Payments care pathways	4	18
8	Not qualified	4	18
9	Renting production capacity	2	9
10	Other	1	5

Frequency (#) indicates the number of panellists who have selected the item and Frequency (%) indicates the corresponding percentage of the total number of panel respondants.
Netflix pricing model refers to an annual subscription fee de-linked from volume for a population and a certain period of time.

Expert Quotes

Outcome-based risk-sharing agreements (i.e. conditional coverage):
"We need to ask those drugs to proof that they are doing what they say they are doing, right? So, the only thing that, in my view, has worked really well for certain diseases or therapeutic areas are this type of, I think it's working well also in Europe, is this type of early launches *[Managed entry agreements (MEAs)/risk-sharing agreements]* ***so that you can start using the drug for severe use for certain patients in a very controlled manner. So that the drug gets to the patient as early as possible, which is also, should be also a driver***" – Payer expert (E08)

Netflix model (annual subscription fee de-linked from volume):
***"We needed some mechanism** [payment method for new antimicrobial products], **that allowed to reward companies when they bring products to market. (…) The de-link model, where companies get paid a setamount per year directly for the antibiotic but it's not proportionated to the volume of sales. And… payer perspective, health service perspective, the last option** [Netflix model] **is the most attractive because it directly addresses the problem, and it allows us to use contracts to not only bring new products to market, but also support the stewardship. If it both aligns the financial incentives to companies and the health service priority is stewardship"** – Payer expert (E25)

***"A very simple message, price-volume. Very simple message, let's start there. The value is a starting point, and then we negotiate from there. (…) I strongly advocate against value being the only criteria, because we've got to be realistic about your ability to pay and volumes"** – Shaper expert (E24)*

***"Sometimes we might build into some sorts of volume, some sort of "value cap" say, if we use higher volumes (…) spending doesn't go up, so the cost per patient comes down. That's a sort of way of trying to mitigate the risk to the health payer with the cost"** – Shaper expert (E25)*

See quotes in section 7.3.1 Case study 3 on pooled procurement for COVID-19 vaccines.

G. PSM Governance

The PSM implies rethinking the role of the government that empowers states to manage both individually and collectively the industry to reach the global health goals. Table 7.23 (R3 STMT 3.42) shows the ranking of the most suited institutions to lead the shift towards equitable PSM. Statements were selected from the R2 survey and interviews. The top one consensus organism to **lead** the **change** is the **EU,** given its characteristics and ongoing initiatives related to the EU pharmaceutical strategy and regulation, the definition and regulation of the Health Data Space, the EU4Health Programme in progress, among others. It is followed by a comprehensive **public-private consortium** representing the ecosystem. Third, a **reformulated WHO** that is more empowered and accountable is proposed. Finally, the **US** is also considered a good candidate to lead change given its dominant market position that involves MEDICARE (federal health insurance for people 65 and older, some young people with disabilities and people with end-stage renal disease) and MEDICAID (public health insurance for people with low income).

38 **Table 7.23** R3 consensus PSM: Governance

R3 Delphi survey (n=27, RR= 81%)

G-GOVERNANCE

STMT 3.42	**Preferred Supplier Governance. Ranked Lead organisations to pilot and implement the model** (with 1 being 'Most important' and 4 being 'Least important').

Rank	Statement	Value
1	EU lead given the European Pharma Strategy Amendment, EU Health Data Space, EU4Health, etc	42
2	Big public-private consortium for a 360º view	57
3	Reformulated WHO (more transparent and empowered)	59
4	USA lead as the main market, engaging MEDICARE and MEDICAID	62

Value indicates the aggregated rank value assigned by the panellists to each statement, meaning that the lowest the value the higher the rank postition.

Kendall's W for the ranked four potential lead organisations was 0.0983 (chi-squared 6.4909, degrees of freedom 3, p-value 0.0983, refer to Annex D, Table D1) reflecting weak agreement among the panel when prioritising the lead institutions. In other words, the panellists have not classified the different leading institutions by applying the same criteria to judge the importance of each of them (Field, 2005; Habibi et al., 2014). Statistically, there is no evidence that the raters are concordant in ordering the lead organisation, as the p-value is higher than 0.05 and the null hypothesis (Kendall's W equal to 0, meaning no consensus) can not be rejected at a significance level of 0.05 (Habibi et al., 2014; Okoli and Pawlowski, 2004).

Besides, Kendall's W for the governance leadership ranking was calculated for each expert segment, resulting in 0.2000 for payers, 0.0367 for performers, 0,467 for users, and 0.2000 for shapers (Annex D, Table D3). Even though the results showed moderate concordance in rating between users and weak concordance for the rest of the segments, the p-value was higher than 0.05 for all of them, so the the null hypothesis could not be rejected at the 0.05 significance level (Habibi et al., 2014; Okoli and Pawlowski, 2004). Thus, there was no concordance in the PSM governance ranking criteria for each key informant segment.

Regarding the **EU** as the top-ranked institution to lead change (Table 7.24), there is wide consensus among the qualified panellists that the PSM could be compatible with the European Pharmaceutical Strategy Amendment and its regulation (under development and approval process) (Table 7.24 (R3 STMT 3.43)). The PSM proposes a **provider accreditation** for public investment and procurement that **stimulates competition** and aims to improve **access** as promoted by the EU Pharmaceutical Strategy referring to ***"actions in the area of public procurement can foster competition and improve access".*** Moreover, the model could be **piloted** in the EU, involving some **member states** and evaluating the results with an **HTA** methodology (Table 7.24 (R3 STMT 3.44).

39 **Table 7.24** R3 consensus PSM: EU Governance

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
G-GOVERNANCE										
STMT 3.43	The **Preferred Supplier** model could be compatible with the **European Pharma Strategy** amendment and its regulation as a "provider accreditation" model aligned with the statement "**actions in the area of public procurement can foster competition and improve access**".	New	1	88	35	53	0	6	6	23
STMT 3.44	**Pilot the model at EU Member States** level (as pricing of medical products is a member state issue in the EU) and perform a Health Technology Assessment (HTA).	New	1	86	48	38	5	10	0	5

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; O, other responses (open text); NQ, participants who indicated that they were not qualified to respond.

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of agreement/disagreement.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Expert Quotes

EU lead:

"In Europe, since we have a larger public health sector, I think it's a good place to start" *– Shaper expert (E27)*

"The US is very fragmented market. Somewhere where you have sort of a central decision maker that can really provide access (…). If the European Union can make the member countries provide coverage and payment, then maybe, but I don't think we've seen that to date" *– Performer expert (E11)*

"The EU government because that's what decides on the financing and so on. And then big corporations, if, if they would change their mindset and would agree to participate in this kind of new model, then together with the government, the rest probably will come, even then the talk should start with academia and the smaller business sector, they adapt quickly" *– Performer expert (E01)*

Big public-private consortium for a 360º view:

"Create an international stable platform for multi-stakeholder agile scientific and public health dialogues to design and implement a public-private partnership consortium, different than current IMI, to address the public health needs" *– Performer expert (E02)*

Reformulated WHO lead:

"If the WHO could be (…) properly reformed, OK, I think that could provide the worldwide body, could give that overall orientation. I'm not asking the WHO to do everything" *– Shaper expert (E27)*

> ***"Kind of reform of WHO where there is more really a democratic environment and where member states are driving the discussions rather than non-state actors, and, you know, other players that somehow are now funding the agency and are, you know, intervening more on the priorities, on the agenda, on the programs. So, yeah, (…) WHO has a really member-state driven multilateral forum would be important and then, in that condition it would be the ideal player. (…) That's why WHO is, you know, what we still see as something that still reminds us of some good representation, at least in terms of countries"*** *– User expert (E14)*
>
> *Pilot the model at EU member states:*
> ***"Start with one example and really give a company credit. I mean, give a company look really good (…) an engaging in that. And then see if it creates momentum, you know, so that others could follow. But, as you say, you know, creating the example for industry instead of always the negatives. Because I think companies do want to meet unmet health needs"*** *– Performer expert (E11)*

7.3.3 Areas of the co-created PSM with no consensus or less agreement

In the final Delphi R3 survey, the co-revision of the PSM by the panel showed **no disagreement statements** in terms of "no consensus" (combined agreement <50%). However, three statements showed a **lower level of agreement** (combined disagreement > 25%) (Annex D, Table D8) as follows, including disagreement by segment and open-ended comments:

- **PSM: definition (less agreement).** Higher disagreement on the de-risk role of the public sector by increasing the R&D funding, especially among the shapers profile. Some panel members object the idea that by increasing public investment in R&D, this would be efficiently used by academia, startups and SMEs (assuming professional competence and impact-oriented R&D), requiring less private investment, thus leading to lower prices (Annex D, Table D8 (R3 STMT 3.8)). Moreover, regarding the comments ("other" open-ended question), a user expert claimed that increasing public R&D funding must include better management and a performer expert mentioned the need for support early and late-stage private sector innovation as well as market access.
- **PSM: risks and rewards (less agreement).** Some panellists, especially shapers and performers, also disagree to a large extent on the voluntary decision of medical companies to disclose private investment in R&I, particularly if it represents a large share (Annex D, Table D8 (R3 STMT 3.16)). One shaper panellist mentioned to prefer compulsory disclosure of private investment over voluntary disclosure. On the contrary, two others were not convinced by the measure, among them a shaper expert mentioned that medical corporates will be reluctant to share the allocation of the investment since much of it goes to marketing actions. On the other hand, price-volume negotiations (with a budget limit, so the cost per patient decreases as volume increases) are less preferred especially by performers (Annex D, Table D8 (R3 STMT 3.20)).

Regarding PSM co-creation in preliminary Delphi surveys, the panel did not reach consensus on 7 statements in R1 and 6 statements in R2 as follows, including open-ended comments (Annex B, Tables B4-B11; Annex C, Tables C3-C7).:

- **PSM specified Normative preferences (no consensus):** Cohort B opposed to the specification of norm 2 on efficiency in the R&I system (Annex B, Table B4 (R1 STMT 12)), as well as the PSM "4 Share" principles (Annex B, Table B4 (R1 STMT 10)). Given its relevance, the first statement was carefully revised and the second was reformulated into other statements included in R3.
- **PSM governance (no consensus)**: Cohort A disagreed with the creation of a public-private consortium to lead the PSM (Annex B, Table B7 (R1 STMT 31, 32, 33). It preferred either a wide syndicate to promote dialogue between stakeholders and define a value framework of values, or the leadership of a regional government institution such as the EU or the African Union, or of a revised WHO for priority setting. Cohort A expressed concern about the consortium being viable and nations ceding autonomy to regional governments or multilateral institutions like the WHO. Cohort A was also skeptical about undertaking PSM as an incremental change in the industry with business as usual but redirected (Annex B, Table B7 (R1 STMT 34)).
- **PSM needs (no consensus**): Cohort A considered it difficult for governments to determine a list of health priorities based on the UN SDGs and establish incentives that include market access facilities (Annex B, Table B8 (R1 STMT 36)). In this sense, there are concerns about how the SDGs are respected and agreed upon. Cohort B resisted endorsing the "citizen-in" strategy that includes prevention and promotion (Annex B, Table B8 (R2 STMT 18)).
- **PSM risks and rewards (no consensus**): Cohort A differed in prioritising disruptive versus incremental innovation (Annex B, Table B9 (R1 STMT 40)). It also considered the difficulty to implement a bundled payment that covers all services involved in a patient's episode and therefore linked to health care outcomes (large population indicators) (Annex B, Table B9 (R1 STMT 42)). Cohort B disagreed to tracking public and private R&D investment to affect the product price in exchange for market access commitment (Annex B, Table B9 (R2 STMT 19)). This cohort also refused to link price to impact (related to disruptive innovation) modulated by tracking R&D cost and investment (Annex B, Table B9 (R2 STMT 20)). Concerns about the use of disruptive innovation in the latest statement required revision.
- **PSM outcomes (no consensus**): Cohort B showed no agreement on measuring outcomes holistically with the triple or quadruple aim approach, with two experts requiring clarification of the definition of the statement and one requiring inclusion of the economic perspective of the contribution of the biomedical sector to national income (Annex B, Table B10 (R2 STMT 25)).

7.4 BARRIERS AND ENABLERS OF THE CO-CREATED PREFERRED SUPPLIER MODEL (O4)

This section presents the ranking of the main barriers (Table 7.25) and enablers (Table 7.26) to pilot and implement the new model. The statements were identified during R1 and R2 interviews and surveys. The results presented correspond to the R3 final survey, complemented by the calculation of Kendall's W for ranked questions and selected quotes from interviews and surveys.

Barriers

Lack of health system capacities in **LMIC** is the top-ranked barrier noted by the panel to implementing the co-created PSM (Table 7.25). The second barrier is the challenge of reaching an international agreement that stablish a **tiered pricing system** based on the **ability to pay** (i.e. GDP per capita). **Industry lobbying** on health policy and the **postponement of data legislation** in terms of ownership and access are mentioned equally in third and fourth position. Finally, **dispersion** in government healthcare decision-making is the fifth top barrier. Other difficulties are the insufficient orientation and training of the academia towards the open innovation approach, an R&I system led by venture capital with a short-term ROI, long development timelines of up to ten years and the cognitive dissonance (inconsistent thoughts, beliefs, and attitudes related to behavioral decisions).

40 **Table 7.25** R3 consensus PSM: Barriers

R3 Delphi survey (n=27, RR= 81%)

STMT 4.1	Rank the following main barriers to implement the new co-created PSM (with 1 being 'Most important' and 9 being 'Least important').	
Rank	**Statement**	**Value**
1	Lack of health system capabilities, especially in LMIC	86
2	Difficulty of global commitments to reward innovation based on the ability to pay	92
3	Industry lobby in health policies	108
4	Delay in data ownership and access legislation	108
5	Governments decentralized decision making	114
6	Lack of academia preparation for Open Innovation	115
7	US Venture Capital led by short-term ROI	118
8	R&D length of time (i.e. a decade)	120
9	Cognitive dissonance between the sectors	129

Value indicates the aggregated rank value assigned by the panellists to each statement meaning that the lowest the value the higher the rank postition.

Kendall's W test applied to the nine ranked PSM barriers was 0.0508 (test of significance: chi-squared 8.9333, degrees of freedom 8, p-value 0.3480, see Annex D, Table D1), reflecting a weak level of agreement among the panellists on the priority range assigned to each barrier. The raters were **not** significantly **concordant** when **prioritising** the barriers, since the p-value is greater than 0.05 (Habibi et al., 2014; Okoli and Pawlowski, 2004). That is, the experts disagreed with each other in the classification of each barrier.

Furthermore, Kendall's W for PSM barriers was calculated for each expert segment to detect possible rating concordance in each cluster. The result was a Kendall's W of 0.2667 for payers, 0.0762 for performers, 0.4889 for users, and 0.1074 for shapers (Annex D, Table D4). Even if the results showed moderate agreement between the rating preferences of the users and a weak agreement among payers, performers and shapers, the p-value higher than 0.05 implied that the null hypothesis could not be rejected at the level of significance of 0.05 (Habibi et al., 2014; Okoli and Pawlowski, 2004). Accordingly, there was no concordance in the criteria for classifying PSM barriers for each key informant segment.

Expert Quotes

Barrier – Lack of health system capabilities:
"Pricing really is not independent of the (…) health care infrastructure. So, (…), the charge in a particular country is certain amount for a pharmaceutical because there is the capacity to utilize and absorb the pharmaceutical because the appropriate number of specialists, and clinicians, and hospital beds, and diagnostic procedures, and diagnostic infrastructure, and distribution infrastructure exist, and that is hardly consistent from country to country*" – Funder expert (E22)*

Barrier – Lack of health system capabilities and Difficulty of global commitments to reward innovation based on the ability to pay (tier pricing):
"Absolutely, there needs to be a differential pricing approach based on the ability to pay. The challenge is how do you actually implement something like that? I mean, again, differential pricing is not new. It's just very difficult to implement in countries where there is no infrastructure (…) or where there is very little government oversight and overview of how much money people are living off" *– Payer expert (E18)*

Barrier – Difficulty of global commitments to reward innovation based on the ability to pay (tier pricing):
"It would be much more efficient if we had certain overall agreements that say, I mean, this is the principal how we set the price for Nigeria and for Kenya and other countries, so if we have a price of 100 that has been set in Europe, then, is automatically clear that these countries pay 17 or 15 or 20 depending on these things *[economic ability]****"*** *– Shaper expert (E12)*

Barrier – Industry lobby in health policies:
"Pharma companies have so much money for lobbying, and that's what prevents us in many ways from making progress. So, (…) we need either to limit that lobbying or we need to have as much lobbying" *– Shaper expert (E17)*

Barrier – Delay in data ownership and access legislation:
"How acceptable is all of this? What would it generate? and also what could be the unintended consequences of having all this data? What are we trying to achieve with all of this? Before talking about data privacy and data security*" – Shaper expert (E13)*

"It's important to develop a common approach, or a common concept of ownership and sharing of the results, failure or not failure" *– Shaper expert (E26)*

Enablers

The **incremental change** balancing risks and rewards proposed by the PSM is considered the top driver of its pilot and implementation. The other two highest-ranked facilitators are the **industry** embracing equity practices as **"responsible capitalism"** and **investors claiming** that the industry **disclose** fair practices. As an example of the former, Pfizer launched the "Accord for a Healthier

World" initiative to close the health equity gap, committing access to its full portfolio of patent-protected drugs and vaccines at non-for-profit prices for all 45 lower-income countries. Current available **digital technology** is the fourth ranked enabler. The **Access to Medicine Index,** as a benchmark measure of health equity, closes the top half of ranked facilitators. Other drivers are **standardized** sets of **indicators** based on **value-based outcomes,** such as COMET (Core Outcome Measures in Effectiveness Trials) in clinical trials and ICHOM (International Consortium for Health Outcomes Measurement) in healthcare. Moreover, the pharmaceutical industry reaction to maintain its **leadership** against newcomers from other sectors, such as Google, Amazon and Apple. The progressive adoption of **compulsory ESG** KPI reporting in several countries and the formulation of a **WHO Pandemic Treaty** close the ranking of facilitators.

41 **Table 7.26** R3 consensus PSM: Enablers

R3 Delphi survey (n=27, RR= 81%)

STMT 4.2	Rank the following main enablers to implement the new co-created PSM (with 1 being 'Most important' and 9 being 'Least important').	
Rank	**Statement**	**Value**
1	Incremental change with balanced Risks & Rewards	90
2	"Responsible Capitalism" by industry i.e. Pfizer with ACCORD	98
3	Investors requiring company disclosures	100
4	Digital technology available	108
5	Access to Medicine Index as a reference	113
6	Outcome standards with COMET & ICHOM for data aggregation	115
7	Pharma leadership in front of Amazon, Google, Apple incomers	115
8	Compulsory ESG KPI in different countries	125
9	WHO International Pandemic Treaty	126

Pfizer with ACCORD patent-protected drugs & vaccines at cost price for 45 lower-income countries.

Value indicates the aggregated rank value assigned by the panellists to each statement meaning that the lowest the value the higher the rank postition.

Kendall's W for the nine ranked enablers was 0.0409 (chi-squared 7.2, degrees of freedom 8, p-value 0.5152, refer to Annex D, Table D1), reflecting a very low degree of agreement on the panel. That is, the experts applied different criteria to judge the importance of each driver (Habibi et al., 2014; Okoli and Pawlowski, 2004). In addition, Kendall's W was calculated for enablers for each expert segment, resulting in 0.4296 for payers, 0.1150 for performers, 0.3000 for users, and 0.1255 for shapers (Annex D, Table D5). Although the results showed moderate agreement among payers' rating preferences and weak agreement among the other segments, the p-values greater than 0.05 implied that the null hypothesis could not be rejected at the 0.05 level of significance (Habibi et al., 2014; Okoli and Pawlowski, 2004). Hence, there was no concordance in the ranking criteria of PSM enablers for each expert segment.

Expert Quotes

Enabler – Incremental change with balanced Risks & Rewards:
"I do support the idea of the basic concept of, you know, trying to introduce change in a way that looks good, that sort of (…) looks incremental. (…) I think the Preferred Supplier model is clever. I think it's a very promising way forward" *– Funder expert (E03)*

"Restructure the current incentive system somehow. (…) Incentives to increase profitability in areas where we need it. Then, in the other

direction, try to (…) use measures to try to, yeah, basically to not have payers pay so much for those certain areas already too lucrative" – *Shaper expert (E17)*

Enabler – "Responsible capitalism" by industry (i.e. Pfizer with ACCORD patent-protected drugs):
"I noticed recently Pfizer started advertising that they're making their products more available for LMICs. So, I assume their motivation is just publicity in the US or Europe to make them look like good corporate citizens rather than they've got somebody who's genuinely interested in low income, low- and middle-income countries. But, again, that maybe sounds cynical… But it'd be interesting to know what it was that influence that decision process? So, how they are being threatened with something else that made preferential to do something themselves? Start making things available before they are pushed into that" *– Payer expert (E25)*

Enabler – Investors requiring company disclosures:
"The definition of success has to be changed or altered. Some companies have created Global Health business units, Novartis, Sanofi, that have different KPIs that are where they measure success based on (…), in the case of Novartis, for example, the number of patients reached. Now, it turns out that, (…) increasing the number of patients reached also created a modest profit, so that worked out well. (…) And the reason why Novartis did it that way, as they actually would get success and recognize success in the form of better ESG metrics, and there is potentially more investment from a pool of investors who are interested in ESG. The fact that they also turned a profit, it's a nice bonus" *– Payer expert (E18)*

Enabler – Digital technology available:
"I think that one of the drivers that really can bring costs down is things like digitalization, everything that happen now is accelerated by COVID" *– Funder expert (E08)*

"We have smartphones and we have electronic prescribing even in these places *[LMICs],* ***some of these countries are more advanced than Europe when it comes to electronic money and the use of smartphones, so I think (…) the technology exists in order to implement these things"*** *– Shaper expert (E12)*

7.5 POLICY RECOMMENDATIONS (O5)

This section identifies the main **policy recommendations** emerging from the final R3 Delphi consensus statements of the co-created PSM, leveraging the ranked barriers and enablers, as well as lessons learnt from the case studies. Incentives and regulation are included to facilitate the implementation of the new model backed by the literature review. The expert panel involved in co-creating the PSM encourages national and international stakeholders to consider

the following six recommendations and related actions to promote equitable health innovation (National Academies SEM, 2023).

Policy Recommendations for equitable health innovation based on the co-created Preferred Supplier model (PSM)

Target: national/regional goverments, intergovernmental forums (i.e. G7, G20), multilateral institutions (i.e. WHO and other UN Agencies, WTO, World Bank, IMF), philanthropists, venture capital firms, venture philanthropists, impact investors and large corporations, among other interested parties.

1. **Governance:** EU leadership in a collaborative public-private ecosystem.
2. **Social choice:** open dialogue for a value framework defining Global Health challenges.
3. **Transparency**: disclosure of publicly funded health innovation.
4. **Social business**: Preferred Supplier as a social business accreditation.
5. **Intellectual property**: foster the implementation of the WTO TRIPS flexibilities.
6. **Impact investment**: strong push for impact investment in health innovation.

GOVERNANCE

REC1. EU leadership in a collaborative public-private ecosystem.

- **The UE is the institution best positioned to further develop and test the co-created PSM**, accompanied with a collaborative private-public ecosystem, a reformulated WHO and the US, as the leading market. Key factors favoring the EU leadership are the social security system, EU Pharmaceutical strategy regulation, European Health Data Space, New European Innovation Agenda, EU Global Health Strategy, the Next Generation EU funds, the European HTA network (EUnetHTA), among others (De Jongh, Velten, Schrijver, 2021).
- **Combine a centralised decision process with a decentralised national approach** with high-profile managers.
- **Promote strategic public-private partnerships** as key enablers of equitable and sustainable health outcomes (Akomea-Frimpong et al., 2023; Ballantyne and Stewart, 2019; Baxter and Casady, 2020; Davis et al., 2021).

Main statements (Tables 7.13 – 7.26): R3 STMT 3.42, 3.43 and 3.44.
Case studies (Tables 7.10 – 7.12): Rare diseases and COVID-19.

SOCIAL CHOICE

REC2. Open dialogue for a value framework defining Global Health challenges.

- **Establish a value framework with equity and efficiency principles** as a normative social choice defined by countries and regions with underlying social values (Cairney et al., 2022; Charlton et al., 2023). Value criteria should balance epidemiology (i.e. burden of disease), market failures (i.e. small populations, low ability to pay, restricted use) and public health emergencies (i.e. pandemics) maximising population health in terms of health system perspective.

- **Define and align priority global health challenges** with the value framework as demand-driven R&I and conduct constant **horizon scanning** of **needs** (National Academies of SEM, 2023; Tong et al., 2019).
- **Reinforce health emergency prevention, preparedness, response and resilience (HEPR)** contributing to the efforts of WHO and the Member States to translate ideas into concrete actions to save lives and reduce morbidity (WHO, 2023m).
- **Incorporate the One Health and Planetary Health approach** to address the Triple Planetary Crisis: climate change, biodiversity loss, and pollution and waste management (IPCC, 2023; Talukder and Hipel, 2022; UN Climate Change, 2022).
- **Strengthen health prevention and the promotion** of the planned innovative solutions.
- **Expand culture, knowledge and participation in Open Innovation** in health (Bullinger et al., 2012; Liu and Yang, 2022; Prado, Sánchez-Gómez, Casamitjana, Espriu et al., 2023).
- **Promote the health in All policies** (HiAP) approach with whole-of-government and whole-of-society initiatives (Ortenzi et al., 2022; Ramírez-Rubio et al., 2019).
- **Regulate industry lobby** in health policies.

Main statements (Tables 7.13 – 7.26): R3 STMT 3.1, 3.11, 3.41. 4.1.
Case studies (Tables 7.10 – 7.12): Rare diseases, HIV/AIDS and COVID-19.

TRANSPARENCY

REC3. Disclosure of publicly funded health innovation.

- **Enforce regulation on health data ownership, sharing and use of Artificial Intelligence (AI)** resulting in a public database for all publicly funded R&I projects. Legislation on ethical innovation, such as the application of AI in health (European Parliament, 2023b; Guenat et al., 2023; Morley et al., 2020; National Academies of SEM, 2023) and digital health equity (Crawford and Serhal, 2020) should be included, as well as an efficient privacy and security management (Dhasarathan et al., 2023).
- **Regulate the mandatory disclosure of scientific data** for all biomedical R&I projects that receive public funding (not only for Preferred Suppliers). Create health data spaces, such as the European Health Data Space (EHDS) (EC, 2023e, European public-private partnership Health Outcomes Observatory H2O, 2023; Shabani, 2022) to incorporate patient-reported outcome measures (PROMs) and patient-reported experience measures (PREMS) into decision-making (Stamm et al., 2021). Take advantage of the NIH clinical trials registry (clinicaltrials.gov). The health data space should share and integrate scientific data at 3 levels: R&I project pipeline, raw data and results (clinical trial, real-world evidence), including failure, allowing the use of advanced analytics (Odone et al., 2019; Tanveer et al., 2022), and complemented by R&I connecting platforms (i.e. EC Horizon Results Platform). Apply Medicine Adaptive Pathway to Patients (MAPPs) with iterative development for patients' progressive access to medications (Bouvy, Sapede and Garner, 2018). For results, it could be given a certain period of time and/or a license, except in the case of a Global Public Health Emergency. This action is aligned with the concept of scientific knowledge as man-made global public good (Kaul et al., 1999)
- **Regulate compulsory disclosure of public R&I funding** for all publicly funded health projects (not just Preferred Suppliers). Establish a public R&I funding tracking system linked to commercial asset (i.e. patents, registered software) and tagged with the SDGs

by applying blockchain technology (Leeming, Ainsworth and Clifton, 2019; Roychowdhury, Shroff and Verdi, 2019; Xie et al., 2021).

Main statements (Tables 7.13 – 7.26): R3 STMT 3.15, 3.16, 3.17, 3.30, 3.31, 3.35, 3.36, 4.1.
Case studies (Tables 7.10 – 7.12): Rare diseases, HIV/AIDS and COVID-19.

SOCIAL BUSINESS

REC4. Preferred Supplier as social business accreditation.

- **Develop the Preferred Supplier accreditation as a condition for public health funding and procurement**. In the PSM, biomedical companies engaged with environmental and social practices (health equity and data sharing) get credit through incentives and sales of innovative solutions as preferred providers of the public sector for priority health challenges. In this sense, the PSM promotes social businessess as a responsible capitalism approach (doing good and making profit).
- **Outline a hybrid PSM Risk-Impact pricing model modulated by the ability to pay.** Identify the impact (value-based, i.e. MEAs) (A Vreman et al., 2020) adjusted for the risk assumed throughout the development pipeline defined by the disclosure of public (and private) R&I funding linked to the asset (i.e. patent, registered software). Moreover, encourage Preferred Suppliers to modulate prices in LMICs through price segmentation according to the countries' ability to pay (i.e. GDP per capita) (i.e. VAMOHS initiative, USAID, 2020b) and voluntary licenses (Biancalani, Gnecco and Riccaboni, 2022; Moon et al., 2020). The hybrid model would promote market competition with early access to low-cost healthcare innovation.
- **Define an Access to Medicine Index (ATMi)-like to measure the PSM "4 Share"** principles (sharing needs, results, risks and rewards, and outcomes) as an outcome-based KPI for biomedical companies to be audited annually. Include voluntary licensing and avoidance of evergreeeing as a favourable practice (sharing risks and rewards) to become a Preferred Supplier.
- **Elaborate the PSM regulation for the 4 audited indicators** (ESG, ATMi-like, disclosure of scientific and financial data) that the company must present when submitting the regulatory file. This would define the PSM accreditation status once the product has marketing approval, allowing the Preferred Supplier company to be eligible for innovative public procurement for better health oucomes (García-Altés et al., 2023; Torvinen and Jansson, 2023).
- **Design the PSM push and pull competitive incentive scheme conditional on commitment to global access and data sharing** that leads to equitable and faster outcomes. Promote push incentives that reinforce R&I public grants and investment as well as R&I tax credits that crows-in privatively financed investments (Bloom et al., 2019; Soete, Verspagen and Ziesemer, 2022; UK Government, 2020). This measure could especially accelerate the growth of deep tech startups and SMEs, as proposed by the new European Innovation Agenda (EU, 2022) with funding of €45 billion of private capital for deep tech scale-ups by 2025. Pull incentives such as regulatory procedures (i.e. regulatory and HTA aligment, FDA-EMA alignment, fast-track, regulatory extensions), new pricing models with Managed Entry Agreements (MEAs) (i.e. risk-sharing, Netflix decoupled model) (A Vreman et al., 2020), centralised purchasing (McEvoy and Ferri, 2020; So and Woo, 2020), "beyond the pill" approaches, premarket purchasing commitments, among others.

- **Define PSM target companies.** Preferred Supplier accreditation could initially apply to **large and listed biomedical companies** (i.e. >500 employees or > €500 million turnover) and progressively incorporate SMEs. Push incentives would mainly benefit academia, startups and SMEs discovering potential solutions, while pull incentives would mainly benefit large accredited Preferred Supplier companies and progressively include SMEs.
- **Promote early partnerships and accelerators around moonshot missions and open innovation environments**, spanning Preferred Suppliers and patients, academia, SMEs, providers, regulators, payers and policy makers networks and clusters. For instance, the Plug and Play Tech Center innovation platform to develop and deploy new technologies with an ecosystem of 50,000 startups, 500 world-leading corporations and hundreds of VC firms, universities and governmental agencies across multiple industries.
- **Leverage PSM enablers to engage industry and investors,** such as the incremental change proposed by the model with balanced risks and rewards, the growing role of the industry as a responsible market player, investors demanding company disclosures, the digital technology available and the Access to Medicine Index as an existing reference measure, among others.
- **Pilot the model and evaluate impact.** Develop the model further and test it, for example, with one or two companies and EU countries. As leaders of the process, public payers could take on more risk initially, avoiding putting too much risk on providers. That is, payers could pay providers the traditional fee-for-service or product and collect outcomes-based data that shows providers how much they would have been payed (ICHOM, 2023). Sharpen the monitoring and evaluation along the innovation life cycle (National Academies of SEM, 2023), carrying out HTAs and HIAs for the population and health systems. Measure industry KPIs such as R&D elasticity (percentage increase in output resulting from a 1-percent increase in R&D inputs) (Coluccia et al., 2020; National Academies of SEM, 2023; Paolone et al., 2022) to increase the buy-in of the private sector.

Main statements (Tables 7.13 – 7.26): R3 STMT 3.2, 3.3, 3.5, 3.6, 3.7, 3.8, 3.9, 3.10, 3.12, 3.13, 3.14, 3.17, 3.18, 3.19, 3.20, 3.21, 3.23, 3.24, 3.25, 3.26, 3.27, 3.29, 3.30, 3.31, 3.32, 3.33, 3.34, 3.35, 3.36, 3.37, 3.38, 3.39, 3.40, 3.41, 4.2.
Case studies (Tables 7.10 – 7.12): Rare diseases, HIV/AIDS and COVID-19.

INTELLECTUAL PROPERTY

REC5. Foster the implementation of the WTO TRIPS flexibilities.

- **Fast-track TRIPS IPR flexibilities to ease waivers and compulsory licenses.** This measure would apply to the production and export of WTO member states for health priorities in application of TRIPs flexibilities (Correa, 2022; Correa and Hilty, 2022; El Said, 2022; Mercurio and Upreti, 2022; Tenni et al., 2022; Vawda, 2022; Vawda and Shozi, 2020; Wong, 2020).
- **Advocate for voluntary licensing by industry patent holders to low-cost manufacturing countries** (i.e. Brazil, Russia, India, China and South Africa, BRICS) to market in LMICs (Morin et al., 2023; Pandey, de Coninck and Sagar, 2022). This measure side-steps compulsory license accelerating and facilitating TT. It can be

channelled through a governed technology access fund, such as the MPP (Van De Pas et al., 2022) or the Health Impact Fund (HIF) (Lee, Yao and Zhang, 2021). Include this criterion in the PSM accreditation.

- **Increase competition avoiding patent abuse by strengthening national or regional patent offices** to fight against the practice of multiple patenting (evergreening). Potentially include this criterion in the Preferred Supplier accreditation (Vawda, 2022).

Main statements (Tables 7.13 – 7.26): R3 STMT 3.1, 3.2, 3.4, 3.5, 3.7, 3.8, 3.11, 3.14, 3.15, 3.17, 3.19, 3.21.
Case studies (Tables 7.11 and 7.12): HIV/AIDS and COVID-19.

IMPACT INVESTMENT

REC6. Strong push for Impact Investment in health innovation

- **Catalyse investment in health innovation in LMICs through global consortia.** Support partnership between Preferred Suppliers and global development actors (i.e. World Bank, philanthropists, impact investors) investing in health innovation infrastructure (including laboratories, digital information systems, surveillance platforms, production, distribution), negotiation, implementation and evaluation skills in LMICs (Cortes et al., 2020; Harman et al., 2021; Hemerijck, Mazzucato and Reviglio, 2020; Inrate, 2023; Lee, Lee and Liu, 2023; Malekzadeh et al., 2020; Panzer et al., 2020; Sparkes et al., 2019; Uppal et al., 2021). In return, governments would simplify procedures for private sector participation and facilitate market access with, for example, regional HTA Agencies (i.e. in West and East Africa) to produce high-quality evidence and facilitate TT (Mueller, 2020; Falkowski et al., 2023; Hollingworth et al., 2020; Hollingworth et al., 2021; Kumar et al., 2021; Panzer et al., 2020). This initiative could be fueled by mobilising impact investments with performance-based returns (i.e. social bonds) (Peeters, Schmitt and Volk, 2020) that provide fiscal incentives to private investors by national or regional governments. The new WHO International Treaty on Pandemic Preparedness and Response (in preparation) could contribute to strengthening capacities in the Global South (Hannon et al., 2022; Phelan, 2023; Velásquez and Syam, 2021; Vinuales et al., 2021). The activation of the US-led G7 Build Back Better World (B3W) (Chatham House, 2022; Savoy and McKeown, 2022) and the EU Global Gateway (EC, 2023f) initiatives, both launched in 2021 to invest in key infrastructure and establish economic associations, could be possible enablers of investment in R&I. Cooperation with China and other non-Western development partners is considered necessary for success (Chatham House, 2022).

Main statements (Table 7.16): 3.22.
Case studies (section 7.3.1): HIV/AIDS and COVID-19.

In general, the PSM should embrace the **5 "S"** for change (Newman, 2020) among stakeholders: surprise (create an experience to share the idea that will surprise them), strategy (show what's in it for them), seductive (be part of the global good), sustainable and simple.

8 DISCUSSION

The unanimous desire to improve health equity claimed by the broad panel of experts in this study contrasts with the little policy action taken. As a main objective, the study reached consensus on the principles and specifications of a new co-created health R&I process based on the Preferred Supplier model (PSM).

Which are the consensus grounds and conditions for equitable health innovation?

We hypothesised that the new model should be built on a social choice, with the values and interests of the different stakeholders, and be based on public purchasing power. It was also assumed that the new model should provide the necessary incentives and risk-leveraging practices aligned with public health priorities, resulting in a new fair play for equitable, agile and sustainable outcomes. To co-design the new model, we specified five objectives, research questions and hypotheses, including policy recommendations. The validation of the hypotheses is shown in Table 8.1.

42 **Table 8.1** Hypotheses validation

HYPOTHESES		CONFIRMATION
H1	There is a moral dilemma in health innovation that, when incentives are not aligned with public health priorities, efficiency (in terms of commercial rewards) takes preference over equity, resulting in a health equity problem.	Equity and efficiency (cost-effectiveness) were considered the main consensus values of the health R&I model. This research confirmed the moral dilemma, as meeting efficiency often prevents meeting equity when incentives are not fully aligned with public health challenges. This moral conflict results in an equity and speed problem with health innovation not reaching citizens fast enough and in an equitable and sustainable manner.
H2	Consensus main causes that prevent equitable health innovation are related to the lack of sharing needs, results, risks and rewards, and outcomes, in addition to the lack of governance.	There was consensus on the main causes of the problem due to the lack of the "4 Share" (4S) principles and leadership. The top-ranked consensus causes were the lack of alignment between incentives and public health priority agenda (comprising the SDGs), followed by unequal distribution of risks and rewards; early-stage developers lack of funds and alignment with priority health challenges; high prices due to patent abuse and value-based pricing; as well as lack of transparency in scientific and financial data.
H3	Governments, as major investors and buyers of biomedical innovation, are well positioned to drive industry toward environmental and health equity practices and get credit as Preferred Suppliers, by aligning incentives to public health priorities in accordance with the "4 Share" principles (sharing needs, results, risks	The panel agreed on the public sector driving health innovation through the PSM 4S principles and conditions as follows: 1) The efficiency norm was specified incentivising health challenges affected by market failure to solve the moral dilemma and reach equilibrium between equity and efficiency principles.

	and rewards, and outcomes) and adequate governance.	2) Provide meaningful incentives for health priorities conditioned on global health equity and environmental practices through the application of the 4S principles (sharing needs, results, risks and rewards and outcomes), and with the appropiate PSM accreditation regulation and governance. Push incentives (R&I funding) mainly targeting early-stage developers (academia, start-ups, SMEs) and pull incentives (commercialization) mainly benefiting accredited Preferred Supplier large corporates. Four annually audited KPIs would be reported to the regulatory agency: ESG, disclosure of R&I scientific and financial data of publicly funded projects as general indicators and, additionally, Preferred Suppliers would be required to report an Access to Medicine index-like to measure the PSM "4S" principles, as an outcome-based KPI for biomedical companies. 3) The EU is well positioned to lead the PSM due to the social security provision and the programmatic, funding and regulatory framework.
H4	The key PSM barriers are related to the health systems capabilities, the pricing scheme and the dominant position of the industry in health policies. The key PSM enablers are related to expanding ESG practices.	The need to increase health systems capacities in LMICs, the difficulty of a transparent global tier pricing scheme and the industry lobby in health policies were confirmed as the main limitations of the PSM. Instead, the main PSM drivers agreed were the PSM balance of risk and rewards as incremental system change, increasing social responsibility practices by industry (and getting credit as Preferred Suppliers), and investors requiring industry disclosures.
H5	Policy recommendations should consider appropriate incentives and regulation to promote the implementation of the consensus PSM.	This research has identified six policy recommendations related to governance, social choice, transparency, social business, IPR and impact invesment derived from the consensus PSM. They include the necessary incentives and regulation to further develop and pilot the model (see section 7.5 and a summary in the conclusions).

Six main strengths define the contribution of this PhD study to the literature. Among them, three can be considered internal strengths: the consensus on PSM as a new equitable R&I model, obtained with a diversified elite panel and a high response rate. The three remaining strengths are the contribution of the PSM to the previous models (see section 2.2), namely the ethical approach of the PSM, its specification (principles, indicators, incentives and regulation requirements), and the PSM as a social business for greater collective reward (Pareto efficiency).

As for the three main internal strengths of the PSM, first, I believe the main study contribution is a **consensus new equitable health R&I model** applying a multi-stakeholder constructive HTA

and an iterative Delphi methodology. By completing the model with new and revised statements, and by demonstrating greater agreement in each successive Delphi round, this method has proven to be effective in sharing and valuing the views of different stakeholders among the panel. As a result, all co-created PSM statements in the final R3 survey have shown simple or supermajority consensus and, in some cases, reached unanimity. Second, the choice of a representative **elite panel** to collect the views of various stakeholders was the core of this study. The sequential sampling approach with the elite group, the two expert cohorts and the snowball process (refer to 6.4.2 Expert panel member sample) contributed to maximize the value of the purposive sampling with a diverse, knowledgeable and motivated panel. In terms of validity, participants are representative of the group of knowledge in terms of segment, sub-segment, gender, public-private sector, followed by sector, country and region of work, age, and years of work experience (Keeney et al., 2001). And third, the **high response rates** to the initial survey (R1 RR=90%), the one-hour interviews (R1 RR=100%; R2 RR=100%), and the three rounds of Delphi scoring suveys (R1 RR=80%; R2 RR=88%; R3 RR=81%) reflect the rigorous implementation of the method and the high level of commitment of the experts. The panel has counted on candidates highly motivated by the topic of the study applying the snowball technique and the ratification of their suitability based on profile and availability. In addition, the design of two sequential cohorts significantly reduced the experts' dedication to two or three surveys (cohort B and A, respectively) and one hour-long in-depth interview per expert. Regarding ethics, we consider that experts responded with honesty and according to their perception of what the researcher expected (Keeney et al., 2001).

Moreover, the PSM creates value with respect to the previous models, the "public value" and the "shareholder" models (see section 2.2) as an alternative desired and potentially plausible model bringing in the values and interests of the different stakeholders. In this sense, the PSM has three main comparative strengths regarding the preceding models. First, **PSM ethical approach,** raising this question*: is equity in medical R&I a societal or individual responsibility, in terms of requiring the government or the industry lead?* Probably both, but necessarily catalised by the government. In a market economy, health industry is led by profit, driving the R&I agenda and delivery. Thus, individual behavior of medical companies plays a significant role in the equity gap. Nonetheless, there is a strong social pressure and an increasing policy regulation for responsible innovation fulfilling social and environmental practices. Investors and donors demand transparency and evidence that the industry walk the talk. As a reaction, governments should be the market shaper rather than mere regulators, pulling together public, private and civil society actors for the **common good** (Mazzucato, 2023b). The PSM proposes that governments and multilateral organisations set the scene to attract companies and investors as relevant **social actors** in a **responsible capitalism**, leading health solutions for public health needs yet making reasonable profit. The PSM fosters competition amongst biomedical developers and producers to create better innovative and equitable solutions for the common good. The identification of values and appropriate policy strategies should be defined per region due to epidemiological, cultural, and socio-economic specifics. The second comparative strength refers to the **PSM specifications**. The PSM was perceived by the panel as an **incremental change** in the current R&I system, balancing risks and benefits (*business as usual but re-directed*) facilitating its implementation. The PSM "4S" principles were defined in ISGlobal's policy brief (Alonso et al., 2021a and 2021b). The foremost difference between the initial PSM proposed in the ISGlobal brief and the final consensus model peer-reviewed by the panel of this research concerns the specifications of the model for achieving equitable innovation: 1) **Accreditation** through **4 KPIs,** namely the **ESG, ATMi-like** as well as **scientific** and **funding data sharing** of all innovations receiving public R&I funding to be reported to the regulatory agency when submitting the regulatory file; 2) **Tracking public R&I funding** linked to the commercial asset (i.e. patent, registered software) along the value chain using blockchain technology; 3) **Hybrid risk-impact pricing**, where risk is measured by the funding mix (involving the publication of public

R&I funds) and impact by the revised value-based pricing (i.e. MEAs) (A Vreman et al., 2020; Bouvy et al., 2018) **modulated** by the **ability to** pay (i.e. GDP per capita) through tier pricing and voluntary licensing (Biancalani et al., 2022). The PSM could apply to deep-tech pharmaceutical, biotech and digital health companies developing innovative solutions for health impact (Brewer et al., 2020; WHO, 2021b). The third strength refers to the **social business** for higher collective reward. Overall, consensus on PSM among stakeholders is a way to solve the prisoner's dilemma to reach a **Pareto efficient equilibrium** as a social choice through the necessary incentives and regulation (Horne and Heath, 2022). The prisoners' dilemma game theory represents a paradox in decision analysis in which two rational agents acting in their own self-interest do not produce the optimal collective outcome. Agents have the choice to cooperate with their partners (i.e. other firms) for higher mutual reward (efficient Pareto equilibrium) or betray their partner ensuring some individual reward (sub-optimal Nash equilibrium), which is the strong equilibrium point reached with the current health R&I system. Cooperation to maximize everybody's rewards (Pareto equilibrium) requires **incentives, trust** (or **regulation**), and **communication**. That is what the PSM aims to provide, promoting a turning point towards social business, embracing **open innovation** (Liu and Yang, 2022), **responsible KPIs** and **fair reward**. The open innovation approach is an opportunity to integrate expertise in early-stage R&I contributing to de-risk the projects. In addition, the model proposes the **ATMi-like index** as an international standard such as the financial statements (i.e. International Financial Reporting Standard (IFRS), Generally Accepted Accounting Principles (GAAP)) along with ESG indicators and the scientific and financial transparency as a common practice to promote fair return for health equity.

Regarding limitations, even though the Delphi technique is a robust approach to assess the levels of agreement, it presents some limitations that may affect the results. The principal study limitations are the following six. First, geographical panel representation of BRICS and LMICs. The purposive sample prioritized regions and countries leading R&I and at least one emerging country. Panel members from Europe have been purposively over represented (78%), given the characteristics of the European healthcare system, North America has been moderately represented (11%) as a leading market, whereas experts from LMICs underrepresented (11%, from Latin America and Caribbean region). Only Brazil, as a BRICS country, was represented with two members in the panel (7%). This unbalance should be assessed in further studies including more LMICS and BRICS as panel members. Moreover, conducting the study in English limited participation to English speakers, although English is a fairly common language in the sector. Second, reliability of qualitative data. The nature of qualitative studies provides no guarantee that the same results would be obtained with other panels (Keeney et al., 2001). Further qualitative and quantitative studies are needed to increase the robustness of results. Third, causes of disagreement. The Delphi technique used controlled survey feedback and the cHTA involved interviews. This means that ideas were not openly discussed between participants, who may not have been able to elaborate on them in the same way as with other research techniques such as focus groups. The anonymous collection of narratives during individual interviews was a method priority for participants to freely express ideas. Less agreed points of the Delphi surveys have been reported in specific results sections of this thesis (see sections 7.2.3 and 7.3.3), but have not been further developed by the experts, difficulting the interpretation (Blackwood and Currie, 2016). Moreover, additional studies should consider to include qualitative comments (open question remarks) separately in the surveys (i.e. at the end of each question or category), rather than as part of the answer options, to increase the qualitative data collection without interfering the survey results. Another possible limitation to deep dive in the dissent opinions could have been performing the interviews virtually (due to COVID-19 pandemic and the global location of the interviewees) rather than in person (see sections 6.5.1 and 6.7). Fourth, low Kendall's W coefficients of concordance and high p-values for the four ranked questions in R3 show little (for the main causes of the problem) or no agreement (for PSM governance, barriers and enablers) between the judges in the priority rank assigned in each set of categories. The

concordance in the ranked questions did not improve when analysing Kendall's W by expert segment. Thus, it requires additional understanding of these variables with further discussion in qualitative studies, as well as quantification in quantitative studies to try to reach priorisation consensus. Fifth, the mitigation of barriers requires further analysis on how to overcome each barrier to be conveyed in future studies. Sixth, procurement policies in healthcare (i.e. innovative public procurement) and other sectors (such as defence) were not analysed in this study.

Concerning competing interests, the author declares that there are no conflicts of interests. The PhD tuition fee at the University of Barcelona has been funded by ISGlobal. The author reports research and innovation grants received by her institution from different public and private donors, all of which are unrelated to the present work. As a disclaimer, the panel's comments reflect solely their individual views based on their professional backgrounds and personal beliefs and not necessarily those of their institutions.

In the light of the study results, suggestions for future research and working groups to upgrade the PSM could include, but are not limited to, the following topics:

- Develop an ATMi-like indicator to assess the performance of the medical industry as Preferred Supplier in accordance with the 4S principles and aligned with the ESG (Inrate, 2023; MSCI, 2023; PwC, 2023).
- Design a public R&I funding tracking tool that explores the option of linking it to the commercial asset (i.e. patents, registered software) by applying blockchain technology.
- Build an open Health Data ecosystem that comprises the list of R&I projects, raw data, clinical trial results and real-world evidence, including failure, and PROMs and PREMs (Bastemeijer et al., 2020) and link it to ESG (Inrate, 2023).
- Address the challenges of implementing impact investment especially for start-ups and SMEs (WEF, 2023) and for LMICs.
- Define new pricing mechanisms, particularly an agreement to segment prices based on countries' ability to pay (i.e. GDP per capita).
- Complete qualitative PSM research, with a deeper analysis of dissent statements, including focus group discussions among experts.
- Conduct quantitative PSM research with greater representation of low-cost manufacturing countries (i.e. BRICS) and LMICs.
- Test and evaluate the PSM with HTA and HIA methodologies (Dini et al., 2023).

9 CONCLUSIONS

This PhD thesis presents a desired and plausible model of responsible innovation for health equity. The former through shared values, the latter through changing incentives and creating the required regulation. This study achieved expert consensus on a co-designed equitable biomedical R&I process based on the Preferred Supplier model (PSM) as the primary objective. The PSM proposes a transition from a shareholder dominance to a collaborative multi-

stakeholder approach for equitable, agile and sustainable health outcomes. The PSM emphasises the role of the government as a market shaper aligning incentives and regulations with public health priorities to accelerate equitable innovation that is, the equitable transfer of innovative solutions. The PSM is a social enterprise model in which companies developing competitive solutions for priority health challenges and committed to environmental and health equity practices of the 4S principles get credit as preferred providers of the public sector.

The PSM accreditation is based on four annually audited KPIs: ESG and R&I scientific and financial data sharing for publicly funded assets as standard indicators, in addition to the ATMi-like for Preferred Suppliers. Accredited providers are eligible for competitive public incentives and procurement that drive the market towards innovative and equitable solutions for the common good. Significant push (especially for academia and SMEs) and pull incentives (mainly for large accredited companies) would be provided for public health priorities. The PSM risk-benefit balance was ranked as the best enabler to implement the new model, representing an incremental rather than radical change. Such a smooth transition would facilitate the engagement of investors and industry in defining the innovation agenda. In addition, increased industry social responsibility actions likely linked to investors requiring ESG disclosure are key additional facilitators agreed by the panel. Available digital technology and the Access to Medicine index (ATMi) as a reference measure round out the top half of the list. The main drawbacks are the lack of health system capacities in less developed countries and the difficulty of global commitments to reward innovation based on the ability to pay. The EU could lead the trial and implement the model together with other global stakeholders.

Specifically, the first significant conclusion (O1) is that equity and speed are the main problem with the health R&I system and the unanimous claim to solve it. Equity (equal access according to need) and efficiency (cost-effectiveness as value for money) are the agreed health values. In market economies, when incentives (risks and rewards) are not fully aligned with public health needs, these norms can involve an ethical dilemma because rewarding efficiency often prevents equity from being met (Culyer, 2001). Furthermore, there is mutual distrust between the public and private sector due to the high risk of R&I and the difficulty of managing it.

The second finding (O2) is that the causes of the problem with the current R&I model are the limitations in governance and the “4 Share” principles (sharing needs, results, risks and rewards and outcomes) that ultimately define the PSM as a solution. The top consensus cause is the lack of alignment between incentives and public health needs, followed by poor management of risks and rewards during the R&I cycle. The third cause is the lack of developer funds and the mismatch with priority health challenges. Abusive patent protection practices (Feldman, 2018) and value-based pricing applied by industry (Mazzucato and Roy, 2019), and the lack of data sharing (scientific and financial) (Mazzucato, 2016b; Ramstrand et al., 2019) close the list of the five main causes of the problem.

The third and core conclusion (O3) is the co-created consensus PSM as a social enterprise model for medical R&I. The model aligns incentives and regulations with priority public health challenges identified by governments and comprised in the SDGs (Roychowdhury, et al., 2019). In the PSM, health companies that comply with health equity and green practices get return as preferred providers of the public sector for health priorities. The model represents a social safety net mechanism for health challenges to be activated by governments and multilateral organizations (i.e. WHO) and supported key stakeholders (i.e. investors, philanthropists, civil society organizations). There was consensus on the articulation of the PSM as follows:

- The efficiency norm was redefined by incentivising the health challenges affected by market failure to solve the moral dilemma and balance equity and efficiency (Cairney et al., 2022; Charlton et al., 2023).
- The experts mainly agreed on the PSM 4S principles. 1) Sharing needs with a tangible part of the R&I portfolio devoted to health priorities based on epidemiology, market failure and public health emergencies (National Academies of SEM, 2023). 2) Sharing results, contributing to the opening of "Health Data Spaces" (EC, 2023e; Shabani, 2022) that include the portfolio of R&I projects, raw data, clinical trial results and RWE (including failure), and embracing adaptative pathways. 3) Sharing risks and rewards, with a hybrid Risk-Impact pricing model (ICER, 2023; WHO, 2020d; Wouters et al., 2020), where risk is measured by the funding mix (which involves the disclosure of public R&I funds) and impact is measured by the revised value-based pricing (i.e. MEAs) (A Vreman et al., 2020; Bouvy et al., 2018), modulated by the countries' ability to pay (i.e. GDP per cacpita) through price segmentation and voluntary licensing (Biancalani et al., 2022; Moon et al., 2020). The creation of investment consortia and early cooperation with health regulators and payers were also agreed. 4) Sharing outcomes involving HIA and HTA, including ethical, legal and social aspects when necessary (Dini et al., 2023).
- In return, the public sector would provide significant push and pull incentives. Push incentives (funding) for early stages of R&I, especially with grants and investment in academia and SMEs (Bloom et al., 2019; Soete et al., 2022). Moreover, growth-stage funding for phase II-III clinical trials, with long-term public-private matching venture capital investment, especially for SMEs, which encourages social impact investment and supportive corporate holding investment. Pull incentives (market access) to reward successful industry innovation ranging from regulatory policies (i.e. regulatory-HTA alignment, FDA-EMA alignment, regulatory fast track approval, regulatory exclusivity extension, regional HTA agencies in LMIC), to new value-based pricing (i.e. outcome-based risk-sharing agreements, financial risk-sharing agreements such as price-volume, de-link Netflix model), and pooled procurement (McEvoy and Ferri, 2020; So and Woo, 2020).
- The PSM accreditation could apply to listed and large companies and progressively incorporate SMEs. It is a recognition of good practices, therefore there is no initial contract with Preferred Suppliers who compete to develop the best possible solution.
- The regulation consists on 4 KPIs audited annually: ESG (PwC, 2023), disclosure of scientific data of publicly funded projects and disclosure of public R&I funding received as general indicators. In addition, Preferred Suppliers would be required to report the ATMi-like to measure the PSM "4S" principles to be eligible for public procurement and incentives. These indicators could be reported by industry to the regulatory agency when submiting the dossier.
- Regarding governance, the panel agreed on the EU leadership to further develop and test the PSM, given its social security provision system and the programmatic, funding and regulatory environment, in collaboration with other interested stakeholders.

The fourth conclusion (O4) is about the main barriers and enablers of the PSM. The lack of health system capacities in LMICs; the difficulty in reaching global commitments on price segmentation (i.e. rewarding innovation based on the country's ability to pay); and industry lobbying in health policies are the principal constraints. Instead, the main drivers are the incremental change that balances risks and rewards proposed by the PSM; the growing practices of responsible capitalism by industry (i.e. Pfizer Accord); and investors requiring corporate disclosure (Bernow et al., 2019;

Blankespoor, deHaan and Marinovic, 2020; Kalkanci and Plambeck, 2020). Available digital technology and ATMi-like are additional agreed facilitators.

The final conclusion (O5) refers to policy recommendations (REC) for an equitable R&I model based on the consensus findings and supported by literature review. REC1 proposes EU leadership in a collaborative public-private ecosystem (Akomea-Frimpong et al., 2023; Ballantyne and Stewart, 2019; Baxter and Casady, 2020; Davis et al., 2021) jointly with a revised WHO and the US. REC2 promotes dialogue for a value framework as a social choice that defines global health challenges (Cairney et al., 2022; Charlton et al., 2023) based on One Health, Planetary Health (IPCC, 2023) and open innovation (Liu and Yang, 2022). The framework should strengthen health emergencies, preparedness and response, and stimulate whole-of-government and whole-of-society action (Ortenzi et al., 2022). It is necessary to delimit the lobby of the industry in health policies. REC3 stimulates transparency of publicly funded R&I including regulation on the ownership, sharing and use of AI (Dhasarathan et al., 2023; Morley et al., 2020; European Parliament, 2023b), as well as mandatory disclosure of scientific and funding data of publicly funded health R&I projects. REC4 seeks to establish the conditions of Preferred Suppliers as social businesses for public funding and procurement by defining the principles, accreditation criteria, incentives and governance of the PSM. It involves defining an ATMi-like index, outlining a hybrid Risk-Impact pricing model modulated by countries' ability to pay, and promoting early partnerships and acceleration platforms. Building on the PSM drivers, industry and investors can participate to pilot the PSM in the EU and assess impact. REC5 aims to encourage the adoption of TRIPS flexibilities fast-tracking IPR waivers and compulsory licensing for WTO member states' health priorities (Correa, 2022; El Said, 2022). The PSM advocates for voluntary licensing by industry in low-cost manufacturing countries (i.e. BRICS) to sell generic products in LMICs (Biancalani et al., 2022; Moon et al., 2020). In addition, it increases competition by avoiding extensions of the useful life of patents (evergreening practices). Ultimately, REC6 calls for boosting impact investment, including investment in health innovation in LMICs (Malekzadeh et al., 2020) by global consortia. In return, governments would facilitate market access (i.e. with regional HTA agencies) and TT (Falkowski et al., 2023; Hollingworth et al., 2021) and provide tax incentives for investment. The new WHO Pandemic Preparedness Treaty (Hannon et al., 2022; Phelan, 2023), the G7 B3W (Savoy and McKeown, 2022) and the EU Global Gateway (EC, 2023f), among others, could be an opportunity to strengthen capacities in the Global South.

The consensus PSM resulting from this study is valuable common ground. We look forward to future research on this topic.

REFERENCES

Abbas, M. Z., & Riaz, S. (2017). Compulsory licensing and access to medicines: TRIPS amendment allows export to least-developed countries. Journal of Intellectual Property Law & Practice, 12(6), 451–452. https://doi.org/10.1093/jiplp/jpx065.

Abdalla, S. M., Maani, N., Ettman, C. K., & Galea, S. (2020). Claiming health as a public good in the post-COVID-19 era. *Development*, *63*(2), 200-204.

Abraham, J. (2010). Pharmaceuticalization of society in context: Theoretical, empirical and health dimensions. Sociology. https://doi.org/10.1177/0038038510369368.

Access to Medicine Foundation (15 November 2022). *Some companies engaging in R&D for emerging infectious diseases, but pipeline mainly empty.* Key Finding 1: R&D Priorities. [online]. Available on: https://accesstomedicinefoundation.org/resource/some-companies-engaging-in-r-and-d-for-emerging-infectious-diseases-but-pipeline-mainly-empty. [Retrieved 2 December 2023].

ACT-Accelerator (3 May 2023). *Global COVID-19 Access Tracker (GCAT).* [online]. Available on: https://www.COVID19globaltracker.org/. [Retrieved 2 December 2023].

Adams, C. P., & Van Brantner, V. (2006). Market watch: Estimating the cost of new drug development: Is it really $802 million? In *Health Affairs*. https://doi.org/10.1377/hlthaff.25.2.420.

Akomea-Frimpong, I., Jin, X., Osei-Kyei, R., & Tumpa, R. J. (2023). A critical review of public–private partnerships in the COVID-19 pandemic: key themes and future research agenda. *Smart and Sustainable Built Environment*, *12*(4), 701-720.

Alford, J. (2014). The Multiple Facets of Co-Production: Building on the work of Elinor Ostrom. *Public Management Review*. https://doi.org/10.1080/14719037.2013.806578.

Alkire, S. (2022). *The capability approach and human development*. [online]. Available on: https://resources.equityinitiative.org/bitstream/handle/ei/430/Alkire%20Intro-to-the-Capability-Approach.pdf?sequence=1. [Retrieved 24 February 2023].

Alonso, A., Espriu M., Bigorra, J., Fanjul G., Vilasanjuan R. (2021a). *Biomedic R&D: How can we protect the public interest after COVID-19?* Barcelona Institute for Global Health (ISGlobal) Policy Brief, 30. [online]. Avalable on: https://www.isglobal.org/en/-/i-d-i-biomedico-como-proteger-el-interes-publico-tras-la-covid-19-. [Retrieved 7 May 2024].

Alonso, A., Espriu M., Bigorra, J., Vilasanjuan R., Fanjul G. (2021b). COVID-19 and the Reform of the Biomedical R&D System: A Proposal for a Preferred Supplier Model. Barcelona Institute for Global Health (ISGlobal) Discussion Paper, June 2021. [online]. Available on: https://www.isglobal.org/en/-/covid-19-y-la-reforma-del-sistema-de-i-d-biomedico-propuesta-para-un-modelo-de-proveedor-preferente. [Retrieved 7 May 2024].

Andrews, M. R., Long, P. A., Ahlberg, M., Balvert, F., Alessandrello, R., Lazzari, A., ... & Stamm, T. (2023). A European arena for joint innovation in healthcare: The Platform for Innovation of Procurement and Procurement of Innovation (PiPPi). Frontiers in Public Health, 10, 1000590.

Angelis, A., Lange, A., & Kanavos, P. (2018). Using health technology assessment to assess the value of new medicines: results of a systematic review and expert consultation across eight European countries. *European Journal of Health Economics*. https://doi.org/10.1007/s10198-017-0871-0.

Annett, S. (2021). Pharmaceutical drug development: high drug prices and the hidden role of public funding. Biologia Futura, 72(2), 129-138.

Årdal, C., Outterson, K., Hoffman, S. J., Ghafur, A., Sharland, M., Ranganathan, N., Smith, R., Zorzet, A., Cohn, J., Pittet, D., Daulaire, N., Morel, C., Rizvi, Z., Balasegaram, M., Dar, O. A., Heymann, D. L., Holmes, A. H., Moore, L. S. P., Laxminarayan, R., … Røttingen, J. A. (2016). International cooperation to improve access to and sustain effectiveness of antimicrobials. *The Lancet*. https://doi.org/10.1016/S0140-6736(15)00470-5.

Aronson, J. K., & Green, A. R. (2020). Me-too pharmaceutical products: History, definitions, examples, and relevance to drug shortages and essential medicines lists. *British Journal of Clinical Pharmacology*, *86*(11), 2114-2122.

Arora, A., & Gambardella, A. (1994). The changing technology of technological change: general and abstract knowledge and the division of innovative labour. *Research Policy*. 23 (5): 523–532. https://doi.org/10.1016/0048-7333(94)01003-X.

Asundi, A., O'Leary, C., & Bhadelia, N. (2021). Global COVID-19 vaccine inequity: The scope, the impact, and the challenges. Cell host & microbe, 29(7), 1036–1039. https://doi.org/10.1016/j.chom.2021.06.007.

Austin, C. P., Cutillo, C. M., Lau, L. P., Jonker, A. H., Rath, A., Julkowska, D., ... & International Rare Diseases Research Consortium. (2018). Future of rare diseases research 2017–2027: an IRDiRC perspective. Clinical and translational science, 11(1), 21.

Avella, J. R. (2016). Delphi panels: Research design, procedures, advantages, and challenges. International Journal of Doctoral Studies, 11, 305.

Avorn, J. (2015). The $2.6 Billion Pill — Methodologic and Policy Considerations. *New England Journal of Medicine*. https://doi.org/10.1056/nejmp1500848.

A Vreman, R., F Broekhoff, T., GM Leufkens, H., K Mantel-Teeuwisse, A., & G Goettsch, W. (2020). Application of managed entry agreements for innovative therapies in different settings and combinations: a feasibility analysis. International Journal of Environmental Research and Public Health, 17(22), 8309.

Baker, S. and Koons, C. (29 October 2020). *Inside Operation Warp Speed's $18 billion sprint for a vaccine*. Bloomberg. [online]. Available on: https://www.bloomberg.com/news/features/2020-10-29/inside-operation-warp-speed-s-18-billion-sprint-for-a-vaccine. [Retrieved 7 March 2024].

Ballantyne, A., & Stewart, C. (2019). Big data and public-private partnerships in healthcare and research: the application of an ethics framework for big data in health and research. Asian Bioethics Review, 11(3), 315-326.

Barel, A., Boman, L., & Morten, C. (2020). Clinical Trial Cost Transparency at the National Institutes of Health: Law and Policy Recommendations. Engelberg Center on Innovation Law and Policy, NYU School of Law.

Bastemeijer, C. M., Boosman, H., Zandbelt, L., Timman, R., de Boer, D., & Hazelzet, J. A. (2020). Patient Experience Monitor (PEM): The Development of New Short-Form Picker Experience Questionnaires for Hospital Patients with a Wide Range of Literacy Levels. Patient related outcome measures, 11, 221–230. https://doi.org/10.2147/PROM.S274015.

Baxter, D., & Casady, C. B. (2020). Proactive and strategic healthcare public-private partnerships (PPPs) in the coronavirus (COVID-19) epoch. Sustainability, 12(12), 5097.

Beall, R. and Kuhn R. (2012). Trends in Compulsory Licensing of Pharmaceuticals Since the Doha Declaration: A Database Analysis. PLoS Med 9(1): e1001154. https://doi.org/10.1371/journal.pmed.1001154.

Beall, R. F., Kuhn, R., & Attaran, A. (2015). Compulsory licensing often did not produce lower prices for antiretrovirals compared to international procurement. Health affairs (Project Hope), 34(3), 493–501. https://doi.org/10.1377/hlthaff.2014.0658.

Becerra, X., & Jha, A. (2023). Project NextGen—Defeating SARS-CoV-2 and Preparing for the Next Pandemic. New England Journal of Medicine.

Beiderbeck, D., Frevel, N., von der Gracht, H. A., Schmidt, S. L., Schweitzer, V. M. (2021). Preparing, conducting, and analyzing Delphi surveys: Cross-disciplinary practices, new directions, and advancements. MethodsX 8. https://doi.org/10.1016/j.mex.2021.101401

Bennet, F. and Ruxton S. (2015). Common social values in the European Union: stocktaking, with a focus on social inclusion and social protection. For Luxembourg Presidency of the Council of the European Union.

Bernow, S., Godsall, J., Klempner, B., & Merten, C. (2019). More than values: The value-based sustainability reporting that investors want. McKinsey and Company.

Biancalani, F., Gnecco, G., & Riccaboni, M. (2022). Price-volume agreements: A one principal/two agents model. European Journal of Operational Research, 300(1), 296–309. https://doi.org/https://doi.org/10.1016/j.ejor.2021.10.050.

Bill & Melinda Gates Foundation (September 2020). 2020 Goalkeepers report. COVID-19 A Global Perspective. [online]. Available on: https://www.gatesfoundation.org/goalkeepers/report/2020-report/#GlobalPerspective. [Retrieved 7 March 2024].

BioNTech (13 July 2020). *Project Lightspeed.* Fact Sheet 2*.* [online]. Available on: https://www.biontech.com/content/dam/corporate/pdf/BioNTech_Factsheet_Project_Lightspeed_mRNA_Technology.pdf. [Retrieved 7 March 2024].

Blackwood, R. and Currie, C. (2016). The use of Delphi methods. UK Faculty of Public Health. Health Knowledge. [online]. Available on: https://www.healthknowledge.org.uk/public-health-textbook/research-methods/1c-health-care-evaluation-health-care-assessment/use-delphi-methods. [Retrieved 7 March 2024].

Blankespoor, E., deHaan, E., & Marinovic, I. (2020). Disclosure processing costs, investors' information choice, and equity market outcomes: A review. Journal of Accounting and Economics, 70(2-3), 101344.

Bleda, M., & Chicot, J. (2020). The role of public procurement in the formation of markets for innovation. Journal of Business Research, 107, 186-196.

Bloom, N., Van Reenen, J., & Williams, H. (2019). A toolkit of policies to promote innovation. Journal of economic perspectives, 33(3), 163-184.

Boddy, C. R. (2016). Sample size for qualitative research. Qualitative Market Research: An international Journal, 19(4), 426–432. https://doi.org/10.1108/QMR-06-2016-0053.

Bourla, A. (7 May 2021). *An Open Letter from Pfizer Chairman and CEO to Colleagues*. *Pfizer*. [online]. Available on: https://www.pfizer.com/news/articles/why_pfizer_opposes_the_trips_intellectual_property_waiver_for_covid_19_vaccines. [Retrieved 7 March 2024].

Bouvy, J. C., Sapede, C., & Garner, S. (2018). Managed entry agreements for pharmaceuticals in the context of adaptive pathways in Europe. Frontiers in pharmacology, 280.

Brewer, L. C., Fortuna, K. L., Jones, C., Walker, R., Hayes, S. N., Patten, C. A., & Cooper, L. A. (2020). Back to the future: achieving health equity through health informatics and digital health. *JMIR mHealth and uHealth*, *8*(1), e14512.

Brown, J. (2018). Interviews, focus groups, and Delphi techniques. Advanced research methods for applied psychology: Design, analysis and reporting, 95-106.

Bryan, K. A., & Williams, H. L. (2021). Innovation: market failures and public policies. In Handbook of industrial organization (Vol. 5, No. 1, pp. 281-388). Elsevier.

Bullinger, A. C., Rass, M., Adamczyk, S., Moeslein, K. M., & Sohn, S. (2012). Open innovation in health care: Analysis of an open health platform. Health policy, 105(2-3), 165-175.

Butchard, P., & Balogun, B. (2022). What is the proposed WHO Pandemic Preparedness Treaty? UK Parliament, House of Commons Library. Research Briefing. Published 2 June 2023.

Cairney, P., St Denny, E., Kippin, S., & Mitchell, H. (2022). Lessons from policy theories for the pursuit of equity in health, education and gender policy. Policy & Politics, 50(3), 362-383.

Canoy, M., & Tichem, J. (2018). Lower drug prices can improve innovation. European Competition Journal. https://doi.org/10.1080/17441056.2018.1512231.

Carrier, M.A. (2019). Higher Drug Price from Anticompetitive Conduct: Three Case Studies. J Leg Med. 2019 Apr-Jun;39(2):151-167. doi: 10.1080/01947648.2019.1645540. PMID: 31503532.

Castor, J., Bacha, K., & Nerini, F. F. (2020). SDGs in action: A novel framework for assessing energy projects against the sustainable development goals. Energy research & social science, 68, 101556.

CDC (1 December 2021). *First Confirmed case of omicron variant detected in the United States*. [online]. Available on: https://archive.cdc.gov/#/details?url=https://www.cdc.gov/media/releases/2021/s1201-omicron-variant.html. [Retrieved 7 March 2024].

Chan, A. Y. L., Chan, V. K. Y., Olsson, S., Fan, M., Jit, M., Gong, M., Zhang, S., Ge, M., Pathadka, S., Chung, C. C. Y., Chung, B. H. Y., Chui, C. S. L., Chan, E. W., Wong, G. H. Y., Lum, T. Y., Wong, I. C. K., Ip, P., & Li, X. (2020). Access and Unmet Needs of Orphan Drugs in 194 Countries and 6 Areas: A Global Policy Review With Content Analysis. Value in Health, 23(12), 1580–1591. https://doi.org/https://doi.org/10.1016/j.jval.2020.06.020.

Chandra, A., Foroughi, C., & Mostrom, L. (2022). Venture Capital–Led Entrepreneurship in Health Care. The Role of Innovation and Entrepreneurship in Economic Growth, 475-98.

Charlton, V., DiStefano, M., Mitchell, P., Morrell, L., Rand, L., Badano, G., ... & Wester, G. (2023). We need to talk about values: a proposed framework for the articulation of normative reasoning in health technology assessment. Health Economics, Policy and Law.

Chatham House (24 June 2022). *The role of the G7 in mobilizing a global recovery. Achieving progress and action in G7 development activities.* [online]. Available on: https://www.chathamhouse.org/2022/06/role-g7-mobilizing-global-recovery. [Retrieved 7 March 2024].

Chirazi, J., Wanieck, K., Fayemi, P. E., Zollfrank, C., & Jacobs, S. (2019). What do we learn from good practices of biologically inspired design in innovation? Applied Sciences, 9(4), 650.

Claxton, K., Lindsay, A. B., Buxton, M. J., Culyer, A. J., McCabe, C., Walker, S., & Sculpher, M. J. (2008). Value based pricing for NHS drugs: An opportunity not to be missed? In BMJ. https://doi.org/10.1136/bmj.39434.500185.25.

Cohen, D. (2017). Cancer drugs: high price, uncertain value. Bmj, 359.

Cohen, J. (2020). Unveiling 'Warp Speed,'the White House's America-first push for a coronavirus vaccine.

Collins, F. S., & Varmus, H. (2015). A New Initiative on Precision Medicine. New England Journal of Medicine. https://doi.org/10.1056/nejmp1500523.

Coluccia, D., Dabić, M., Del Giudice, M., Fontana, S., & Solimene, S. (2020). R&D innovation indicator and its effects on the market. An empirical assessment from a financial perspective. Journal of Business Research, 119, 259-271.

Conti, R. M., Bernstein, A. C., Villaflor, V. M., Schilsky, R. L., Rosenthal, M. B., & Bach, P. B. (2013). Prevalence of off-label use and spending in 2010 among patent-protected chemotherapies in a population-based cohort of medical oncologists. *Journal of Clinical Oncology*. https://doi.org/10.1200/JCO.2012.42.7252.

Cook, R. J. (2020). International human rights and women's reproductive health. Women, Medicine, Ethics and the Law, 37-50.

Coreil J. (1995). Group interview methods in community health research. Med Anthropol. 1995 Jul;16(3):193-210. doi: 10.1080/01459740.1994.9966115. PMID: 8643022.

Correa, C. M. (2022). Interpreting the Flexibilities under the TRIPS Agreement. *Access to Medicines and Vaccines*, 1.

Correa, C. M., & Hilty, R. M. (2022). *Access to Medicines and Vaccines: Implementing Flexibilities Under Intellectual Property Law* (p. 369). Springer Nature.

Cortes, J., Perez-García, J. M., Llombart-Cussac, A., Curigliano, G., El Saghir, N. S., Cardoso, F., ... & Arribas, J. (2020). Enhancing global access to cancer medicines. CA: a cancer journal for clinicians, 70(2), 105-124.

Cosgriff, C. V., Ebner, D. K., & Celi, L. A. (2020). Data sharing in the era of COVID-19. The Lancet Digital Health, 2(5), e224.

Cossio-Gil, Y., Omara, M., Watson, C., Casey, J., Chakhunashvili, A., Gutiérrez-San Miguel, M., ... & Stamm, T. (2022). The roadmap for implementing value-based healthcare in European university hospitals—consensus report and recommendations. Value in Health, 25(7), 1148-1156.

COVID-19 Vaccine Tracker (2 December 2022). *COVID-19 Vaccine Tracker*. [online]. Available on: https://covid19.trackvaccines.org/. [Retrieved 7 March 2024].

Crawford, A., & Serhal, E. (2020). Digital health equity and COVID-19: the innovation curve cannot reinforce the social gradient of health. Journal of medical Internet research, 22(6), e19361.

Cross, S., Rho, Y., Reddy, H., Pepperrell, T., Rodgers, F., Osborne, R., ... & Keestra, S. (2021). Who funded the research behind the Oxford–AstraZeneca COVID-19 vaccine? *BMJ global health*, *6*(12), e007321.

Cubanski, J., Kates, J., Tolbert, J., Guth, M., Pollitz, K., & Freed, M. (31 January 2023b). *What happens when COVID-19 emergency declarations end? Implications for coverage, costs, and access*. *Kaiser Family Foundation*. [online]. Available on: https://www.kff.org/coronavirus-covid-19/issue-brief/what-happens-when-covid-19-emergency-declarations-end-implications-for-coverage-costs-and-access/. [Retrieved 7 March 2024].

Cubanski, J., Neuman, T., True, S., & Freed, M. (23 July 2023a). What's the latest on Medicare drug price negotiations? Kaiser Family Foundation. [online]. Available on: https://www.kff.org/medicare/issue-brief/whats-the-latest-on-medicare-drug-price-negotiations/. [Retrieved 7 March 2024].

Cullinan, K. (1 December 2022). *Twenty Years On, HIV Activist is Still Fighting for Access to Cheaper Medicine.* HIV and AIDS. Health Policy Watch. [online]. Available on: https://healthpolicy-watch.news/twenty-years-on-hiv-activist-is-still-fighting-for-access-to-cheaper-medicine/. [Retrieved 7 March 2024].

Culyer, A. J. (1992). The morality of efficiency in health care—some uncomfortable implications. Health economics, 1(1), 7-18.

Culyer, A. J. (2001). Equity-some theory and its policy implications. Journal of medical ethics, 27(4), 275-283.

Daems, R., & Maes, E. (2022). The race for COVID-19 vaccines: Accelerating innovation, fair allocation and distribution. *Vaccines*, *10*(9), 1450.

Daniels, N., Porteny, T., & Urritia, J. (2016). Expanded HTA: Enhancing fairness and legitimacy. In International Journal of Health Policy and Management.

Davies, L. (2023). Compulsory licensing: an effective tool for securing access to COVID-19 vaccines for developing states? Legal Studies, 43(1), 86-103.

Davis, A. M., Engkvist, O., Fairclough, R. J., Feierberg, I., Freeman, A., & Iyer, P. (2021). Public-private partnerships: Compound and data sharing in drug discovery and development. *SLAS DISCOVERY: Advancing the Science of Drug Discovery*, *26*(5), 604-619.

Dawkins, H. J. S., Draghia-Akli, R., Lasko, P., Lau, L. P. L., Jonker, A. H., Cutillo, C. M., Rath, A., Boycott, K. M., Baynam, G., Lochmüller, H., Kaufmann, P., Le Cam, Y., Hivert, V., Austin, C. P., & International Rare Diseases Research Consortium (IRDiRC) (2018). Progress in Rare Diseases Research 2010-2016: An IRDiRC Perspective. Clinical and translational science, 11(1), 11–20. https://doi.org/10.1111/cts.12501.

deBoer, J. & Hale, J. (2002, November/December). The oracle at Delphi: Was she really stoned? Archeolo y Odyssey, 6/2002. [online]. Available on: http://www.biblicalarchaeology.org/daily/ancient-cultures/daily-life-and-practice/the-oracle-of-delphi%E2%80%94was-she-really-stoned/. [Retrieved 7 March 2024].

De Jongh, T., Velten, L. & Schrijver, L. (June 2021). *Access to medicinal products*. European Parliament. Available on: https://www.europarl.europa.eu/RegData/etudes/STUD/2021/662910/IPOL_STU(2021)662910_EN.pdf. [Retrieved 2 December 2023].

Deneulin, S., & Townsend, N. (2007). Public goods, global public goods and the common good. *International journal of social economics*, *34*(1/2), 19-36

De Oliveira, T., & Baxter, C. (2024). Investing in Africa's scientific future. Science, 383(6678), eadn4168.

Detel, W. (2015). Social Constructivism. 10.1016/B978-0-08-097086-8.63081-7.

Dhasarathan, C., Hasan, M. K., Islam, S., Abdullah, S., Mokhtar, U. A., Javed, A. R., & Goundar, S. (2023). COVID-19 health data analysis and personal data preserving: A homomorphic privacy enforcement approach. Computer Communications, 199, 87–97. https://doi.org/https://doi.org/10.1016/j.comcom.2022.12.004.

Diamond, I. R., Grant, R. C., Feldman, B. M., Pencharz, P. B., Ling, S. C., Moore, A. M., & Wales, P. W. (2014). Defining consensus: a systematic review recommends methodologic criteria for reporting of Delphi studies. Journal of clinical epidemiology, 67(4), 401–409. https://doi.org/10.1016/j.jclinepi.2013.12.002.

Diez-Busto, E., Sanchez-Ruiz, L., & Fernandez-Laviada, A. (2021). The B Corp movement: A systematic literature review. *Sustainability*, *13*(5), 2508.

DiMasi, J. A., Grabowski, H. G., & Hansen, R. W. (2016). Innovation in the pharmaceutical industry: new estimates of R&D costs. Journal of health economics, 47, 20-33.

DiMasi, J. A., Hansen, R. W., Grabowski, H. G., & Lasagna, L. (1991). Cost of innovation in the pharmaceutical industry. Journal of Health Economics. https://doi.org/10.1016/0167-6296(91)90001-4.

Dini, L., Maceira, D., Rabanal, J. A., Boccia, S., Pezullo, A., Stranges, S., ... & Ogawa, S. (2023). Research methods for global public health oriented health services research-what can we learn from each other? Population Medicine, 5.

DNDi (2013). *Research & Development for Diseases of the Poor: A 10-Year Analysis of Impact of the DNDi Model. Drugs for Neglected Diseases Initiative*. [online]. Available on: http://www.dndi.org/wp-content/uploads/2009/03/DNDi_CostOfDev_FactsFigures.pdf. [Retrieved 2 December 2023].

Dolderer, J., Felber, C., & Teitscheid, P. (2021). From neoclassical economics to common good economics. *Sustainability*, *13*(4), 2093.

Donaldson, T. (2023). Value creation and CSR. Journal of Business Economics, 1-21.

Dron, L., Dillman, A., Zoratti, M. J., Haggstrom, J., Mills, E. J., & Park, J. J. (2021). Clinical trial data sharing for COVID-19–related research. *Journal of Medical Internet Research*, *23*(3), e26718.

Dron, L., Kalatharan, V., Gupta, A., Haggstrom, J., Zariffa, N., Morris, A. D., ... & Park, J. (2022). Data capture and sharing in the COVID-19 pandemic: a cause for concern. The Lancet Digital Health, 4(10), e748-e756.

Druedahl, L. C., Minssen, T., & Price, W. N. (2021). Collaboration in times of crisis: A study on COVID-19 vaccine R&D partnerships. Vaccine, 39(42), 6291-6295.

EC (2016). *Strengthening of the EU cooperation on Health Technology Assessment (HTA). DG Santé.* [online]. Available on: https://ec.europa.eu/smart-regulation/roadmaps/docs/2016_sante_144_health_technology_assessments_en.pdf. [Retrieved 7 March 2024].

EC (2017). *European Consensus of Development – "our world, our dignity, our future".* [online]. Available on: https://international-partnerships.ec.europa.eu/system/files/2019-09/european-consensus-on-development-final-20170626_en.pdf. [Retrieved 7 March 2024].

EC (2019). *Defining Value in "Value-Based Healthcare".* Report of the Expert Panel on effective ways of investing in Health (EXPH). [online]. Available on: https://health.ec.europa.eu/system/files/2019-11/024_defining-value-vbhc_en_0.pdf. [Retrieved 7 March 2024].

EC (29 January 2021). *Vaccines: contract between European Commission and AstraZeneca now published*. Brussels. [online]. Available on: https://ec.europa.eu/commission/presscorner/detail/en/ip_21_302. [Retrieved 7 March 2024].

EC (30 November 2022). *EU Global Health Strategy to improve global health security and deliver better health for all.* [online]. Available on: https://ec.europa.eu/commission/presscorner/detail/en/ip_22_7153 and https://health.ec.europa.eu/system/files/2023-10/international_ghs-report-2022_en.pdf. [Retrieved 7 March 2024].

EC (2023a). *International Partnerships*. Aid, Development cooperation, Fundamental rights. [online]. Available on: https://international-partnerships.ec.europa.eu/policies/human-development/health-and-demography_en. [Retrieved 7 March 2024].

EC (26 April 2023b). *Reform of the EU pharmaceutical legislation.* [online]. Available on: https://health.ec.europa.eu/medicinal-products/pharmaceutical-strategy-europe/reform-eu-pharmaceutical-legislation_en. [Retrieved 7 March 2024].

EC (2023c). *Big Buyers Working Together*. Public Buyers Community. [online]. Available on: https://public-buyers-community.ec.europa.eu/about/big-buyers-working-together and https://sustainable-procurement.org/fileadmin/user_upload/Big_Buyers_Initiative/General/Big_Buyers_-_Recruitment_Brief.pdf. [Retrieved 7 March 2024].

EC (2023d). *EU Vaccines Strategy*. [online]. Available on: https://commission.europa.eu/strategy-and-policy/coronavirus-response/public-health/eu-vaccines-strategy_en. [Retrieved 7 March 2024].

EC (2023e). *European Health Data Space*. [online]. Available on: https://health.ec.europa.eu/ehealth-digital-health-and-care/european-health-data-space_en. [Retrieved 7 March 2024].

EC (2023f). *Global Gateway.* [online]. Available on: https://commission.europa.eu/strategy-and-policy/priorities-2019-2024/stronger-europe-world/global-gateway_en. [Retrieved 7 March 2024].

EC NGEU (2023). *Recovery plan for Europe.* [online]. Available on: https://commission.europa.eu/strategy-and-policy/recovery-plan-europe_en. [Retrieved 7 March 2024].

El Said, M. (2022). The Impact of 'TRIPS-Plus' Rules on the Use of TRIPS Flexibilities: Dealing with the Implementation Challenges. *Access to Medicines and Vaccines*, 297.

Ellemers, N. (2021). Science as collaborative knowledge generation. British Journal of Social Psychology, 60(1), 1-28. doi:10.1111/bjso.12430.

EMA (4 May 2020). *COVID-19: how EMA fast-tracks development support and approval of medicines and vaccines*. European Union. [online]. Available on: https://www.ema.europa.eu/en/news/covid-19-how-ema-fast-tracks-development-support-approval-medicines-vaccines. [Retrieved 7 March 2024].

EMA (8 March 2023a). *Human Regulatory. Orphan Designation. Orphan Designation.* European Medicines Agency. European Union. [online]. Available on: https://www.ema.europa.eu/en/human-regulatory/overview/orphan-designation-overview. [Retrieved 7 March 2024].

EMA (26 July 2023b). *Human Regulatory. COVID-19 guidance: evaluation and marketing authorisation. European Union.* [online]. Available on: https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/covid-19-public-health-emergency-international-concern-2020-23/guidance-developers-companies/covid-19-guidance-evaluation-marketing-authorisation. [Retreived 7 March 2024].

Endocrinology, T. L. D. (2019). Spotlight on rare diseases. *The lancet. Diabetes & endocrinology*, *7*(2), 75.

Espriu, M., Bigorra, J., Gallo, P., & Sampietro-Colom, L. (2022). A New Equitable Biomedical Research And Development Model: Preliminary Findings From A Pilot Study Applying VALIDATE Value Methods. International Journal of Technology Assessment in Health Care, 38(S1), S94-S94. doi:10.1017/S0266462322002768.

EU (16 December 1999). *Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products.* [online]. Available on: https://eur-lex.europa.eu/eli/reg/2000/141/oj. [Retrieved 7 March 2024].

EU (22 June 2006). *Council Conclusions on Common values and principles in European Union Health Systems.* (2006/C 146/01). [online]. Available on: https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:52006XG0622(01)&rid=1. [Retrieved 7 March 2024].

EU (25 November 2020). *Pharmaceutical Strategy for Europe.* Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions. Brussels, 25/11/2020, COM (2020) 761 final. [online]. Available on: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52020DC0761. [Retrieved: 7 March 2024].

EU (5 July 2022). *"A New European Innovation Agenda".* [online]. Available on: https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A52022DC0332. [Retrieved 7 March 2024].

EU Rare2030 (2023). Rare 2030. Foresight in Rare Disease Policy. Available on: https://www.rare2030.eu/. [Retrieved 7 March 2024].

European Parliament (10 June 2021). *Parliament calls for temporary COVID-19 vaccine patent waiver*. [online]. Available on: https://www.europarl.europa.eu/news/en/press-room/20210604IPR05514/parliament-calls-for-temporary-covid-19-vaccine-patent-waiver. [Retrieved 7 March 2024].

European Parliament (3 May 2022). *European Health Data Space*. 2022/0140(COD) – 03/05/2022. Legislative Observatory. [online]. Available on: https://oeil.secure.europarl.europa.eu/oeil/popups/summary.do?id=1703041&t=e&l=en. [Retrieved 7 March 2024].

European Parliament (25 January 2023a). *New EU global health strategy: A recalibrated agenda*. [online]. Available on: https://www.europarl.europa.eu/RegData/etudes/BRIE/2023/739306/EPRS_BRI(2023)739306_EN.pdf. [Retrieved 7 March 2024].

European Parliament (15 June 2023b). *EU AI Act: first regulation on artificial intelligence.* [online]. Available on: https://www.europarl.europa.eu/news/en/headlines/society/20230601STO93804/eu-ai-act-first-regulation-on-artificial-intelligence. [Retrieved 7 March 2024].

EURORDIS Rare Diseases Europe (17 January 2021). *The development and market launch of orphan drugs from 1980–2019: a quantitative analysis*. Project Rare20230. [online]. Available from: https://download2.eurordis.org/rare2030/deliverables/D5.3%20R%26D%20and%20market%20launch%20of%20orphan%20drugs.pdf. [Retrieved 7 March 2024].

Falkowski, A., Ciminata, G., Manca, F., Bouttell, J., Jaiswal, N., Farhana Binti Kamaruzaman, H., ... & Grieve, E. (2023). How least developed to lower-middle income countries use health technology assessment: a scoping review. Pathogens and Global Health, 117(2), 104-119.

Fang, F. C., & Casadevall, A. (2015). Competitive science: Is competition ruining science? Infection and Immunity, 83(4), 1229-1233. doi:10.1128/IAI.02939-14.

Fanjul G., Villanueva E. (2016). *Biomedical Innovation and Access to Essential Medicines: Alternatives to a Broken Model.* Barcelona Institute for Global Health (ISGlobal) Analysis Brief, 24. [online]. Available on: https://www.isglobal.org/documents/10179/5353835/Informe+24+Innovaci%C3%B3n+y+acceso+medicamentos+ENG/442662a5-cc8d-401b-baae-3c5f6ae7781a. [Retrieved 7 March 2024].

FDA (13 December 2022a). *Rare Diseases at FDA*. [online]. Available on: https://www.fda.gov/patients/rare-diseases-fda and https://www.fda.gov/patients/rare-diseases-fda. [Retrieved 7 March 2024].

FDA (2022b). *Rare Disease Cures Accelerator. To support innovation and quality in rare disease drug development.* [online]. Available on: https://www.fda.gov/drugs/regulatory-science-research-and-education/rare-disease-cures-accelerator. [Retrieved 7 March 2024].

FDA (2023a). *New Drug Therapy Approvals 2022.Advancing health through innovation*. [online]. Available on: https://www.fda.gov/drugs/new-drugs-fda-cders-new-molecular-entities-and-new-therapeutic-biological-products/new-drug-therapy-approvals-2022#rare-disease. [Retrieved 7 March 2024].

FDA (10 March 2023b). *COVID-19 Vaccines. Updated 16 June 2023*. [online]. Available on: https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines. [Retrieved 7 March 2024].

Feachem, R. G. A., Chen, I., Akbari, O., Bertozzi-Villa, A., Bhatt, S., Binka, F., Boni, M. F., Buckee, C., Dieleman, J., Dondorp, A., Eapen, A., Sekhri Feachem, N., Filler, S., Gething, P., Gosling, R., Haakenstad, A., Harvard, K., Hatefi, A., Jamison, D., … Mpanju-Shumbusho, W. (2019). Malaria eradication within a generation: ambitious, achievable, and necessary. The Lancet Commission. https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(19)31139-0.pdf

Feinmann, J. (2021). COVID-19: global vaccine production is a mess and shortages are down to more than just hoarding. bmj, 375. https://doi.org/10.1136/bmj.n2375.

Feldman, R. (2018). May your drug price be evergreen. Journal of Law and the Biosciences, 5(3), 590-647.

Feloni (2019). *The entrepreneur behind the coveted B Corp label shares why he's partnering with the UN to solve our most pressing workforce problems.* [online]. Available on: https://www.businessinsider.com/the-nonprofit-behind-b-corp-is-making-tools-for-companies-like-danone-2019-4?r=US&IR=T. [Retrieved 7 March 2024].

Fetro, C., & Scherman, D. (2020). Drug repurposing in rare diseases: Myths and reality. Therapie, 75(2), 157–160. https://doi.org/10.1016/j.therap.2020.02.006.

Field, A. P. (2005). Kendall's coefficient of concordance. Encyclopedia of Statistics in Behavioral Science, 2, 1010-11.

Fischer, F. (1995). Evaluating Public Policy. Chicago, Nelson-Hall Publishers.

Fischer, F., & Gottweis, H. (2013). Introduction. *The Argumentative Turn Revisited*. Duke University Press. https://doi.org/10.1215/9780822395362-001.

Fletcher, A. J., & Marchildon, G. P. (2014). Using the Delphi Method for Qualitative, Participatory Action Research in Health Leadership. International Journal of Qualitative Methods, 13(1), 1–18. https://doi.org/10.1177/160940691401300101

Fogel, D. B. (2018). Factors associated with clinical trials that fail and opportunities for improving the likelihood of success: a review. Contemporary clinical trials communications, 11, 156-164.

Fojo, T., & Lo, A. W. (2016). Price, value, and the cost of cancer drugs. In *The Lancet Oncology*. https://doi.org/10.1016/S1470-2045(15)00564-1.

Fontanet, A., & Cauchemez, S. (2020). COVID-19 herd immunity: where are we? Nature Reviews Immunology, 20(10), 583–584. https://doi.org/10.1038/s41577-020-00451-5.

Fontrier, A.M. (2022). Market access for medicines treating rare diseases: Association between specialised processes for orphan medicines and funding recommendations. Social Science and Medicine, 306. https://doi.org/10.1016/j.socscimed.2022.115119.

Friedman, J., Gu, F., & Klausner, J. D. (2019). Pursuing Global Equity in Access to Cancer Drugs: Lessons Learned from the HIV Epidemic. JAMA oncology, 5(11), 1535-1536.

Gagne, J. J., & Choudhry, N. K. (2011). How many "me-too" drugs is too many? *Jama*, *305*(7), 711-712.

Gahilod, R. S., Veeranna, B., & Thakre, S. (2023). Orphan Drug Development Policies in India and the United States: A Comparison. *INDIAN JOURNAL OF PHARMACEUTICAL EDUCATION AND RESEARCH*, *57*(2), 329-336.

Galea, S. (10 January 2016). *Public Health as Public Good*. Boston University School of Public Health. [online]. Available on: https://www.bu.edu/sph/news/articles/2016/public-health-as-a-public-good/. [Retrieved 7 March 2024].

García-Altés, A., McKee, M., Siciliani, L., Barros, P. P., Lehtonen, L., Rogers, H., ... & De Maeseneer, J. (2023). Understanding public procurement within the health sector: a priority in a post-COVID-19 world. Health Economics, Policy and Law, 18(2), 172-185.

GAVI (8 May 2023). *COVAX Facility and COVAX Advanced Market Commitment (AMC) Formative Review and Baseline Study*. [online]. Available on: https://www.gavi.org/our-impact/evaluation-studies/covax-facility-and-covax-advance-market-commitment-amc-formative-review-and-baseline-study. [Retrieved 7 March 2024].

Gaviria, M., & Kilic, B. (2021). A network analysis of COVID-19 mRNA vaccine patents. Nature Biotechnology, 39(5), 546-548.

Geertz, C. (1973). The interpretation of cultures (Vol. 5019). Basic books. Selected Essays, New York: Basic Books, pp. 3–30.

Geiger, S., & Gross, N. (2023). Tech sharing, not tech hoarding: COVID-19, global solidarity, and the failed responsibility of the pharmaceutical industry organization, 13505084221145666.

Gilead Sciences (February 2016). *HIV Treatment Expansion*. [online]. Available on: https://www.gilead.com/mobile/~/media/files/pdfs/other/hivtreatmentexpansion020816.pdf. [Retrieved 7 March 2024].

Global Fund (2020). *Pooled Procurement Mechanism Reference Pricing: Strategic Medicines used in HIV programs*. [online]. Available on: https://www.theglobalfund.org/media/7500/ppm_strategicmedicineshivreferencepricing_table_en.pdf. [Retrieved 7 March 2024].

Goodland, R., & Ledec, G. (1987). Neoclassical economics and principles of sustainable development. Ecological modelling, 38(1-2), 19-46.

Goodman, C.M. (1987). The Delphi technique: a critique. Journal of Advanced Nursing 12 (6), 729-734. https://doi.org/10.1111/j.1365-2648.1987.tb01376.x

Govindaraj, R. G., Naderi, M., Singha, M., Lemoine, J., & Brylinski, M. (2018). Large-scale computational drug repositioning to find treatments for rare diseases. Npj Systems Biology and Applications, 4(1). https://doi.org/10.1038/s41540-018-0050-7.

Goyeneche, O. Y. R., Ramirez, M., Schot, J., & Arroyave, F. (2022). Mobilizing the transformative power of research for achieving the Sustainable Development Goals. Research Policy, 51(10), 104589.

Gozzi, N., Chinazzi, M., Dean, N. E., Longini, I. M., Jr, Halloran, M. E., Perra, N., & Vespignani, A. (2023). Estimating the impact of COVID-19 vaccine inequities: a modeling study. Nature communications, 14(1), 3272. https://doi.org/10.1038/s41467-023-39098-w.

Grande, T. (2017). Kendall's Coefficient of Concordance (Kendall's W) in excel. [video]. Available on: https://www.youtube.com/watch?v=BW5vCZwpTxY. [Retrieved 7 March 2024].

Green, J., & Thorogood, N. (2004). Qualitative methodology and health research. In *Qualitative methods for health research*.

Gregson, N., Sparrowhawk, K., Mauskopf, J., & Paul, J. (2005). Pricing medicines: Theory and practice, challenges and opportunities. In Nature Reviews Drug Discovery.https://doi.org/10.1038/nrd1633.

Grin, J., van de Graaf, H., & Hoppe, R. (1997). Technology Assessment through Interaction: A guide. (Working document; No. 57). Rathenau Institute.

Gronde, T. V. D., Uyl-de Groot, C. A., & Pieters, T. (2017). Addressing the challenge of high-priced prescription drugs in the era of precision medicine: a systematic review of drug life cycles, therapeutic drug markets and regulatory frameworks. PloS one, 12(8), e0182613.

Guba, E. G., & Lincoln, Y. S. (1989). Fourth generation evaluation. Sage. pp.149-1 5 5; pp. 177 -179.

Guba, E. G., & Lincoln, Y. S. (2001). Guidelines and checklist for constructivist (aka fourth generation) evaluation.

Guenat, S., Purnell, P., Davies, Z. G., Nawrath, M., Stringer, L. C., Babu, G. R., ... & Dallimer, M. (2022). Meeting sustainable development goals via robotics and autonomous systems. Nature communications, 13(1), 3559.

Gupta, R., Srivastava, D., Sahu, M., Tiwari, S., Ambasta, R. K., & Kumar, P. (2021). Artificial intelligence to deep learning: machine intelligence approach for drug discovery. Molecular diversity, 25, 1315-1360.

Gurgula, O. (2021a). Accelerating COVID-19 vaccine production via involuntary technology transfer. The South Centre policy brief, 102.

Gurgula, O. (2021b). Compulsory licensing vs. the IP waiver: what is the best way to end the COVID-19 pandemic? Policy brief, 104.

Gustafsson, D. (2019). Analysing the Double diamond design process through research & implementation.

Guterres, A. (2020). Tackling the inequality pandemic: A new social contract for a new era. *Nelson Mandela Annual Lecture*.

H2O (2023). *Health Outtcomes Observatory*. [online]. Available on: https://health-outcomes-observatory.eu/. [Rerieved 2 December 2023].

Habibi, A., Sarafrazi, A., & Izadyar, S. (2014). Delphi technique theoretical framework in qualitative research. The International Journal of Engineering and Science, 3(4), 8-13.

Hall, A. K., & Carlson, M. R. (2014). The current status of orphan drug development in Europe and the US. Intractable & rare diseases research, 3(1), 1–7. https://doi.org/10.5582/irdr.3.1.

Hamilton, L. (2019). Amartya Sen. John Wiley & Sons.

Hannon, E., Hanbali, L., Lehtimaki, S., & Schwalbe, N. (2022). Why we still need a pandemic treaty. The Lancet Global Health, 10(9), e1232-e1233.

Harman, S., Erfani, P., Goronga, T., Hickel, J., Morse, M., & Richardson, E. T. (2021). Global vaccine equity demands reparative justice—not charity. BMJ Global Health, 6(6), e006504.

Harvard Business School, *Value-based Health Care Key Concepts*. [online]. Available on: https://www.isc.hbs.edu/health-care/value-based-health-care/key-concepts/Pages/default.aspx. [Retrieved 7 March 2024].

Hasson, F., Keeney, S., McKenna, H. (2000). Research guidelines for the Delphi survey technique. Journal of Advanced Nursing 32 (4), 1008–1015. https://doi.org/10.1046/j.1365-2648.2000.t01-1-01567.

Haverfield, M. C., Tierney, A., Schwartz, R., Bass, M. B., Brown-Johnson, C., Zionts, D. L., ... & Zulman, D. M. (2020). Can patient–provider interpersonal interventions achieve the quadruple aim of healthcare? A systematic review. Journal of General Internal Medicine, 35, 2107-2117.

Hemerijck, A., Mazzucato, M., & Reviglio, E. (2020). Social investment and infrastructure. Open Book Publishers.

Henein, M., & Ells, C. (2021). Identifying and classifying tools for health policy ethics review: A systematic search and review. Health Care Analysis, 29, 1-20.

Henry B. (2018). Drug. Pricing & Challenges to Hepatitis C treatment access. *Journal of health & biomedical law*, *14*, 265–283.

Hoen E.F.M. (2016). Indian hepatitis C drug patent decision shakes public health community. Lancet 2016; 387: 2272–73.

Hoen E.F.M., Veraldi J., Toebes B., Hogerzeil H.V. (2018). Medicine procurement and the use of flexibilities in the agreement on trade-related aspects of intellectual property rights, 2001-2016. Bulletin of the World Health Organization, 96 (3), pp. 185 - 193, Cited 40 times. DOI: 10.2471/BLT.17.199364

Hollingworth, S., Fenny, A. P., Yu, S. Y., Ruiz, F., & Chalkidou, K. (2021). Health technology assessment in sub-Saharan Africa: a descriptive analysis and narrative synthesis. *Cost Effectiveness and Resource Allocation*, *19*(1), 39.

Hollingworth, S., Gyansa-Lutterodt, M., Dsane-Selby, L., Nonvignon, J., Lopert, R., Gad, M., ... & Chalkidou, K. (2020). Implementing health technology assessment in Ghana to support universal health coverage: building relationships that focus on people, policy, and process. *International Journal of Technology Assessment in Health Care*, *36*(1), 8-11.

Honeyman, R., & Jana, T. (2019). The B Corp handbook: How you can use business as a force for good. Berrett-Koehler Publishers.

Horne, L. C., & Heath, J. (2022). A market failures approach to justice in health. Politics, Philosophy & Economics, 21(2), 165-189.

Hotez, P. J. (2016). Blue marble health: An innovative plan to fight diseases of the poor amid wealth. In Blue Marble Health: An Innovative Plan to Fight Diseases of the Poor amid Wealth. Johns Hopkins University Press. https://doi.org/10.3201/eid2302.161801.

Hotez, P. J. (2017). Neglected tropical diseases in the time of Dr Tedros. In *Transactions of the Royal Society of Tropical Medicine and Hygiene*. https://doi.org/10.1093/trstmh/trx040.

Hotez, P. J., Damania, A., & Naghavi, M. (2016). Blue Marble Health and the Global Burden of Disease Study 2013. In *PLoS Neglected Tropical Diseases*. https://doi.org/10.1371/journal.pntd.0004744.

Houston, L., Martin, A., Yu, P., & Probst, Y. (2021). Time-consuming and expensive data quality monitoring procedures persist in clinical trials: a national survey. Contemporary Clinical Trials, 103, 106290.

Howard, D. H., Bach, P. B., Berndt, E. R., & Conti, R. M. (2015). Pricing in the market for anticancer drugs. *Journal of Economic Perspectives*. https://doi.org/10.1257/jep.29.1.139.

Hsu, C. & Sandford, B. (2007). The Delphi Technique: Making Sense Of Consensus. Practical Assessment, Research and Evaluation. 12.

Huff, A. L., Jaffee, E. M., & Zaidi, N. (2022). Messenger RNA vaccines for cancer immunotherapy: progress promotes promise. The Journal of clinical investigation, 132(6), e156211. https://doi.org/10.1172/JCI156211.

Hurst, L., Mahtani, K., Pluddemann, A., Lewis, S., Harvey, K., Briggs, A., ... & Heneghan, C. (2019). Defining Value-based Healthcare in the NHS. Centre for Evidence-Based Medicine Report 2019/04, (4).

Hutin Y, Desai S, Bulterys M. (2018). Preventing hepatitis B virus infection: milestones and targets. Bull World Health Organ 2018; 96: 443A.

ICER (25 September 2023). *Value Assessment Framework*. 2023. [online]. Available on: https://icer.org/wp-content/uploads/2023/09/ICER_2023_VAF_For-Publication_092523.pdf. [Retrieved 7 March 2024].

ICHOM (9 October 2023). ICHOM Conference 2023. [online]. Available on: https://conference.ichom.org/. [Retrieved 7 March 2024].

Ikilezi, G., Augusto, O. J., Dieleman, J. L., Sherr, K., & Lim, S. S. (2020). Effect of donor funding for immunization from Gavi and other development assistance channels on vaccine coverage: evidence from 120 low and middle income recipient countries. Vaccine, 38(3), 588-596.

Inrate (12 July 2023). *Current ESG Trends to Watch for 2023*. [online]. Available on: https://inrate.com/blog/latest-esg-trends-2023/. [Retrieved 7 March 2024]

IPCC (2023). *Climate Change 2023.* AR6 Synthesis Report. [online]. Available on: https://www.ipcc.ch/report/ar6/syr/. [Retrieved 7 March 2024].

IQVIA (2020). *Orphan Drugs in the United States. Rare Disease innovaiton and cost trends through 2019.* Report 2020. [online]. Available on: https://www.iqvia.com/form-pages/institute-gated?redirectUrl=%2f-%2fmedia%2fiqvia%2fpdfs%2finstitute-reports%2forphan-drugs-in-the-united-states-rare-disease-innovation-and-cost-trends-through-2019%2forphan-drugs-in-the-united-states.pdf&title=Orphan+Drugs+in+the+United+States. [Retrieved 7 March 2024].

IQVIA (27 February 2023). *Recent advancements in the rare diseases landscape. How RWE can accelerate development, approval, and access to new ground-breaking therapies*. [online]. Available on: https://www.iqvia.com/locations/united-kingdom/blogs/2023/02/recent-advancements-in-the-rare-disease-landscape. [Retrieved 7 March 2024].

Jackson, J. K., Weiss, M. A., Schwarzenberg, A. B., Nelson, R. M., Sutter, K. M., & Sutherland, M. D. (2020). Global economic effects of COVID-19.

Jamison, D. T. (2018). Disease control priorities: improving health and reducing poverty. The Lancet, 391(10125), e11-e14.

Jayasundara, K., Hollis, A., Krahn, M., Mamdani, M., Hoch, J. S., & Grootendorst, P. (2019). Estimating the clinical cost of drug development for orphan versus non-orphan drugs. *Orphanet journal of rare diseases*, *14*, 1-10.

Jeffery, G., Hache, G., Lehr, R. (1995). A group-based Delphi application: defining rural career counselling needs. Measurement and Evaluation in Counselling and Development 28, 45-60.

Jünger, S., Payne, S. A., Brine, J., Radbruch, L., & Brearley, S. G. (2017). Guidance on Conducting and REporting DElphi Studies (CREDES) in palliative care: Recommendations based on a methodological systematic review. Palliative medicine, 31(8), 684-706.

Kalkanci, B., & Plambeck, E. L. (2020). Managing supplier social and environmental impacts with voluntary versus mandatory disclosure to investors. Management Science, 66(8), 3311-3328.

Kampers, L. F., Asin-Garcia, E., Schaap, P. J., Wagemakers, A., & Dos Santos, V. A. M. (2021). From innovation to application: bridging the valley of death in industrial biotechnology. Trends in Biotechnology, 39(12), 1240-1242.

Katella, K. (5 October 2023). *What to Know About EG.5 (Eris) – the Latest Coronavirus Strain*. Yale Medicine. [online]. Available on: https://www.yalemedicine.org/news/covid-eg5-eris-latest-coronavirus-strain. [Retrieved 7 March 2024].

Kaul, I., Grunberg, I., & Stern, M. (1999). Global public goods. *New York-Oxford*.

Kawalec, P., Sagan, A., & Pilc, A. (2016). The correlation between HTA recommendations and reimbursement status of orphan drugs in Europe. Orphanet Journal of Rare Diseases, 11(1), 122. https://doi.org/10.1186/s13023-016-0501-4.

Keeney, S., Hasson, F., McKenna, H. P. (2001). A critical review of the Delphi technique as a research methodology for nursing. International Journal of Nursing Studies (2), 195–200. https://doi.org/10.1016/S0020-7489(00)00044-4.

Keeney, S., McKenna, H. A., & Hasson, F. (2011). *The Delphi technique in nursing and health research*. John Wiley & Sons.

Kelly, T. R., Machalaba, C., Karesh, W. B., Crook, P. Z., Gilardi, K., Nziza, J., Uhart, M. M., Robles, E. A., Saylors, K., Joly, D. O., Monagin, C., Mangombo, P. M., Kingebeni, P. M., Kazwala, R., Wolking, D., Smith, W., & Mazet, J. A. K. (2020). Implementing One Health approaches to confront emerging and re-emerging zoonotic disease threats: lessons from PREDICT. One Health Outlook. https://doi.org/10.1186/s42522-019-0007-9.

Kesselheim A.S. (2020). *Improving competition to lower U.S. prescription drug costs, Washington Center for Equitable Growth*. [online]. Available on: https://equitablegrowth.org/improving-competition-to-lower-u-s-prescription-drug-costs/. [Retrieved 7 May 2024].

Kesselheim, A. S., Avorn, J., & Sarpatwari, A. (2016). The high cost of prescription drugs in the United States: origins and prospects for reform. Jama, 316(8), 858-871.

Kesselheim, A. S., Tan, Y. T., & Avorn, J. (2015). The roles of academia, rare diseases, and repurposing in the development of the most transformative drugs. *Health Affairs*. https://doi.org/10.1377/hlthaff.2014.1038.

Khetrapal, S., & Bhatia, R. (2020). Impact of COVID-19 pandemic on health system & Sustainable Development Goal 3. The Indian journal of medical research, 151(5), 395.

Kieny, M. P., Viergever, R. F., Adam, T., Boerma, T., & Røttingen, J. A. (2016). Global platform to inform investments for health R&D. The Lancet. https://doi.org/10.1016/S0140-6736(16)00705-4.

Kim, J. H., Hotez, P., Batista, C., Ergonul, O., Figueroa, J. P., Gilbert, S., ... & Bottazzi, M. E. (2021). Operation Warp Speed: implications for global vaccine security. The Lancet Global Health, 9(7), e1017-e1021.

Kimble, L., & Massoud, M. R. (2017). What do we mean by innovation in healthcare. Eur Med J, 1, 89-91.

Kobus, J., & Westner, M. (2016). Ranking-type delphi studies in IS research: step-by-step guide and analytical extension. In *IADIS Int. Conf. Inf. Syst* (pp. 28-38).

Kohler, J., Wong, A., & Tailor, L. (2022). Improving access to COVID-19 vaccines: an analysis of TRIPS waiver discourse among WTO Members, civil society organizations, and pharmaceutical industry stakeholders. Health and Human Rights, 24(2), 159.

Koplan, J. P., Bond, T. C., Merson, M. H., Reddy, K. S., Rodriguez, M. H., Sewankambo, N. K., & Wasserheit, J. N. (2009). Towards a common definition of global health. The Lancet, 373(9679), 1993-1995.

Krieger, J., Li, D., & Papanikolaou, D. (2022). Missing novelty in drug development. The Review of Financial Studies, 35(2), 636-679.

Kristensen, F. B., Lampe, K., Wild, C., Cerbo, M., Goettsch, W., & Becla, L. (2017). The HTA Core Model®—10 years of developing an international framework to share multidimensional value assessment. Value in Health, 20(2), 244-250.

Kumar, R., Chakwin, M., Suharlim, C., Gilmartin, C., Caruso, A. A., Mehra, M., & Castro, H. (2021). PNS76 The Growing Demand for HTA in Sub-Saharan Africa. Value in Health, 24, S186-S187.

Kwon, H. Y., & Kim, Y. (2020). Global access to cancer medicines. In *Global Pharmaceutical Policy*. https://doi.org/10.1007/978-981-15-2724-1_4.

Laplane, A., & Mazzucato, M. (2020). Socializing the risks and rewards of public investments: Economic, policy, and legal issues. Research Policy: X. https://doi.org/10.1016/j.repolx.2020.100008.

Lawson, T. (2013). What is this 'school'called neoclassical economics? Cambridge Journal of Economics, 37(5), 947-983.

Lazarus, J. V., Romero, D., Kopka, C. J., Karim, S. A., Abu-Raddad, L. J., Almeida, G., ... & El-Mohandes, A. (2022). A multinational Delphi consensus to end the COVID-19 public health threat. *Nature*, 1-14.

Lazonick, W. (2014). Profits without prosperity. Harvard Business Review.

Ledley, F. D., McCoy, S. S., Vaughan, G., & Cleary, E. G. (2020). Profitability of large pharmaceutical companies compared with other large public companies. Jama, 323(9), 834-843.

Lee, K. (2020). *Mind the Gap: Bridging the 'Valley of Death' for U.S. Biomanufacturing.* NIST. [online]. Available on: https://www.nist.gov/blogs/taking-measure/mind-gap-bridging-valley-death-us-biomanufacturing. [Retrieved 28 April 2023].

Lee, C., Lee, J. M., & Liu, Y. (2023). Catalysing innovation and digital transformation in combating the Covid-19 pandemic: Whole-of government collaborations in ICT, R&D, and business digitization in Singapore. Public Money & Management, 43(4), 340-348.

Lee, T., & Porter, M. (2013). The strategy that will fix healthcare (Vol. 91, pp. 1-19). Boston: Harvard Business Review.

Lee, V. C. J., Yao, J., & Zhang, W. (2021). The Health Impact Fund: making the case for engagement with pharmaceutical laboratories in Brazil, Russia, India, and China. *Globalization and Health*, *17*, 1-7.

Leeming, G., Ainsworth, J., & Clifton, D. A. (2019). Blockchain in health care: hype, trust, and digital health. The Lancet, 393(10190), 2476-2477.

Lenert, L., & McSwain, B. Y. (2020). Balancing health privacy, health information exchange, and research in the context of the COVID-19 pandemic. Journal of the American Medical Informatics Association, 27(6), 963-966.

Light, D. W., & Warburton, R. (2011). Demythologizing the high costs of pharmaceutical research. *BioSocieties*. https://doi.org/10.1057/biosoc.2010.40.

Littlejohns, P., Chalkidou, K., Culyer, A. J., Weale, A., Rid, A., Kieslich, K., ... & Knight, S. (2019). National Institute for Health and Care Excellence, social values and healthcare priority setting. *Journal of the Royal Society of Medicine*, *112*(5), 173-179.

Liu, S. (2020). DARPA: A global innovation differentiator. IEEE Engineering Management Review, 48(2), 65-71.

Liu, K., & Lou, Y. (2022). Optimizing COVID-19 vaccination programs during vaccine shortages. Infectious Disease Modelling, 7(1), 286–298. https://doi.org/https://doi.org/10.1016/j.idm.2022.02.002

Liu, Z., Shi, Y., & Yang, B. (2022). Open innovation in times of crisis: An overview of the healthcare sector in response to the COVID-19 Pandemic. *Journal of Open Innovation: Technology, Market, and Complexity*, *8*(1), 21.

Lore, A. (28 February 2023). Pharma Research Progress Hope. *Celebrating 40 years of the Orphan Drug Act on Rare Disease Day*. [online]. Available on: https://phrma.org/en/Blog/Celebrating-40-years-of-the-Orphan-Drug-Act-on-Rare-Disease-Day. [Retrieved 7 March 2024].

Love, J., & T. Hubbard. (2009). Prizes for Innovation of New Medicines and Vaccines. Annals of Health Law/Loyola University Chicago, School of Law, Institute for Health Law 18 (2): 155–186.

Lucero-Prisno III, D. E., Shomuyiwa, D. O., Kouwenhoven, M. B. N., Dorji, T., Odey, G. O., Miranda, A. V., ... & Wong, M. C. (2023). Top 10 public health challenges to track in 2023: Shifting focus beyond a global pandemic. *Public Health Challenges*, *2*(2), e86.

Lynn, M.R., Layman, E.L., Englebardt, S.P. (1998). Nursing administration research priorities: A National Delphi study. Journal of Nursing Administration 28 (5), 7-11.

Makurvet, F. D. (2021). Biologics vs. small molecules: Drug costs and patient access. Medicine in Drug Discovery, 9, 100075.

Malekzadeh, A., Michels, K., Wolfman, C., Anand, N., & Sturke, R. (2020). Strengthening research capacity in LMICs to address the global NCD burden. *Global Health Action*, *13*(1), 1846904.

Marseille, E., & Kahn, J. G. (2019). Utilitarianism and the ethical foundations of cost-effectiveness analysis in resource allocation for global health. *Philosophy, Ethics, and Humanities in Medicine*, *14*(1), 1-7.

Maxmen, A. (2016). Big pharma's cost-cutting challenger. *Nature*, *536*(7617), 388-390.

Mayer, I. S., Van Daalen, C. E., & Bots, P. W. G. (2004). Perspectives on policy analyses: A framework for understanding and design. In International Journal of Technology, Policy and Management, 4(2), 169–191. https://doi.org/10.1504/IJTPM.2004.004819.

Mazzoleni, R., & Nelson, R. R. (1998). Economic theories about the benefits and costs of patents. In Journal of Economic Issues. https://doi.org/10.1080/00213624.1998.11506108.

Mazzucato, M. (2013). The Entrepreneurial State. London: Anthem Press.

Mazzucato, M. (2016a). High cost of new drugs. In British Medical Journal (*BMJ)*. 354 (4136). https://doi.org/10.1136/bmj.i4136.

Mazzucato, M. (2016b). From market fixing to market-creating: a new framework for innovation policy. Industry and Innovation. https://doi.org/10.1080/13662716.2016.1146124.

Mazzucato, M. (2018). The Value of Everything. London: Penguin.

Mazzucato, M. (2021). Mission economy: A moonshot guide to changing capitalism. Penguin UK.

Mazzucato, M. (1 May 2023a). *Financing the Common Good*. [online]. Available on: https://www.project-syndicate.org/commentary/new-economic-paradigm-common-good-market-shaping-by-mariana-mazzucato-2023-05?barrier=accesspaylog. [Retrieved 7 March 2024].

Mazzucato, M. (2023b). *A collective response to our global challenges: a common good and 'market-shaping' approach*. UCL Institute for Innovation and Public Purpose, Working Paper Series. Available on: https://www. ucl. ac. uk/bartlett/public-purpose/publications/2023/jan/collective-response-our-global-challenges-common-good-and-market-shaping. [Retrieved 7 March 2024].

McEvoy, E., & Ferri, D. (2020). The role of the joint procurement agreement during the COVID-19 Pandemic: Assessing Its usefulness and discussing its potential to support a european health union. European Journal of Risk Regulation, 11(4), 851-863.

McKinsey (21 January 2023). *5 takeaways from the World Economic Forum's 2023 meeting. Davos*. [online]. Available on: https://www.mckinsey.com/featured-insights/themes/5-takeaways-from-the-world-economic-forums-2023-meeting. [Retrieved 7 March 2024].

McPake, B., Normand, C., Smith, S., & Nolan, A. (2020). Health economics: an international perspective. Routledge.

Mercurio, B., & Upreti, P. N. (2022). From necessity to flexibility: a reflection on the negotiations for a TRIPS waiver for COVID-19 vaccines and treatments. *World Trade Review*, *21*(5), 633-649.

Micah, A. E., Su, Y., Bachmeier, S. D., Chapin, A., Cogswell, I. E., Crosby, S. W., ... & Moghadaszadeh, M. (2020). Health sector spending and spending on HIV/AIDS, tuberculosis, and malaria, and development assistance for health: progress towards Sustainable Development Goal 3. The Lancet, 396(10252), 693-724.

Miethke, M., Pieroni, M., Weber, T., Brönstrup, M., Hammann, P., Halby, L., ... & Müller, R. (2021). Towards the sustainable discovery and development of new antibiotics. Nature Reviews Chemistry, 5(10), 726-749.

Miles, M. B., & Huberman, A. M. (1994). Qualitative data analysis: An expanded sourcebook. sage.

Miller, K. L., Fermaglich, L. J., & Maynard, J. (2021). Using four decades of FDA orphan drug designations to describe trends in rare disease drug development: substantial growth seen in development of drugs for rare oncologic, neurologic, and pediatric-onset diseases. *Orphanet journal of rare diseases*, *16*(1), 265. https://doi.org/10.1186/s13023-021-01901-6.

Moch, F., Arabi, W., NA, A., & Pre, A. C. (2021). What the Moderna–NIH COVID vaccine patent fight means for research. Nature, 600.

Moeckli, D., Shah, S., Sivakumaran, S., & Harris, D. (Eds.). (2022). International human rights law. Oxford University Press.

Moliner, A.M., Waligora, J. (2017). The European Union Policy in the Field of Rare Diseases. In: Posada de la Paz, M., Taruscio, D., Groft, S. (eds) Rare Diseases Epidemiology: Update and Overview. Advances in Experimental Medicine and Biology, vol 1031. Springer, Cham. https://doi.org/10.1007/978-3-319-67144-4_30.

Moon, S., Mariat, S., Kamae, I., & Pedersen, H. B. (2020). Defining the concept of fair pricing for medicines. bmj, 368.

Moore, C.M. (1987). Technique and the mail questionnaire in Group Techniques for Idea Building: Applied social research methods. Series 9. Sage, Newbury Park, CA, pp. 50-77.

Moreno, S. G., & Epstein, D. (2019). The price of innovation-the role of drug pricing in financing pharmaceutical innovation. A conceptual framework & Health Policy, 7(1), 1583536. https://doi.org/10.1080/20016689.2019.1583536.

Morin, S., Segafredo, G., Piccolis, M., Das, A., Das, M., Loffredi, N., ... & Burrone, E. (2023). Expanding access to biotherapeutics in low-income and middle-income countries through public health non-exclusive voluntary intellectual property licensing: considerations, requirements, and opportunities. The Lancet Global Health.

Morley, J., Machado, C. C. V, Burr, C., Cowls, J., Joshi, I., Taddeo, M., & Floridi, L. (2020). The ethics of AI in health care: A mapping review. Social Science & Medicine, 260, 113172. https://doi.org/https://doi.org/10.1016/j.socscimed.2020.113172.

Mowbray, C. E., Braillard, S., Glossop, P. A., Whitlock, G. A., Jacobs, R. T., Speake, J., ... & Wyllie, S. (2021). DNDI-6148: a novel benzoxaborole preclinical candidate for the treatment of visceral leishmaniasis. Journal of medicinal chemistry, 64(21), 16159-16176.

MPP (16 November 2021). *Pfizer and Medicines Patent Pool (MPP) sign licensing agreement for COVID-19 oral antiviral treatment candidate to expand access in Low-and Middle-Income Countries.* [online]. Available on: https://medicinespatentpool.org/news-publications-post/pfizer-and-the-medicines-patent-pool-mpp-sign-licensing-agreement-for-covid-19-oral-antiviral-treatment-candidate-to-expand-access-in-low-and-middle-income-countries. [Retrieved 7 March 2024].

MPP (30 November 2022). *Medicines Patent Pool*. [online]. Available on: https://covid19response.org/medicines-patent-pool/. [Retrieved 7 March 2024].

MPP (10 August 2023a). *Annual Report 2022: Greater Access to Medicines and health Technologies for those who need them*. [online]. Available on: https://medicinespatentpool.org/who-we-are/annual-reports. [Retrieved 7 March 2024].

MPP (2023b). *mRNA Technology Transfer Programme*. [online]. Available on: https://medicinespatentpool.org/what-we-do/mrna-technology-transfer-programme. [Retrieved 7 March 2024].

MSCI. *ESG And Climate Trends to Watch for 2023.* [online]. Available on: https://www.msci.com/documents/1296102/35124068/ESG+and+Climate+Trends+to+Watch+for+2023.pdf. [Retrieved 7 March 2024].

MSF Access Campaign (October 2020). *Voluntary Licenses and Access to Medicines*. Médecins sans Frontières Technical Briefing. [online]. Available on: https://msfaccess.org/sites/default/files/2020-10/IP_VoluntaryLicenses_full-brief_Oct2020_ENG.pdf. [Retrieved 7 March 2024].

MSF Access Campaign (27 May 2021). *Analysis of EU position on compulsory licensing and TRIPS waiver in* the COVID-19 pandemic. Médecins sans Frontières Technical Brief. [online]. Available on: https://msfaccess.org/analysis-eu-position-compulsory-licensing-and-trips-waiver-covid-19-pandemic. [Retrieved 7 March 2024].

Mueller, B. (23 February 2023). *After Long delay, Moderna pays N.I.H. for COVID Vaccine Technique. The New York Times.* [online]. Available on: https://www.nytimes.com/2023/02/23/science/moderna-covid-vaccine-patent-nih.html. [Retrieved 7 March 2024].

Mueller, D. (2020). Addressing the challenges of implementing a Health Technology Assessment Policy framework in South Africa. *International journal of technology assessment in health care*, *36*(4), 453-458.

Murphy, T., & Parkey, J. (2016). An economic analysis of the philosophical common good. *International Journal of Social Economics*, *43*(8), 823-840.

National Academies of Sciences, Engineering, and Medicine (2018). *Making Medicines Affordable: A National imperative.* [online]. Available on: https://www.nap.edu/catalog/24946/making-medicines-affordable-a-national-imperative (describing the drug pricing crisis in the United States). [Retrieved 7 March 2024].

National Academies of Sciences, Engineering, and Medicine (2023). *Toward Equitable Innovation in Health and Medicine*. A framework. 2023. [online]. Available on: https://nap.nationalacademies.org/catalog/27184/toward-equitable-innovation-in-health-and-medicine-a-framework. [Retrieved 7 March 2024].

Neumann, P. J., & Weinstein, M. C. (2010). Legislating against use of cost-effectiveness information. N Engl J Med, 363(16), 1495-1497.

Newman, T. (20 August 2020). *The 5 S's to embracing change.* [video]. Available on: https://www.youtube.com/watch?v=hnqjQrSWbGQ. [Retrieved 7 March 2024].

Nguengang Wakap, S., Lambert, D. M., Olry, A., Rodwell, C., Gueydan, C., Lanneau, V., ... & Rath, A. (2020). Estimating cumulative point prevalence of rare diseases: analysis of the Orphanet database. European Journal of Human Genetics, 28(2), 165-173.

Niederberger, M., & Spranger, J. (2020). Delphi Technique in Health Sciences: A Map. Frontiers in Public Health, 8. https://doi.org/10.3389/fpubh.2020.00457.

NIH National Library of Medicine (2023). ClinicalTrials.gov. [online]. Available from: https://clinicaltrials.gov/. [Retrieved 7 March 2024].

Odone, A., Buttigieg, S., Ricciardi, W., Azzopardi-Muscat, N., & Staines, A. (2019). Public health digitalization in Europe: EUPHA vision, action and role in digital public health. European Journal of Public Health, 29(Supplement_3), 28–35. https://doi.org/10.1093/eurpub/ckz16.

OECD (29 April 2019). *Licensing of IP rights and Competition Law.* [online]. Available on: https://one.oecd.org/document/DAF/COMP(2019)3/en/pdf. [Retrieved 7 March 2024].

OECD (March 2023). *Collaborative mechanisms for sustainaible health innovation. The case of vaccines and antibiotics*. OECD science, technology and industry. Policy paper. No. 145. [online]. Available on:

https://www.oecd-ilibrary.org/docserver/3e8d40dcen.pdf?expires=1700760949&id=id&accname=guest&checksum=C76B7BFCB8BEE6C2C4AAEC10FC834267. [Retrieved 7 March 2024].

Okoli, C., & Pawlowski, S. D. (2004). The Delphi method as a research tool: an example, design considerations and applications. Information & management, 42(1), 15-29.

O'Rourke B, Oortwijn W, Schuller T, & the International Joint Task Group (2020). The new definition of health technology assessment: A milestone in international collaboration. *International Journal of Technology Assessment in Health Care* 1-4. https://doi.org/10.1017/S0266462320000215.

Orphanet (13 October 2023). The portal for rare diseases and orphan drugs. *Diagnostic Test*. [online]. Available from: https://www.orpha.net/consor4.01/www/cgi-bin/ClinicalLabs.php. [Retrieved 7 March 2024].

Ortenzi, F., Marten, R., Valentine, N. B., Kwamie, A., & Rasanathan, K. (2022). Whole of government and whole of society approaches: call for further research to improve population health and health equity. BMJ Global Health, 7(7), e009972.

Palladino, L., & Lazonick, W. (2022). Regulating stock buybacks: the $6.3 trillion question. International Review of Applied Economics, 1-25.

Pandey, N., de Coninck, H., & Sagar, A. D. (2022). Beyond technology transfer: Innovation cooperation to advance sustainable development in developing countries. *Wiley Interdisciplinary Reviews: Energy and Environment*, *11*(2), e422.

Panzer, A. D., Emerson, J. G., D'Cruz, B., Patel, A., Dabak, S., Isaranuwatchai, W., ... & Kim, D. D. (2020). Growth and capacity for cost-effectiveness analysis in Africa. *Health Economics*, *29*(8), 945-954.

Paolone, F., Cucari, N., Wu, J., & Tiscini, R. (2022). How do ESG pillars impact firms' marketing performance? A configurational analysis in the pharmaceutical sector. *Journal of Business & Industrial Marketing*, *37*(8), 1594-1606.

Paré, G., Cameron, A. F., Poba-Nzaou, P., & Templier, M. (2013). A systematic assessment of rigor in information systems ranking-type Delphi studies. *Information & management*, *50*(5), 207-217.

Paul, B., & R. Langreth. (2015). Pharma Execs Don't Know Why Anyone Is Upset by a $94,500 Miracle Cure. Bloomberg Businessweek, [online]. Available on: https://www.bloomberg.com/news/articles/ 2015-06-03/specialty-drug-costs-gilead-s-hepatitis-c-cures-spur-backlash [Accessed 2nd February 2021].

Pedrana, A., Howell, J., Scott, N., Schroeder, S., Kuschel, C., Lazarus, J. V, Atun, R., Baptista-Leite, R., 't Hoen, E., Hutchinson, S. J., Aufegger, L., Peck, R., Sohn, A. H., Swan, T., Thursz, M., Lesi, O., Sharma, M., Thwaites, J., Wilson, D. P., & Hellard, M. (2020). Global hepatitis C elimination: an investment framework. The Lancet Gastroenterology and Hepatology, 5(10), 927 – 939. https://doi.org/10.1016/S2468-1253(20)30010-8.

Peeters, S., Schmitt, M., & Volk, A. (2020). Social bonds can help mitigate the economic and social effects of the COVID-19 Crisis.

Perehudoff, K., Hoen, E. T., & Boulet, P. (2021). Overriding drug and medical technology patents for pandemic recovery: a legitimate move for high-income countries, too. BMJ global health, 6(4), e005518.

Perehudoff K, Wirtz VJ, Wong A, Rusu, V.& Kohler, J. (2022), A global social contract to ensure access to essential medicines and health technologies. BMJ Global Health 2022;7: e010057. http://dx.doi.org/10.1136/bmjgh-2022-010057.

Pereno, A., & Eriksson, D. (2020). A multi-stakeholder perspective on sustainable healthcare: From 2030 onwards. Futures, 122, 102605.

Pfizer (25 May 2022). *Pfizer launches 'An Accord for a healthier World' to improve health equity for 1.2 Billion people living in 45 lower-income countries*. [online]. Available on: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-launches-accord-healthier-world-improve-health. [Retrieved 7 March 2024].

Phelan, A. L. (2023). The World Health Organization pandemic treaty. BMJ, 380. https://doi.org/10.1136/bmj.p463.

Philipsborn, P., Steinbeis, F., Bender, M. E., Regmi, S., & Tinnemann, P. (2015). Poverty-related and neglected diseases - an economic and epidemiological analysis of poverty relatedness and neglect in research and development. *Global health action*, *8*, 25818. https://doi.org/10.3402/gha.v8.25818.

Plackett, B. (2020). Why big pharma has abandoned antibiotics. Nature, 586(7830), S50-S50.

Plug and Play (2023). Plug and Play Tech Center. [online]. Available on: https://www.plugandplaytechcenter.com/. [Retrieved 7 March 2024].

Policy Cures Research (2020). Landscape of emerging infectious disease research and development: Preventing the next pandemic. G-Finder 2020 report. [online]. Available on: https://s3-ap-southeast-2.amazonaws.com/policy-cures-website-assets/app/uploads/2020/10/30095357/EID_Report.pdf. [Retrieved 7 March 2024].

Policy Cures Research (23 January 2023). *G-Finder*. [online]. Available on: https://gfinderdata.policycuresresearch.org/pages/data-visualisations/allNeglectedDiseases. [Retrieved 7 March 2024].

Porter, M. E. (2010). What is value in health care. N Engl J Med, 363(26), 2477-2481.

Porter, M. E., & Teisberg, E. O. (2006). *Redefining health care: creating value-based competition on results.* [online]. Available on: https://www.hbs.edu/ris/Publication%20Files/20060502%20NACDS%20-%20Final%2005012006%20for%20On%20Point_db5ede1d-3d06-41f0-85e3-c11658534a63.pdf. [Retrieved 7 March 2024].

Prado, A. M., Sánchez-Gómez, J. I., Casamitjana, N., Espriu, M., Kumar, P., Ngoye, B., ... & Rosenmoller, M. (2023). Building management and innovation capabilities for global health: a senior executive program. Frontiers in Public Health, 11.

Prahalad, D. (2019). The new fortune at the bottom of the pyramid. Strategy+ business, 94, 1-13.

Prudêncio, M., & Costa, J. C. (2020). Research funding after COVID-19. Nature Microbiology, 5(8), 986-986.

PwC (April 2023). *ESG trends in 2023. Key ESG areas to keep a watch this year*. [online]. Available on: https://www.pwc.com/kz/en/publications/new_publication_assets/esg-trends-in-2023-eng.pdf. [Retrieved 7 March 2024].

Quigley, F. (2017). Prescription for the People: An Activist's Guide to Making Medicine Affordable for All. Ithaca, NY: Cornell University Press.

Qunaj, L., Kaltenboeck, A., & Bach, P. B. (2022). Compulsory Licensing of Pharmaceuticals in High-Income Countries: A Comparative Analysis. *Milbank Quarterly*, *100*(1), 284 – 313. https://doi.org/10.1111/1468-0009.12557.

Rahimi, A., Mirzazadeh, A., & Tavakolpour, S. (2021). Genetics and genomics of SARS-CoV-2: A review of the literature with the special focus on genetic diversity and SARS-CoV-2 genome detection. Genomics, 113(1), 1221-1232.

Ramirez-Rubio, O., Daher, C., Fanjul, G., Gascon, M., Mueller, N., Pajín, L., ... & Nieuwenhuijsen, M. J. (2019). Urban health: an example of a "health in all policies" approach in the context of SDGs implementation. Globalization and health, 15, 1-21.

Ramstrand, N., Fatone, S., Dillon, M. P., & Hafner, B. J. (2019). Promoting quality and transparency in clinical research. *Prosthetics and orthotics international*, *43*(5), 474-477.

Reinhardt, U. (2015). Probing our moral values in health care: The pricing of specialty drugs. In JAMA - Journal of the American Medical Association. https://doi.org/10.1001/jama.2015.9593.

Rejon-Parrilla, J. C., Espin, J., & Epstein, D. (2022). How innovation can be defined, evaluated and rewarded in health technology assessment. *Health Economics Review*, *12*(1), 1-11.

Revilla, M. a., Saris, W. E., & Krosnick, J. a. (2013). Choosing the Number of Categories in Agree-Disagree Scales. Sociological Methods & Research, 43(1), 73-97. http://doi.org/10.1177/0049124113509605.

Ricciardi, W., & Fehr, R. (2013). Health Technology Assessment (HTA) and Health impact Assessment (HIA)–Opportunities for mutual benefit: Walter Ricciardi. The European Journal of Public Health, 23(suppl_1), ckt126-006.

Richardson, H. (2019). Specifying Norms as a Way to Resolve Concrete Ethical Problems. In *Ethics and Medical Decision-Making*. (Original version 1990). https://doi.org/10.4324/9781315209692-12.

Rodríguez, V., Rocamora, A., Plasència, A. (May 2023). *What opportunities and challenges does the EU Global Health Strategy present?* Barcelona Institute for Global Health (ISGlobal). Policy brief number 51. [online]. Available on: https://www.isglobal.org/documents/10179/12351497/51_Estrategia+Salud+Global+UE_EN.pdf/4a382398-a49d-4d79-abcd-3bd1c3259841?t=1686131668000. [Retrieved 7 March 2024].

Roe, E. M. (1994). Narrative Policy Analysis: Theory and Practice. Durham: Duke University Press.

Rosati, F., Rodrigues, V. P., Cosenz, F., & Li-Ying, J. (2023). Business model innovation for the Sustainable Development Goals. Business Strategy and the Environment, 32(6), 3752-3765.

Rosenkötter, N., Vondeling, H., Blancquaert, I., Mekel, O. C., Kristensen, F. B., & Brand, A. (2011). The contribution of health technology assessment, health needs assessment, and health impact assessment to the assessment and translation of technologies in the field of public health genomics. Public health genomics, 14(1), 43–52. https://doi.org/10.1159/000318317.

Røttingen, J. A., Regmi, S., Eide, M., Young, A. J., Viergever, R. F., Årdal, C., Guzman, J., Edwards, D., Matlin, S. A., & Terry, R. F. (2013). Mapping of available health research and development data: what's there, what's missing, and what role is there for a global observatory? The *Lancet*.; **382**: 1286-1307. https://doi.org/10.1016/S0140-6736(13)61046-6.

Roychowdhury, S., Shroff, N., & Verdi, R. S. (2019). The effects of financial reporting and disclosure on corporate investment: A review. *Journal of Accounting and Economics*, *68*(2-3), 101246.

Rubin, E. J., Baden, L. R., Abraham, J., & Morrissey, S. (2022). Audio Interview: Viral Evolution and the Future of Monoclonal Antibodies. The New England journal of medicine, 386(24), e75. https://doi.org/10.1056/NEJMe2207933.

Rutstein, S. E., Price, J. T., Rosenberg, N. E., Rennie, S. M., Biddle, A. K., & Miller, W. C. (2017). Hidden costs: the ethics of cost-effectiveness analyses for health interventions in resource-limited settings. Global public health, 12(10), 1269-1281.

Ryle, G. (1996). The Thinking of Thoughts: What is 'Le Penseur' Doing? *Studies in Anthropology* 11:11. ISSN 1363-1098.

Sachs, J. D., Schmidt-Traub, G., Mazzucato, M., Messner, D., Nakicenovic, N., & Rockström, J. (2019). Six transformations to achieve the sustainable development goals. Nature sustainability, 2(9), 805-814.

Samuelson, P. A. (1954). The Pure Theory of Public Expenditure. The Review of Economics and Statistics, 36(4), 387–389. https://doi.org/10.2307/1925895.

Savoy, C. M., & McKeown, S. (2022). Opportunities for Increased Multilateral Engagement with B3W. Center for Strategic and International Studies, 6.

Saxena, A., Baker, B. K., Banda, A., Herlitz, A., Miller, J., Karrar, K., ... & Hassoun, N. (2023). Pandemic preparedness and response: beyond the Access to COVID-19 Tools Accelerator. *BMJ global health*, *8*(1), e010615.

Scherman, D., & Fetro, C. (2020). Drug repositioning for rare diseases: Knowledge-based success stories. Therapie, 75(2), 161–167. https://doi.org/10.1016/j.therap.2020.02.007.

Schlander, M., Hernandez-Villafuerte, K., Cheng, C. Y., Mestre-Ferrandiz, J., & Baumann, M. (2021). How much does it cost to research and develop a new drug? A systematic review and assessment. PharmacoEconomics, 39, 1243-1269.

Schon D., & Rein M. (1994). Frame Reflection: Toward the Resolution of Intractable Policy Controversies, New York: Basis Books.

Sekayi, D., & Kennedy, A. (2017). Qualitative Delphi method: A four round process with a worked example. Qualitative Report, 22, 2755–2763.

Sen, A. (1990). Development as capability expansion. The community development reader, 41, 58.

Shabani, M. (2022). Will the European Health Data Space change data sharing rules? Science, 375(6587), 1357-1359.

Singh, S., Bawa, J., Singh, B., Singh, B., & Bika, S. L. (2022). Analyzing GAVI the Vaccine Alliance as a Global Health Partnership Model: A Constructivist Analysis of the Global Health Crisis. Millennial Asia, 09763996221116283.

Simmons B., Cooke G.S., Miraldo M. (2019). Effect of voluntary licenses for hepatitis C medicines on access to treatment: a difference-in-differences analysis. Lancet Glob Health 2019; 7: e1189–96.

Simoens, S., Cassiman, D., Dooms, M., & Picavet, E. (2012). Orphan drugs for rare diseases: Is it time to revisit their special market access status? Drugs, 72(11), 1437 – 1443. https://doi.org/10.2165/11635320-000000000-00000.

Slaoui, M., & Hepburn, M. (2020). Developing safe and effective COVID vaccines—Operation Warp Speed's strategy and approach. New England Journal of Medicine, 383(18), 1701-1703. https://www.nejm.org/doi/full/10.1056/NEJMp2027405.

Smeeth, L., & Kyobutungi, C. (2023). Reclaiming global health. The Lancet, 401(10377), 625-627.

Smit S., Madgavkar A., Russell K., Woetzel J., Francis T., Ellingrud K., Lath V., Wibowo P. & Anderson R. McKinsey (13 november 2022). *Toward a sustainable, inclusive, growing future: The role of business.* [online]. Available on: https://www.mckinsey.com/featured-insights/sustainable-inclusive-growth/toward-a-sustainable-inclusive-growing-future-the-role-of-business#/. [Retrieved 7 March 2024].

So, A. D., & Woo, J. (2020). Reserving coronavirus disease 2019 vaccines for global access: cross sectional analysis. bmj, 371.

Soete, L., Verspagen, B., & Ziesemer, T. H. W. (2022). Economic impact of public R&D: an international perspective. *Industrial and Corporate Change*, *31*(1), 1–18. https://doi.org/10.1093/icc/dtab066.

Solovy, E. M. (2021). The Doha Declaration at Twenty: Interpretation, Implementation, and Lessons Learned on the Relationship Between the TRIPS Agreement and Global Health. *Nw. J. Int'l L. & Bus.*, *42*, 253.

South Centre (March 2021). *Scope of Compulsory License and Government use of patented Medicines in the context of COVID-19 pandemic*. [online]. Available on: https://www.southcentre.int/wp-content/uploads/2021/03/Compulsory-licenses-table-Covid-19-2-March.pdf. [Retrieved 7 March 2024].

Sparkes, S. P., Kutzin, J., & Earle, A. J. (2019). Financing common goods for health: a country agenda. Health Systems & Reform, 5(4), 322-333.

Spranger, J., Homberg, A., Sonnberger, M., Niederberger, M. (2022). Reporting guidelines for Delphi techniques in health sciences: A methodological review. https://doi.org/https://doi.org/10.1016/j.zefq.2022.04.025.

Stamm, T., Bott, N., Thwaites, R., Mosor, E., Andrews, M. R., Borgdorff, J., ... & Styliadou, M. (2021). Building a Value-based care infrastructure in Europe: the health outcomes observatory. NEJM Catalyst Innovations in Care Delivery, 2(3).

Stevens, A. J., Jensen, J. J., Wyller, K., Kilgore, P. C., Chatterjee, S., & Rohrbaugh, M. L. (2011). The Role of Public-Sector Research in the Discovery of Drugs and Vaccines. *New England Journal of Medicine*. https://doi.org/10.1056/nejmsa100826.

Stirling, A. (2009). Direction, Distribution and Diversity! Pluralising Progress in Innovation, Sustainability and Development. *STEPS Working Paper 32*. http://sro.sussex.ac.uk/16081/.

Storeng, K. T., de Bengy Puyvallée, A., & Stein, F. (2021). COVAX and the rise of the 'super public private partnership'for global health. *Global Public Health*, 1-17.

Strasser, A. (2017). Delphi method variants in information systems research: Taxonomy development and application. Electronic Journal of Business Research Methods (2), 120–133.

Subrahmanian, K., & Swamy, P. (2018). What is global health? In *Springer Briefs in Public Health*. https://doi.org/10.1007/978-3-319-75136-8_1.

Sun, D., Gao, W., Hu, H., & Zhou, S. (2022). Why 90% of clinical drug development fails and how to improve it? Acta Pharmaceutica Sinica B, 12(7), 3049-3062.

Syeed, M. S., Poudel, N., Ngorsuraches, S., Veettil, S. K., & Chaiyakunapruk, N. (2022). Characterizing attributes of innovation of technologies for healthcare: a systematic review. Journal of Medical Economics, 25(1), 1158-1166.

Talukder, B., & Hipel, K. W. (2022). Planetary health & COVID-19: A multi-perspective investigation. One Health, 15, 100416

Tanne, J. H. (2022). Pfizer pledges to provide 23 drugs at not-for-profit prices to lower income countries.

Tanveer, S., Rowhani-Farid, A., Hong, K., Jefferson, T., & Doshi, P. (2022). Transparency of COVID-19 vaccine trials: decisions without data. *BMJ evidence-based medicine*, *27*(4), 199-205.

Teisberg, E., Wallace, S., & O'Hara, S. (2020). Defining and implementing value-based health care: a strategic framework. Academic Medicine, 95(5), 682.

Tenni, B., Moir, H. V., Townsend, B., Kilic, B., Farrell, A. M., Keegel, T., & Gleeson, D. (2022). What is the impact of intellectual property rules on access to medicines? A systematic review. Globalization and health, 18(1), 1-40.

Thakur S. (2022). Advances in orphan drug development: Time to change the status and stereotype. Perspectives in clinical research, 13(3), 123–128. https://doi.org/10.4103/picr.picr_193_21.

Theobald, S., Brandes, N., Gyapong, M., El-Saharty, S., Proctor, E., Diaz, T., Wanji, S., Elloker, S., Raven, J., Elsey, H., Bharal, S., Pelletier, D., & Peters, D. H. (2018). Implementation research: new imperatives and opportunities in global health. *The Lancet*. https://doi.org/10.1016/S0140-6736(18)32205-0.

Tong, A., Sainsbury, P., & Craig, J. (2007). Consolidated criteria for reporting qualitative research (COREQ): A 32-item checklist for interviews and focus groups. International Journal for Quality in Health Care. https://doi.org/10.1093/intqhc/mzm042.

Tong, A., Synnot, A., Crowe, S., Hill, S., Matus, A., Scholes-Robertson, N., ... & Craig, J. C. (2019). Reporting guideline for priority setting of health research (REPRISE). BMC Medical Research Methodology, 19(1), 1-11.

Torvinen, H., & Jansson, K. (2023). Public health care innovation lab tackling the barriers of public sector innovation. Public Management Review, 25(8), 1539-1561.

Towse, A., Chalkidou, K., Firth, I., Kettler, H., & Silverman, R. (2021). How should the world pay for a coronavirus disease (COVID-19) vaccine? *Value in Health*, *24*(5), 625-631.

Towse, A., Hoyle, C. K., Goodall, J., Hirsch, M., Mestre-Ferrandiz, J., & Rex, J. H. (2017). Time for a change in how new antibiotics are reimbursed: Development of an insurance framework for funding new antibiotics based on a policy of risk mitigation. Health Policy, 121(10), 1025–1030. https://doi.org/10.1016/j.healthpol.2017.07.011.

UHC2030 (2023). *Taking action for Universal Health Coverage*. [online]. Available on: https://www.uhc2030.org/. [Retrieved 7 March 2024].

UK Government (March 2020). *The relationship between public and private R&D funding.* BEIS Research Paper Number 2020/010. Department for Science, innovation and Technology and Department for Business, Energy & Industrial Strategy. [online]. Available on: https://www.gov.uk/government/publications/research-and-development-relationship-between-public-and-private-funding. [Retrieved 7 March 2024].

UK Government (28 February 2022). *England Rare Diseases Action Plan 2022. Policy Paper*. [online]. Available on: https://www.gov.uk/government/publications/england-rare-diseases-action-plan-2022/england-rare-diseases-action-plan-2022. [Retrieved 7 March 2024].

UN (2023). *The Sustainable Development Goals report 2023: Special Edition*. [online]. Available on: https://unstats.un.org/sdgs/report/2023/. [Retrieved 7 March 2024].

UN Climate Change (13 April 2022). *What is the Triple Planetary Crisis*? [online]. Available on: https://unfccc.int/blog/what-is-the-triple-planetary-crisis. [Retrieved 7 March 2024].

UNSDG. (2018). Unlocking SDG financing: Findings from early adopters.

UN (1948). *Universal Declaration of Human Rights.* [online]. Available on: https://www.un.org/en/about-us/universal-declaration-of-human-rights. [Retrieved 7 March 2024].

UN (1967). *International Covenant on Economic, Social and Cultural Rights.* [online]. Available on: https://treaties.un.org/doc/treaties/1976/01/19760103%2009-57%20pm/ch_iv_03.pdf. [Retrieved 7 March 2024].

UNAIDS (2013). *TRIPS Transition period extension for least-developed countries.* Issue Brief 2013. [online]. Available on: https://www.unaids.org/sites/default/files/media_asset/JC2474_TRIPS-transition-period-extensions_en_0.pdf. [Retrieved 7 March 2024].

UNAIDS (2015). How AIDS Changed Everthing. [online]. Available on: https://www.unaids.org/sites/default/files/media_asset/MDG6Report_en.pdf. [Retrieved 7 March 2024].

UNAIDS (2000). AIDS epidemic update: December 2000. [online]. Available on: https://data.unaids.org/publications/irc-pub05/aidsepidemicreport2000_en.pdf. [Retrieved 7 March 2024].

UNCTAD (2002). *Hazel Tau & others v. GlaxoSmithKline, Boehringer Ingelheim & others, 2002* (South African Competition Commission, Competition Commission Case No. 2002Sep226). Prepared by UNCTAD Intellectual Property Unit. [online]. https://unctad.org/ippcaselaw/hazel-tau-others-v-glaxosmithkline-boehringer-ingelheim-others-2002-south-african-competition. [Retrieved 7 March 2024].

UNDP (20 December 2011). *The Doha Declaration Ten years on and Its Impact on Access to Medicines and the Right to Health*. Discussion paper. [online]. Available on: https://www.undp.org/sites/g/files/zskgke326/files/publications/Discussion_Paper_Doha_Declaration_Public_Health.pdf. [Retrieved 7 March 2024].

Uppal, A., Chakrabarti, R., Chirmule, N., Rathore, A., & Atouf, F. (2021). Biopharmaceutical industry capability building in India: report from a symposium. Journal of Pharmaceutical Innovation, 1-8.

Uyarra, E., Zabala-Iturriagagoitia, J. M., Flanagan, K., & Magro, E. (2020). Public procurement, innovation and industrial policy: Rationales, roles, capabilities and implementation. Research Policy, 49(1), 103844.

USAID (August 2020a). *Global Health Innovation Index. A tool for identifying the most promising Global Health Innovations*. [online]. Available on: https://www.usaid.gov/sites/default/files/2022-05/CII_Global_Health_Innovation_Index_.pdf. [Retrieved 7 March 2024].

USAID (2020b). *2020 Impact Brief*. [online]. Available on: https://www.usaid.gov/sites/default/files/2022-05/USAID_2020_CII_ImpactBrief.pdf. [Retrieved 7 March 2024].

USAID (2022). *2022 Impact Brief*. [online]. Available on: https://www.usaid.gov/sites/default/files/2022-12/USAID_2022_CII_ImpactBrief_V8_spreads.pdf. [Retrieved 2 December 2023].

US Global Leadership Coalition (2021). *Impact on the Economics of Developing Countries*. COVID-19 Issue Briefs. [online]. Available on: https://www.usglc.org/coronavirus/economies-of-developing-countries/. [Retrieved 7 March 2024].

US Government (1983). *Public Law 97-414. Orphan Drug Act.* [online]. Available on: https://www.govinfo.gov/content/pkg/STATUTE-96/pdf/STATUTE-96-Pg2049.pdf. [Retrieved 7 March 2024].

US Government (2002). *Rare Disease Act of 2002.* [online]. Available on: https://www.govinfo.gov/content/pkg/PLAW-107publ280/html/PLAW-107publ280.htm. [Retrieved 7 March 2024].

US Government (2020a). *Explaining Operation Ward Speed.* U.S. Department of Health and Human Services. [online]. Available on: https://health.mo.gov/living/healthcondiseases/communicable/novel-coronavirus-lpha/pdf/fact-sheet-operation-warp-speed.pdf. [Retrieved 2 December 2023].

US Government (12 December 2020b). *Operation Ward Speed Official: First COVID-19 Vaccines to Arrive Monday. US Department of Defense.* [online]. Available on: https://www.defense.gov/News/News-Stories/Article/Article/2445137/operation-warp-speed-official-first-covid-19-vaccines-to-arrive-monday/. [Retrieved 7 March 2024].

US Government (2021). *Operation Ward Speed: Accelerated COVID-19 Vaccine Development Status and Efforts to Address Manufacturing Challenges*. GAO U.S. Government Accountability Office. [online]. Available on: https://www.gao.gov/products/gao-21-319. [Retrieved 7 March 2024].

UX Planet (19 May 2022). *Quick Steps through the Double Diamond.* [online]. Available on: https://uxplanet.org/quick-steps-through-the-double-diamond-cf2e00b22ba7. Luísa Quinn. [Retrieved 10 March 2024].

Validate (2019). Values in Doing Assessmentts of Health Technologies. [online]. Available on: https://validatehta.eu/. [Retrieved 7 March 2024].

Van De Pas, R., Widdowson, M. A., Ravinetto, R., N Srinivas, P., Ochoa, T. J., Fofana, T. O., & Van Damme, W. (2022). COVID-19 vaccine equity: a health systems and policy perspective. Expert review of vaccines, 21(1), 25-36.

Varkey, B. (2021). Principles of clinical ethics and their application to practice. Medical Principles and Practice, 30(1), 17-28.

Vawda, Y. A. (2022). Compulsory Licenses and Government Use: Challenges and Opportunities. *Access to Medicines and Vaccines: Implementing Flexibilities Under Intellectual Property Law*, 73-104.

Vawda, Y. A., & Shozi, B. (2020). Eighteen years after Doha: An analysis of the use of public health TRIPS flexibilities in Africa. Available at SSRN 3559478.

Velásquez, G., & Syam, N. (2021). A new WHO international treaty on pandemic preparedness and response: can it address the needs of the global south. South Centre Policy Brief, 93.

Vintura (2023). *What is Value-Based Healthcare?* [online]. Available on: https://www.vintura.com/value-based-healthcare/michael-porter. [Retrieved 7 March 2024].

Vinuales, J., Moon, S., Le Moli, G., & Burci, G. L. (2021). A global pandemic treaty should aim for deep prevention. The Lancet, 397(10287), 1791-1792.

Wass, S., & Vimarlund, V. (2016). Healthcare in the age of open innovation–a literature review. Health Information Management Journal, 45(3), 121-133.

Watson, C. (2022). Rise of the preprint: how rapid data sharing during COVID-19 has changed science forever. Nat Med, 28(1), 2-5.

Watson, O. J., Barnsley, G., Toor, J., Hogan, A. B., Winskill, P., & Ghani, A. C. (2022). Global impact of the first year of COVID-19 vaccination: a mathematical modelling study. The Lancet Infectious Diseases, 22(9), 1293 – 1302. https://doi.org/10.1016/S1473-3099(22)00320-6.

Wealth, A., Initiative, J., Sachs, J., Fajans-Turner, M. V., Smith, M. T., Kennedy-Cuomo, M. C., ... & Loni, M. S. S. (2018). Closing the SDG budget gap.

White House Government (9 September 2021). *Executive Order on Requiring Coronavirus Disease 2019 Vaccination for Federal Employees*. Briefing room. Presidential Actions. [online]. Available on: https://www.whitehouse.gov/briefing-room/presidential-actions/2021/09/09/executive-order-on-requiring-coronavirus-disease-2019-vaccination-for-federal-employees/. [Retrieved 7 March 2024].

WHO (2002). Implications of the Doha Declaration on the TRIPS agreement and public health / Carlos M. Correa. [online]. Available on: https://apps.who.int/iris/handle/10665/67345. [Retrieved 7 March 2024].

WHO (1 January 2008). *International Health Regulations (2005).* [online]. Available on: https://www.who.int/publications/i/item/9789241580410. [Retrieved 7 March 2024].

WHO (2015). *International Health Regulations (2005) core capacity workbook: a series of exercises to assist the validation of core capacity implementation levels*. [online]. Available on: https://iris.who.int/handle/10665/190819?search-result=true&query=WHO+International+Health+Regulations.IHR+Core+Capacities&scope=&rpp=10&sort_by=score&order=desc. [Retrieved 7 March 2024].

WHO (2020a). Public pharmaceutical expenditure as % of total pharmaceutical expenditure. World Health Organisation Regional Office for Europe. [online]. Available on: https://gateway.euro.who.int/en/indicators/hfa_580-6790-public-pharmaceutical-expenditure-as-of-total-pharmaceutical-expenditure/?id=19675. [Retrieved 7 March 2024].

WHO (29 June 2020b). *WHO Timeline - COVID-19.* [online]. Available on: https://www.who.int/news/item/27-04-2020-who-timeline---covid-19. [Retrieved 7 March 2024].

WHO (11 March 2020c). *WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020.* [online]. Available on: https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020. [Retrieved 7 March 2024].

WHO (2020d). *WHO guideline on country pharmaceutical pricing policies*. [online]. Available on: https://iris.who.int/bitstream/handle/10665/335692/9789240011878-eng.pdf. [Retrieved 7 March 2024].

WHO (9 December 2021a). *State of inequality: HIV, tuberculosis and malaria.* [online]. Available on: https://www.who.int/publications/i/item/9789240039445. [Retrieved 7 March 2024].

WHO (2021b). *Global strategy on digital health.* [online]. Available on: https://www.who.int/docs/default-source/documents/gs4dhdaa2a9f352b0445bafbc79ca799dce4d.pdf. [Retrieved 7 March 2024].

WHO (12 April 2021c). *ACT-A priortized strategy and budget for 2021.* [online]. Available on: https://www.who.int/publications/m/item/act-a-prioritized-strategy-and-budget-for-2021. [Retrieved 7 March 2024].

WHO (20 April 2022). *Accelerating COVID-19 Vaccine Deployment. Removing obstacles to increase coverage levels and protect those at high risk.* G20 Indonesia 2022. [online]. Available on:

https://www.who.int/publications/m/item/accelerating-covid-19-vaccine-deployment. [Retrieved 7 March 2024].

WHO (2023a). *Health innovation for impact.* [online]. Available on: https://www.who.int/teams/digital-health-and-innovation/health-innovation-for-impact. [Retrieved 7 March 2024].

WHO (2023b). *What is the Global Observatory on Health R&D and why is needed?* [online]. Available on: https://www.who.int/observatories/global-observatory-on-health-research-and-development/about/what-is-the-global-observatory-on-health-and-why-is-it-needed. [Retrieved 7 March 2024].

WHO (13 July 2023c). HIV/AIDS Fact Sheet. [online]. Available on: https://www.who.int/en/news-room/fact-sheets/detail/hiv-aids. [Retrieved 7 March 2024].

WHO (1 June 2023d). *Access to COVID-19 tools funding commitment tracker.* [online]. Available on: https://www.who.int/publications/m/item/access-to-covid-19-tools-tracker. [Retrieved 7 March 2024].

WHO (5 October 2023e). *Coronavirus (COVID-19) Dashboard.* [online]. Available on: https://data.who.int/dashboards/covid19/cases?n=c. [Retrieved 7 March 2024].

WHO (17 May 2023f). *ACT-Accelerator Transition report.* [online]. Available on: https://www.who.int/publications/m/item/act-accelerator-transition-report. [Retrieved 7 March 2024].

WHO (5 May 2023g). *Statement on the fifteeth meeting of the IHR (2005) Emergency Committee on the COVID-19 pandemic*. [online]. Available on: https://www.who.int/news/item/05-05-2023-statement-on-the-fifteenth-meeting-of-the-international-health-regulations-(2005)-emergency-committee-regarding-the-coronavirus-disease-(covid-19)-pandemic?adgroupsurvey={adgroupsurvey}&gclid=Cj0KCQjwib2mBhDWARIsAPZUn_nM-GrQ6d268pxGiKOLgl-NpalaBfhLQbl4fyv_woTemlKUNe1-zlQaAgHnEALw_wcB. [Retrieved 7 March 2024].

WHO (2023h). What is the ACT-Accelerator? [online]. Available on: https://www.who.int/initiatives/act-accelerator/about. [Retrieved 7 March 2024].

WHO (28 June 2023i). *Pandemic Prevention, preparedness and response accord.* [online]. Available on: https://www.who.int/news-room/questions-and-answers/item/pandemic-prevention--preparedness-and-response-accord. [Retrieved 7 March 2024].

WHO (2023j). *The ACT-Accelerator frequently asked questions.* [online]. Available on: https://www.who.int/initiatives/act-accelerator/faq. [Retrieved 7 March 2024].

WHO (20 April 2023k). *mRNA Technology Transfer Programme moves to the next phase of its development*. [online]. Available on: https://www.who.int/news/item/20-04-2023-mrna-technology-transfer-programme-moves-to-the-next-phase-of-its-development. [Retrieved 7 March 2024].

WHO (June 2023l). *COVID-19 Vaccine Delivery* Partnership [online]. Available on: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines/covid-19-vaccine-delivery-partnership. [Retrieved 7 March 2024].

WHO (2023m). *Strengthening health emergency prevention, preparedness, response and resilience* (HEPR). [online]. Available on: https://cdn.who.int/media/docs/default-source/emergency-preparedness/who_hepr_wha2023-21051248b.pdf?sfvrsn=a82abdf4_3&download=true [Retrieved 37 March 2024].

WHO/PAHO (1 September 2021). *PAHO launches new collaborative platform to produce COVID-19 vaccines in Latin America and the Caribbean*. [online]. Available on: https://www.paho.org/en/news/1-9-2021-paho-launches-new-collaborative-platform-produce-covid-19-vaccines-latin-america-and. [Retrieved 7 March 2024].

WHO, WIPO and WTO (May 2023). *An integrated Health, Trade and IP Approach to Respond to the COVID-19 Pandemic.* Second update, May 2023. [online]. Available on: https://www.wto.org/english/res_e/booksp_e/who_wipo_wto_2023_e.pdf. [Retrieved 7 March 2024].

Williams, S. & Tippitt, R. (2022). [online]. *The US Government's Innovation Valley of Death***.** Ain Ventures. Available on**:** https://www.ainventures.com/post/the-valley-of-death. [Retrieved 28 April 2024].

Wirtz, V. J., Hogerzeil, H. V., Gray, A. L., Bigdeli, M., de Joncheere, C. P., Ewen, M. A., Gyansa-Lutterodt, M., Jing, S., Luiza, V. L., Mbindyo, R. M., Möller, H., Moucheraud, C., Pécoul, B., Rägo, L., Rashidian, A., Ross-Degnan, D., Stephens, P. N., Teerawattananon, Y., 't Hoen, E. F., Wagner, A. K., … Reich, M. R. (2017). Essential medicines for universal health coverage. Lancet (London, England), 389(10067), 403–476. https://doi.org/10.1016/S0140-6736(16)31599-9.

Wong, H. (2020). The case for compulsory licensing during COVID-19. *Journal of global health*, *10*(1).

Wong A., Cole C. & Kohler J.C. (2022). TRIPS flexibilities and access to medicines: an evaluation of barriers to employing compulsory licensing for patented pharmaceuticals at the WTO. South Centre Research Paper Series No. 168.

World Economic Forum (April 2023). *Private Market Impact Investing: A Turning Point*. [online]. Available on: https://www3.weforum.org/docs/WEF_Private_Market_Impact_Investing_2023.pdf. [Retrieved 7 March 2024].

WTO (1994). *Agreement on Trade-Related Aspects of Intellectual Property Rights (unamended).* [online]. Available on: https://www.wto.org/english/docs_e/legal_e/27-trips_01_e.htm. [Retrieved 7 March 2024].

WTO (14 November 2001). WTO Ministerial 2001: TRIPS. WT/MIN(01)/DEC/2. *Declaration on the TRIPS agreement and public health.* Adopted on 14 November 2001. [online]. https://www.wto.org/english/thewto_e/minist_e/min01_e/mindecl_trips_e.htm. [Retrieved 7 March 2024].

WTO (September 2006). *Fact Sheet: Trips and Pharmaceutical patents. Obligations and exceptions.* [online]. Available on: https://www.wto.org/english/tratop_e/trips_e/factsheet_pharm02_e.htm. [Retrieved 7 March 2024].

WTO (16 October 2013). *Responding to least developed countries' special needs in intellectual property.* [online]. Available on: https://www.wto.org/english/tratop_e/trips_e/ldc_e.htm. [Retrieved 7 March 2024].

WTO (27 June 2022a). Ministerial Decision on the TRIPS Agreement. Adopted on 17 June 2022. [online]. Available on: https://docs.wto.org/dol2fe/Pages/SS/directdoc.aspx?filename=q:/WT/MIN22/30.pdf&Open=True. [Retrieved 7 March 2024].

WTO (3 May 2022b*). Quad's outcome document on IP COVID-19 response made public*. [online]. Available on: https://www.wto.org/english/news_e/news22_e/trip_03may22_e.htm. [Retrieved 7 March 2024].

WTO (2023). *Compulsory licensing of pharmaceuticals and TRIPS*. [online]. Available on: https://www.wto.org/english/tratop_e/trips_e/public_health_faq_e.htm. [Retrieved 7 March 2024].

Wouters, O. J., McKee, M., & Luyten, J. (2020). Estimated research and development investment needed to bring a new medicine to market, 2009-2018. *Jama*, *323*(9), 844-853.

Xie, Y., Zhang, J., Wang, H., Liu, P., Liu, S., Huo, T., ... & Ye, Z. (2021). Applications of blockchain in the medical field: Narrative review. Journal of Medical Internet Research, 23(10), e28613.

Yale CRIT (2017). *Promoting Transparency in Clinical Research: Why and How.* Policy Paper by Yale Collaboration for Research Integrity and Transparency. [online]. Available on: https://law.yale.edu/sites/default/files/area/center/crit/crit_white_paper_november_2017_best_promoting_transparency_in_clinical_research_why_and_how.pdf. [Retrieved 7 March 2024].

Young, D., & Woods, W. (2019). Innovation is the only way to win the SDG race.

Yu, P. K. (2023). The COVID-19 TRIPS waiver and the WTO ministerial decision. IPR in times of crises: Lessons learned from the COVID-19 Pandemic. Jens Schovsbo, ed., Edward Elgar Publishing.

Zhang, M., Pawar, K. S., & Bhardwaj, S. (2017). Improving supply chain social responsibility through supplier development. *Production Planning and Control*. https://doi.org/10.1080/09537287.2017.1309717.

Zhou, Y., Wang, F., Tang, J., Nussinov, R., & Cheng, F. (2020). Artificial intelligence in COVID-19 drug repurposing. The Lancet Digital Health, 2(12), e667-e676.

Zraick, K. (24 February 2021). *Meet the key members of the BIden's COVID-19 response team.* The New York Times. [online]. Available on: https://www.nytimes.com/2021/02/24/us/bidens-covid-19-response-team.html. [Retrieved 7 March 2024].

DATA AVAILABILITY

Additional data will be shared upon request from the corresponding author for fair use, such as:

- Bioethical resolution of the Bioethics Commission of the University of Barcelona
- Interview transcripts and video recording (R1 and R2)
- Survey questionnaires and answers (R1, R2 and R3)

ANNEXES

Annex A. R3 Minimum consensus criteria and results
Annex B. R1 Delphi results
Annex C. R2 Delphi results
Annex D. R3 Additional results
Annex E. R3 Informational input: R1 and R2 consensus statements
Annex F. R3 Informational input: Summary of the proposed PSM
Annex G. Informed consent and commitment of confidentiality forms

ANNEX A. R3 MINIMUM CONSENSUS CRITERIA AND RESULTS

43 **Table A1** R3 Delphi survey Minimum Consensus Criteria statements and results

R3 Delphi survey (n=27, RR= 81%)

Statement			CON	CA	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
#	**Normative Preferences (social values)**									
1	STMT 1.1	**Norm 1: Equity** "Generally speaking, health systems should secure equal access to affordable, preventive, curative and good quality healthcare according to the need regardless of ethnicity, gender, age, social status or ability to pay".	1	100	91	9	0	0	0	0
2	STMT 1.2	**Norm 2: Efficiency / Cost-effectiveness** "Generally speaking, health systems should reward efficiency, normally quantified by cost-effectiveness analysis, so innovation really improving the patient journey for a certain cost (value for money), contributing to the health systems sustainability".	1	86	55	32	9	0	5	0
3	STMT 1.3	**Ethical dilemma.** In market economies, when incentives (risks & rewards) are not fully aligned with public health needs, these norms may imply an ethical dilemma because complying with rewarding efficiency frequently prevents from complying with equity.	1	77	50	27	5	5	14	0
4	STMT 1.4	**Efficiency dominates equity.** In industry decision-making, when the equity norm conflicts with the efficiency norm, efficiency (rewards) is superior to equity, resulting in a profit-oriented R&I model rather than public health equity-driven approach.	1	72	48	24	5	14	10	5
5	STMT 1.6	**Health equity as a R&I priority.** Improving health equity should be a priority for the biomedical R&I model.	1	100	82	18	0	0	0	0
	Problem Definition									
6	STMT 1.8	**Equity and speed as main problem.** The main problem with the biomedical R&I system is equity and speed, given that health innovation is not reaching citizens around the world fast enough in an equitable and sustainable manner.	1	81	48	33	5	10	5	5
	Causes - Needs									
7	STMT 2.9	**Lack of a "Value frame" as a "social choice" of priority health challenges**, which is country-specific given the heterogeneous epidemiology, income and healthcare costs among countries/regions, resulting in price-based negotiations rather than value proposition-	1	82	41	41	9	9	0	0

Table A1 R3 Delphi survey Minimum Consensus Criteria statements and results (cont.)

R3 Delphi survey (n=27, RR= 81%)

Statement			CON	CA	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
	Causes - Needs									
8	STMT 2.10	**Lack of incentives to fulfill the UN SDG agenda**. Global priorities already set in the UN SDGs but not really impactful in engaging pharmaceutical organizations.	1	85	55	30	5	10	0	9
9	STMT 2.11	**US profit-driven R&D portfolio**. The biomedical corporates tend to target few high-profit therapeutic areas in selected markets, with the USA as the largest one.	1	95	63	32	0	5	0	14
	Causes - Results									
10	STMT 2.21	**Gap in publication of R&D results, including failure**. Reluctance of researchers, institutions and countries to publish all the significant results, including failure, causing excess research waste (outcomes cannot be used) and delays in patient access to innovative medical products.	1	68	41	27	23	0	9	0
	Causes - Risks & Rewards									
	A- R&D Gap									
11	STMT 2.23	**Mismatch between market incentives and Public Health needs**. For certain public health challenges there are no incentives for the private sector to take on the high risk and cost of development and market launch. On the other hand, the current public system is not designed nor capitalized to take on the level of risk to deliver health equity goals.	1	90	52	38	5	0	5	5
12	STMT 2.24	**Venture capital patent-driven R&I based on high prices.** The current biomedical R&I model is led by venture capital to maximise return on investment (ROI), mainly through high prices for patented products, leaving some health needs unattended and resulting in health access challenges of the end products.	1	71	52	19	14	10	5	5
13	STMT 2.25	**Public purchasers failing to use their market power.** Public sector, as significant investor and buyer in biomedical R&I, failing to use their market power to set the agenda, the incentives and the equity goals for public health priorities.	1	80	55	25	15	5	0	9
	Causes - Risks & Rewards									
	B- High prices based on Patents and Value-based Pricing (VBP) as main innovation drivers									
14	STMT 2.33	**De-constructing Value-Based Pricing (VBP).** Value cannot be the only product pricing criteria, but other parameters, such as the R&D risk assumed as well as the ability to pay and volume, should be considered.	1	91	67	24	10	0	0	5
15	STMT 2.36	**Lack of transparency about the R&I investment mix** as it normally involves public R&I co-funding that is not reported and that should modulate the price.	1	67	38	29	10	10	14	5
	Causes - Outcomes									
16	STMT 2.43	**Lack of a differential reward for companies fulfilling environmental and health equity practices** (they don't get credit for it).	1	100	65	35	0	0	0	9

Table A1 R3 Delphi survey Minimum Consensus Criteria statements and results (cont.)

R3 Delphi survey (n=27, RR= 81%)

Statement			CON	CA	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
	Consensus Co-Created Preferred Supplier Model									
	B- RE-SPECIFIED NORMATIVE PREFERENCES									
17	STMT 3.2	To solve the moral dilemma, the efficiency norm could be re-specified as follows: **Norm 2 re-specified:** Efficiency "Generally speaking, health systems should reward risk-taking and efficiency, quantified by cost-effectiveness analysis, so effective innovation really improving the patient journey for a certain cost (value for money), contributing to the sustainability of the health systems AND, in case this reward doesn't happen naturally, preventing from fulfilling health equity, for instance when difficult to show results (i.e. mental health), small populations (i.e. rare diseases), low availability to pay (i.e. LMIC, disregarded socio-economic groups), restricted use (i.e. new antibiotics), and for public health emergencies (i.e. new epidemics), that reward should necessarily be incentivised conditioned to a global access commitment.	1	80	30	50	10	10	0	9
	C- CO-CREATED PREFERRED SUPPLIER MODEL DEFINITION									
18	STMT 3.3	**Get credit for health equity practices.** In the Preferred Supplier model, biomedical companies engaged with environmental and social practices (equity and data sharing) get credit as preferred providers of the public sector for priority health challenges.	1	81	48	33	10	5	5	5
19	STMT 3.6	**Incentives conditioned to equity & data sharing**. The incentives for the health priority challenges should be conditioned to a global access commitment and data sharing practices that lead to equitable and quicker outcomes. By doing so, providers would improve their Preferred Supplier accreditation level.	1	85	40	45	0	10	5	9
	D- ACCREDITATION REQUIREMENTS: 4 "SHARE" PRINCIPLES									
20	STMT 3.11	**Share NEEDS. Priorities** should be defined by governments, according to their value frameworks, mainly considering 1) epidemiology (i.e. burden of disease), 2) market failure in which impact is not rewarded naturally, such as when difficult to show results (i.e. mental health), small populations (i.e. rare diseases), low ability to pay (i.e. LMIC), restricted use (i.e. new antibiotics), etc as well as 3) public health emergencies (i.e. new epidemics).	1	95	41	55	5	0	0	0
21	STMT 3.12	**Share RESULTS. Contribute to open "Health Data Spaces"**. Preferred Suppliers should share scientific data, from R&D project pipeline and raw data to results (clinical trials, real-world evidence), including failure, as projects co-financed with public funds.	1	95	62	33	0	5	0	5
22	STMT 3.14	**Share RISK & REWARDS. Risk-Impact hybrid pricing model.** Rewards for innovative products should balance Impact (outcomes/value-based) modulated by the Risk assumed along the development pipeline defined by the R&I public-private funding mix.	1	85	33	52	5	10	0	5

Table A1 R3 Delphi survey Minimum Consensus Criteria statements and results (cont.)

R3 Delphi survey (n=27, RR= 81%)

Statement			CON	CA	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
	Consensus Co-Created Preferred Supplier Model									
	D- ACCREDITATION REQUIREMENTS: 4 "SHARE" PRINCIPLES									
23	STMT 3.15	**Share RISKS& REWARDS. Disclosure of Public R&I funding to assess the risk assumed.** To assess the R&I risk assumed, Preferred Suppliers should declare the public funding received during the cycle.	1	100	82	18	0	0	0	0
24	STMT 3.17	**Share RISK & REWARDS. Public R&I funding should modulate price.** Disclosure of public (and private) R&I funding should affect the price negotiation between the Preferred Supplier and the public payer in exchange for favorable market access for products with positive evidence.	1	81	48	33	5	10	5	5
25	STMT 3.26	**Share OUTCOMES. Preferred Supplier as "Responsible Capitalism" accreditation.** Incentives should be given to companies with best corporate practices: environmental (i.e. in R&D, manufacturing and distribution), social (i.e. health equity, sharing data), and finance practices (i.e. reduce share buybacks and reinvest part of the profit in R&D) that determine the Preferred Supplier accreditation.	1	89	47	42	0	11	0	14
	E- ACCREDITATION CRITERIA & REGULATION									
	ACCREDITATION									
	The Preferred Supplier accreditation criteria could be defined by these 2 pillars and their corresponding indicators:									
	Pillar 1. Corporate Impat (ESG & Access to Medecine Index)									
26	STMT 3.27	**ESG KPI.** Disclosure by industry of Environmental, Social and Governance (ESG), alongside the financial information. Already mandatory In some countries (i.e. EU, USA) for large and public companies to address their externalities and deliver meaningful impact over the long term.	1	90	65	25	0	5	5	9
27	STMT 3.29	**Access to Medicines Index KPI.** For the biomedical sector, an "Access to Medicines Index (ATMi) like" could stimulate industry to improve global access by getting credit as Preferred Suppliers. The ATMi ranks the world's largest 20 pharma firms according to their ability to expand access in LMIC, assessing Governance (strategy), R&D portfolio and Implementation (pricing and delivery). Since 2008, the biennial index is published by the Access to Medicine Foundation in Netherlands, an international not-for-profit organization. An index similar to ATMi could be adopted considering the Preferred Supplier "4 SHARE" principles and turned into a KPI to be measured and audited.	1	83	22	61	0	6	11	18
	Pillar 2. Data Disclosure (scientific and financial data)									
28	STMT 3.30	**Disclosure of Scientific Data in "Open Data Spaces" for ALL the projects receiving public R&I funding (not only for Preferred Suppliers)**. Share at 3 levels: R&D project pipeline, raw data and results, including failure. For results, it could be given a certain period of time and/or a license, except in case of a Global Public Health Emergency.	1	82	55	27	9	5	5	0

Table A1 R3 Delphi survey Minimum Consensus Criteria statements and results (cont.)

R3 Delphi survey (n=27, RR= 81%)

	Statement		CON	CA	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
	Consensus Co-Created Preferred Supplier Model									
	E- ACCREDITATION CRITERIA & REGULATION									
	ACCREDITATION									
	Pillar 2. Data Disclosure (scientific and financial data)									
29	STMT 3.31	**Disclosure of R&I public Funding for ALL the projects publicly funded (not only for Preferred Suppliers).** The R&D public funding could be tracked during the R&D cycle and linked, for instance, to the commercial asset (i.e. patents, software) applying blockchain technology.	1	80	50	30	0	10	10	9
	REGULATION									
30	STMT 3.32	**Preferred Supplier regulation.** For all the priority products submitted by the Preferred Suppliers to the Regulatory Agencies (i.e. EMA, FDA) for marketing approval, there should be the transparency obligation, at the moment of the submission of the dossier, to present annually audited indicators.	1	83	56	28	0	6	11	18

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%); level 2 simple majority agreement (CA 50%-66%); level 3 no consensus (CA 0-49%).

ANNEX B. R1 DELPHI SURVEY RESULTS

The following tables includes the results of R1 initial survey and Delphi survey of consensus scoring questions only. Results of open-ended questions are not included (refer to 10.1 data availability).

44 **Table B1** R1 consensus Normative Preferences and Problem Definition

R1 Delphi survey (n=10, RR= 80%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Normative Preferences (social values)								
STMT 28	**Norm 1: Equity** " "Generally speaking, health systems should secure universal access to affordable, preventive, curative and good quality healthcare regardless of ethnicity, gender, age, social status or ability to pay".	Y	50	38	13	0	0	0
STMT 29	**Norm 2: Efficiency / Cost-effectiveness** "Generally speaking, health systems should reward efficiency, meaning solution-based disruptive innovation really improving the patient journey and the sustainability of the health systems".	Y	63	38	0	0	0	0

R1 Preliminary survey (n=10, RR= 90%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Normative Preferences (social values)								
STMT 14	**Health equity as a R&I priority.** Improving equity access and outcomes should be a priority for the R&I model.	Y	33	67	0	0	0	0
STMT 15	**Health equity as a priority in decision-making in your organisation.** Improving health equity is a priority in the decision-making of your organization.	Y	22	67	11	0	0	0
STMT 16	**Revision of the R&I model**. The biomedical R&I model should be redefined.	Y	11	78	11	0	0	0
Problem definition								
STMT 10	**Equity R&D gap**. "As little as 1% of all global funding for health R&D is allocated to diseases mostly noted in LMIC countries (such as malaria and TB) even though they account for more than 12.5% of the global burden of disease" (WHO, 2016).	Y	33	33	33	0	0	0

Table B1. R1 Consensus Normative Preferences and Problem Definition (cont.)

STMT 12	**Equity Pricing gap.** "The system of pharmaceutical innovation and access to medicines allows millions of people to die, in LMIC as well as in HIC, when the drug that would save their lives can be produced and sold at a price that would cover costs —including the R&D investment— and yield a reasonable, but not abusive, profit for the company" (Amy, 2016; Canoy and Tichem, 2018; Moreno and Epstein,	N	11	33	33	22	0	0

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree;A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

45 **Table B2** R1 consensus Causes: Governance, Needs and Results

R1 Delphi survey (n=10, RR= 80%)

Statement		**CON**	**SA (%)**	**A (%)**	**N (%)**	**D (%)**	**SD (%)**	**O (%)**
Causes - Governance								
STMT 3	Low alignment between the stakeholders given that the biomedical R&I system has been led by industry with profit-driven motivations that deviate from problems with the greatest health burden worldwide.	N	38	13	13	25	0	13
Causes - Needs								
STMT 4	The main problem is in low-and-middle income countries (LMIC) with Universal Health Coverage and how to develop effective treatments for neglected diseases.	N	25	38	0	13	0	26
STMT 5	Global Health priorities are already set in the UN Sustainable Development Goals, but they aren't really impactful in engaging pharmaceutical organizations.	Y	0	50	38	13	0	0
STMT 6	The main problem is how to reset the agenda in high-income countries dominated by the industry and their lobby through patient groups. This results in smaller and smaller group of patients with more and more expensive drugs (ie. cancer drugs).	N	13	13	13	38	13	13
STMT 7	Health needs are not discussed in advance between the main stakeholders because there is not the culture. Research has been mainly "investigator-led" with only a progressive tiny increase in evidence-based research led by HTA agencies oriented to public health needs.	Y	25	63	0	13	0	0
Causes - Results								
STMT 8	Insufficient R&D data sharing by industry.	N	13	13	25	50	0	0
STMT 9	Insufficient real-world evidence sharing and data integration by national governments.	Y	25	63	13	0	0	0

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree;A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

46 **Table B3** R1 consensus Causes: Risks and rewards

R1 Delphi survey (n=10, RR= 80%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Causes - Risks & Rewards								
A- R&I Gap								
STMT 1	The mismatch between financial incentives (commercial value) for biomedical innovation and public health needs.	Y	25	50	13	13	0	0
STMT 2	Public purchasers failing to use their market power to set a clear and robust priority agenda and financial incentives strategy, including smart	Y	0	63	38	0	0	0
STMT 12	High competition for public and private investment funding with a main funding gap for start-ups and SMEs.	N	0	38	50	13	0	0
STMT 13	Lack of focus on public funding in biomedical R&I that prevents large budgets from being allocated to the best initiatives / projects.	N	13	25	63	0	0	0
STMT 14	Low tolerance to R&D failure and pressure for profit in the value chain: public sector gives funds to universities that are challenged to do tech transfer and be profitable and the chain continues to startups, SME up to pharma.	N	0	38	13	50	0	0
B- High prices based on Patents and Value-based Pricing (VBP) as main innovation drivers								
STMT 10	There is a lot of misunderstanding about what is value in health between private and public sector with current private-public negotiations focused on price rather than value proposition.	Y	38	50	13	0	0	0
STMT 11	Governments are paying for new drugs that don't bring significant added value to patients and health systems.	N	0	25	50	0	25	0
STMT 15	The patent system has failed: it's led by profit-oriented pharma that, instead of having a narrow window to recoup the R&D costs, it's benefiting from large profits and not tackling global health needs.	N	25	13	13	13	38	0
STMT 16	We normally forget about the patients, the more fragile side of the whole picture. The "fee per service" or "fee per drug" do not always solve the cause of the problem for the patient.	N	25	0	50	13	13	0
STMT 17	At EU, prices for new biomedical products are set at national level resulting in lack of transparency since producers and buyers don't want to disclose the price.	N	0	38	50	0	13	0
STMT 18	Even though the procurement system in EU could be improved, it's a good system because there is a strong regulation and analysis.	N	0	38	63	0	0	0

Table B3. R1 Consensus Causes: Risks and rewards (cont.)

R1 Delphi survey (n=10, RR= 80%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Causes - Risks & Rewards								
B- High prices based on Patents and Value-based Pricing (VBP) as main innovation drivers								
STMT 19	Gains for the Government to embrace a new R&I model: The real problem for the governments is sustainability of health systems and affordability of drugs, not unmet needs (although they recognize their existence). Governments are worried about the existing levels of expenditure on health care and relatively low impact of some new technologies.	N	0	50	13	38	0	0
STMT 23	With the current Value-Based Pricing (VBP) model industry finds all sorts of ways of making the value look enormous and without any equity consideration.	N	0	25	13	38	13	13
STMT 24	The value-based model disincentives R&D investment in areas with reasonable good generic drugs due to low return on investment. i.e. a new drug for schizophrenia is going to be priced against the base of the generic. Cancer drugs rarely get to the generic stage: every new drug is compared with the very expensive predecessor, so prices keep hiking up.	N	0	38	13	50	0	0
STMT 25	Products that seek to improve health and wellbeing should be framed as "**global public goods**" allowing a very narrow window of patent protection so the industry can recoup the R&D costs.	N	13	13	38	25	0	13
STMT 26	Pricing and reimbursement based on value means promoting excellence and deliver results. That is, high return on investment resulting from high impact disruptive innovation that really changes the way patients are managed and their health outcomes. You have to look at the total cost of healthcare, not only at the costs of a new drug, so consider the savings in healthcare costs and increase in productivity as a result of the innovation.	Y	75	25	0	0	0	0
STMT 27	Solutions-oriented ("beyond the pill"). Pharma has been really confused during so many years trying to make the product the center of the business. Now they are discovering that healthcare systems are progressively willing to pay for value-added solutions, including health prevention and promotion.	Y	38	50	0	0	0	13

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree;A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

47 **Table B4** R1 consensus PSM: specified Normative Preferences

R1 Delphi survey (n=10, RR= 80%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Normative Preferences (social values)								
STMT 30	**Norm 2 specified:** "Generally speaking, health systems should reward efficiency, meaning solution-based disruptive innovation, really improving the patient journey and the sustainability of the health systems unless there aren't the conditions for this reward to happen naturally, for instance when difficult to show results (i.e. mental health), small populations (i.e. rare diseases), low availability to pay (i.e. LMIC, disregarded socio-economic groups), restricted use (i.e. new antibiotics), that should be necessarily incentivised.	Y	25	50	13	13	0	0

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree; A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

48 **Table B5** R1 consensus PSM: Priority elements

R1 Preliminary survey (n=10, RR= 90%)

STMT 17	**Priority elements of the new equitable R&I mode**l. In the case we decide to re-design the biomedical R&I model to improve health equity - What 5 priority elements of the model should be redefined? (Please tick ONLY 5 boxes).		
Top position	**Items**	**Freq (#)**	**Freq (%)**
1	Orientation to top public health priorities covering	9	100
2	Reward R&I Outcomes (health/environment/financial/social)	7	78
3	Pricing mechanisms (i.e. risk-sharing, Netflix model)	6	67
4	Distribution of risks and rewards	5	56
5	Increase Pull incentives (i.e. AMC, PRV)	4	44
6	Transparency in Financial data	3	33
7	Transparency in Scientific data for publicly funded studies	3	33
8	Increase Push incentives to academia, start-ups, PDPs, etc.	3	33
9	Increase incentives to Venture Capital	3	33
10	Intellectual Property measures to avoid patent abuse	1	11
11	Other (open text)	1	11
12	Voluntary patent licensing	0	0
13	Compulsory patent licensing	0	0

Frequency: Freq (#) indicates the number of panellists who have selected the item and Freq (%) indicates the corresponding percentage of the total number of panel respondants.

AMC, advanced market commitment; PRV, priority review voucher.

49 **Table B6** R1 consensus PSM: Judgement of the solution

R1 Preliminary survey (n=10, RR= 90%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Judgement of the solution								
STMT 20	**PSM 4S principles**. What do you think about other ways of rethinking the R&I model such as the PSM with the 4 "Share" principles in which public investment and procurement can be the market shapers for biomedical R&I?	Y	0	67	22	11	0	0

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree;A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

50 **Table B7** R1 consensus PSM: sharing Governance

R1 Delphi survey (n=10, RR= 80%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Co-created PSM - Governance								
STMT 31	Big public-private consortium for a 360º view and honest dialog including inter-governmental and multilateral organisations, ministries of health, private sector and civil society organisations as a platform to identify priorities, define value in healthcare and foster open innovation based on results.	N	25	38	13	0	13	13
STMT 32	Big public-private consortium with regional leadership by inter-governmental organisations such as the EU and African Union, among others.	N	25	25	25	0	13	13
STMT 33	Big public-private consortium: At global health level, WHO leadership for priority setting with reinforced authority and influence in front of nation states and private sector.	N	13	38	25	0	13	13
STMT 34	Set clear conditions on how you collaborate and the end result should be: "Business as usual but re-directed. The Preferred Supplier model introduces change in a way that looks incremental and pragmatic for the private sector".	N	0	25	63	13	0	0

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree;A,

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

51 **Table B8** R1 consensus PSM: sharing Needs

R1 Delphi survey (n=10, RR= 80%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Co-created PSM - Needs								
STMT 35	Priorisation of Public Health unmet needs to be incentivised should be based on epidemiology (burden of disease, etc) and situations in which impact is not rewarded naturally, for instance when difficult to show results (i.e. mental health), small populations (i.e. rare diseases), low availability to pay (i.e. LMIC, disregarded socio-economic groups), restricted use (i.e. new antibiotics), etc.	Y	13	75	0	13	0	0
STMT 36	At global level, health priorities are already set by the UN Sustainable Development Goals. A priorisation list is needed and make absolutely clear for the private sector what is the incentive model and the market access commitment by the government.	N	0	50	13	25	0	13
STMT 37	Citizen and solution-oriented: In a "customer-in" strategy, pharma should engage at the very beginning the citizens and health practitioners for the prioritization of the problems to the design of solutions, their personalization and validation. The private sector should cooperate and come with a disease area of focus (ie cardiovascular health rather than hypertension, epidemic preparedness rather than Covid-19) and bring a series of interventions including prevention and promotion, so proposing solutions tackling the root of the problem and be rewarded for that.	Y	0	88	0	0	0	13

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree; A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

52 **Table B9** R1 consensus PSM: sharing Risks and rewards

R1 Delphi survey (n=10, RR= 80%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Co-created PSM - Risks and Rewards								
STMT 38	Tracking public and private R&I investment and cost is doable, and should affect the price negotiation between the Preferred Supplier and the Government in return for a market access commitment linked to impact.	Y	0	63	25	13	0	0
STMT 39	Price should be linked to impact, related to disruptive science that brings value to the patients, modulated by the tracked R&I cost and investment record.	Y	13	75	13	0	0	0
STMT 40	Government should align the unmet needs to the disruptive innovation by only paying for what brings real value to the patient, and ultimately be sustainable for the health system. Stop paying for incremental innovation and review the list of reimbursed treatments periodically.	N	13	38	13	38	0	0
STMT 41	Reimbursement agreements between payers and manufacturers for innovative therapies could be Managed Entry Agreements, Advanced Market Commitments, Subscription model (ie. for new antibiotics), among others.	Y	25	63	13	0	0	0
STMT 42	Goverments should promote population-based purchasing agreement bundling payments based on solutions increasing the health care outcomes of the whole population (big indicators).	N	13	63	0	13	0	13

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree;A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

53 **Table B10** R1 consensus PSM: sharing Results and Outcomes

R1 Delphi survey (n=10, RR= 80%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Co-created PSM - Results								
STMT 43	Mobilise scientific data so the development of new treatments can be improved and speed up, accepting and sharing failure results as an important part of the R&I process.	Y	13	88	0	0	0	0
STMT 44	Pharma generates R&D data related to pre-clinical and clinical phases. Real-world evidence related to healthcare outcomes is mainly owned by the government who should facilitate access	Y	38	50	13	0	0	0
Co-created PSM - Outcomes								
STMT 45	Follow the triple/ quadruple aim with clinical endpoints complemented with efficiency indicators (i.e. re-admissions, prevention of transmission), patient-reported outcomes and experience (PROMS, PREMS), caregivers and healthcare professionals' satisfaction; as well as environmental impact and financial practices (i.e. re-investment of profit in R&I).	Y	50	13	25	0	0	13
STMT 46	Evaluate health interventions with full HTA.	Y	50	25	25	0	0	0
STMT 47	Apply the HTA results including ethical, legal and social aspects to better define and quantify value-based pricing in order to promote an equitable, efficient and high-quality health	Y	38	38	25	0	0	0

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree;A, agree; N, neutral; D, Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

54 **Table B11** R1 consensus PSM: Gains for the industry

R1 Delphi survey (n=10, RR= 80%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Co-created PSM - Gains for the industry to embrace a new R&I model								
STMT 20	The current biomedical R&D system is collapsing. The PSM may ensure both sustainability and reputation for the industry since it's better aligned with what government and the general public wants.	N	0	25	37,5	12,5	12,5	12,5
STMT 21	"Responsible capitalism" by truly thinking about the patient. The way big companies are starting to perform in stock market is not just about benefit, it's also about being responsible, giving value to the society, being part of the ecosystem as an efficient actor. And that goes beyond pricing and profit which is something that big pharma are abandoning.	N	37,5	25	12,5	12,5	0	12,5
STMT 22	Pharma leadership in front of Incomers: Pharma wants to be part of this health transformation to survive avoiding that powerful incomers such as Amazon, Google or Apple could come into play and disintermediate pharma. If the R&I system is compared with a bike, the new incomers could be a nice front wheel (customer reach) buying the back wheel (R&I traction) of other companies and acting as a main orchestrator.	N	0	50	13	25	13	0

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree; A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

55 **Table B12** R1 consensus PSM: Enablers

R1 Delphi survey (n=10, RR= 80%)

STMT 48	What are the key success factors that could lead to the successful implementation of the new model? Please tick ONLY 3.		
Top position	**Items**	**Freq (#)**	**Freq (%)**
1	Pilot the model at EU IMI level	5	63
2	Realistic aspiration: incremental change based on shifting incentives	4	50
3	Solution-based model in moonshot missions and increased applicability of solutions	3	38
4	EU Next Generation Europe funds (European Recovery Plan)	3	38
5	Open innovation based on results	3	38
6	Private sector interested in MEAs and need the population to try their innovations	2	25
7	Tolerance to failure	2	25
8	Scale	2	25

Frequency: Freq (#) indicates the number of panellists who have selected the item and Freq (%) indicates the corresponding percentage of the total number of panel respondants.

IMI, Innovative Medicines Initiative (now Innovative Health Initiative).

MEAs, managed entry agreements.

56 **Table B13** R1 consensus PSM: Feasibility and probability

R1 Delphi survey (n=10, RR= 80%)

Statement		Almost Certain	Likely	Possible	Unkikely	Rare
Feasibility and Probability						
STMT 49	How feasible is that the new model will increase health access & equity?	12,5	0	62,5	25	0
STMT 50	How probable is this model to be implemented?	0	12,5	50	37,5	0

ANNEX C. R2 DELPHI SURVEY RESULTS

The following tables includes the results of R2 initial survey and Delphi survey of consensus scoring questions only. Results of open-ended questions are not included (refer to 10.1 data availability).

57 **Table C1** R2 consensus Normative Preferences and Problem Definition

R2 Delphi survey (n=17, RR= 88%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Normative Preferences (social values)								
STMT 1.10	**Norm 1: Equity** "Generally speaking, health systems should secure universal access to affordable, preventive, curative and good quality healthcare regardless of ethnicity, gender, age, social status or ability to pay".	Y	80	13	0	0	7	0
STMT 1.11	**Norm 2: Efficiency / Cost-effectiveness:** "Generally speaking, health systems should reward efficiency, meaning solutions tackling the root of the problem based on disruptive innovation, really improving the patient journey and the sustainability of the health systems".	Y	27	40	20	0	7	7
STMT 0.5	**Health equity as a R&I priority.** Improving equity access and outcomes should be a priority for the R&I model.	Y	27	60	13	0	0	0
STMT 0.6	**Health equity as a priority in decision-making in your organisation.** Improving health equity is a priority in the decision-making of your organization.	Y	47	27	27	0	0	0
STMT 0.7	**Revision of the R&I model**. The biomedical R&I model should be redefined.	Y	27	33	33	0	7	0
Problem definition								
STMT 0.3	**Equity R&D gap**. "As little as 1% of all global funding for health R&D is allocated to diseases mostly noted in LMIC countries (such as malaria and TB) even though they account for more than 12.5% of the global burden of disease" (WHO, 2016).	Y	27	60	13	0	0	0

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree;A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

58 **Table C2** R2 consensus Causes: Needs, Results and Risks and rewards

There were no causes statement linked to governance in R2.

R2 Delphi survey (n=17, RR= 88%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Causes - Needs								
STMT 1.3 (5)	Global Health priorities are already set in the UN Sustainable Development Goals, but they aren't really impactful in engaging pharmaceutical organizations.	Y	7	67	13	7	0	7
STMT 1.4 (7)	Health needs are not discussed in advance between the main stakeholders because there is not the culture. Research has been mainly "investigator-led" with only a progressive tiny increase in evidence-based research led by HTA agencies oriented to public health needs.	Y	27	40	20	0	0	13
Causes - Results								
STMT 1.5 (9)	Insufficient real-world evidence sharing and data integration by national governments.	Y	33	33	33	0	0	0
Causes - Risks & Rewards								
A- R&I Gap								
STMT 1.1 (1)	The mismatch between financial incentives (commercial value) for biomedical innovation and public health needs.	Y	60	27	7	0	7	0
STMT 1.2 (2)	Public purchasers failing to use their market power to set a clear and robust priority agenda and financial incentives strategy, including smart procurement.	N	20	33	20	7	7	13
B- High prices based on Patents and Value-based Pricing (VBP) as main innovation drivers								
STMT 1.6 (10)	There is a lot of misunderstanding about what is value in health between private and public sector with current private-public negotiations focused on price rather than value proposition.	Y	13	60	13	0	0	13
STMT 1.8 (26)	Pricing and reimbursement based on value means promoting excellence and deliver results. That is, high return on investment resulting from high impact disruptive innovation that really changes the way patients are managed and their health outcomes. You have to look at the total cost of healthcare, not only at the costs of a new drug, so consider the savings in healthcare costs and increase in productivity as a result of the innovation.	N	27	33	7	7	0	27
STMT 1.9 (27)	Solutions-oriented ("beyond the pill"). Pharma has been really confused during so many years trying to make the product the center of the business. Now they are discovering that healthcare systems are progressively willing to pay for value-added solutions, including health prevention and promotion.	N	7	40	27	0	0	27

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree;A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

59 **Table C3** R2 consensus PSM: specified Normative Preferences

R2 Delphi survey (n=17, RR= 88%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Normative Preferences (social values)								
STMT 12 (30)	**Norm 2 specified:** "Generally speaking, health systems should reward efficiency, meaning solution-based disruptive innovation, really improving the patient journey and the sustainability of the health systems unless there aren't the conditions for this reward to happen naturally, for instance when difficult to show results (i.e. mental health), small populations (i.e. rare diseases), low availability to pay (i.e. LMIC, disregarded socio-economic groups), restricted use (i.e. new antibiotics), that should be necessarily incentivised.	N	20	33	13	7	7	20

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree;A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

60 **Table C4** R2 consensus PSM: Priority elements

R2 Delphi survey (n=17, RR= 88%)

STMT 17	**Priority elements of the new equitable R&I mode**l. In the case we decide to re-design the biomedical R&I model to improve health equity - What 5 priority elements of the model should be redefined? (Please tick ONLY 5 boxes).		
Top position	**Priority items**	**Freq (#)**	**Freq (%)**
1	Orientation to top public health priorities covering unmet needs	9	60
2	Transparency in Scientific data for publicly funded projects	8	53
3	Reward R&I Outcomes (health/environment/financial/social)	8	53
4	Transparency in Financial data	7	47
5	Pricing mechanisms (risk-sharing, Netflix model, etc)	6	40
6	Increase Push incentives with funding to academia, start-ups, PDPs, etc	6	40
7	Increase Pull incentives (i.e. AMC, PRV)	5	33
8	Other (open text)	5	34
9	Intellectual Property (avoid patent abuse, etc)	5	33
10	Distribution of risks and rewards	4	27
11	Increase incentives to Venture Capital	4	27
12	Compulsory patent licensing	2	13
13	Voluntary patent licensing	1	7

Frequency: Freq (#) indicates the number of panellists who have selected the item and Freq (%) indicates the corresponding percentage of the total number of panel respondants.

AMC, advanced market commitment; PRV, priority review voucher.

61 **Table C5** R2 consensus PSM 4S Principles: Judgement of the solution

R2 Delphi survey (n=17, RR= 88%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Judgement of the solution								
STMT 10 (20)	**PSM 4S principles**. What do you think about other ways of rethinking the R&I model such as the PSM with the 4 "Share" principles in which public investment and procurement can be the market shapers for biomedical R&I?	N	7	20	40	13	20	0

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree;A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

62 **Table C6** R2 consensus PSM: sharing Needs

R2 Delphi survey (n=17, RR= 88%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Co-created PSM - Needs								
STMT 16 (35)	Priorisation of Public Health unmet needs to be incentivised should be based on epidemiology (burden of disease, etc) and situations in which impact is not rewarded naturally, for instance when difficult to show results (i.e. mental health), small populations (i.e. rare diseases), low availability to pay (i.e. LMIC, disregarded socio-economic groups), restricted use (i.e. new antibiotics), etc.	Y	20	47	13	0	0	20
STMT 18 (37)	Citizen and solution-oriented: In a "customer-in" strategy, pharma should engage at the very beginning the citizens and health practitioners for the prioritization of the problems to the design of solutions, their personalization and validation. The private sector should cooperate and come with a disease area of focus (ie cardiovascular health rather than hypertension, epidemic preparedness rather than Covid-19) and bring a series of interventions including prevention and promotion, so proposing solutions tackling the root of the problem and be rewarded for that.	N	13	33	33	0	7	13

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree;A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

63 **Table C7** R2 consensus PSM: sharing Risks and rewards, Results and Outcomes

R2 Delphi survey (n=17, RR= 88%)

Statement		CON	SA (%)	A (%)	N (%)	D (%)	SD (%)	O (%)
Co-created PSM - Risks and Rewards								
STMT 19 (38)	Tracking public and private R&I investment and cost is doable, and should affect the price negotiation between the Preferred Supplier and the Government in return for a market access commitment linked to impact.	N	13	27	27	7	13	13
STMT 20 (39)	Price should be linked to impact, related to disruptive science that brings value to the patients, modulated by the tracked R&I cost and investment record.	N	0	53	7	7	13	20
STMT 21 (41)	Reimbursement agreements between payers and manufacturers for innovative therapies could be Managed Entry Agreements, Advanced Market Commitments, Subscription model (ie. for new antibiotics), among others.	Y	13	40	27	0	7	13
Co-created PSM - Results								
STMT 23 (43)	Mobilise scientific data so the development of new treatments can be improved and speed up, accepting and sharing failure results as an important part of the R&D process.	Y	40	40	7	0	0	13
STMT 24 (44)	Pharma generates R&D data related to pre-clinical and clinical phases. Real-world evidence related to healthcare outcomes is mainly owned by the government who should facilitate access to this aggregate data to improve the design and implementation of solutions.	Y	33	27	33	0	0	7
Co-created PSM - Outcomes								
STMT 25 (45)	Follow the triple/ quadruple aim with clinical endpoints complemented with efficiency indicators (i.e. re-admissions, prevention of transmission), patient-reported outcomes and experience (PROMS, PREMS), caregivers and healthcare professionals' satisfaction; as well as environmental impact and financial practices (i.e. re-investment of profit in R&I).	N	7	40	20	0	0	40
STMT 26 (46)	Evaluate health interventions with full HTA.	Y	13	40	27	0	7	13
STMT 27 (47)	Apply the HTA results including ethical, legal and social aspects to better define and quantify value-based pricing in order to promote an equitable, efficient and high-quality health	Y	13	47	20	7	0	13

N, total number of responses; RR, response rate.

Responses to each statement (STMT) are represented as percentages of the total responses. SA, strongly agree;A, agree; N, neutral; D, disagree; SD, strongly disagree; O, other responses (open text).

Level of consensus (CON). Y, yes; N, no. Based on the percentage of 80-100% agreement strongly agree + agree + neutral and, among them, 50-100% strongly agree + agree.

64 **Table C8** R2 consensus PSM: Enablers

R2 Delphi survey (n=17, RR= 88%)

STMT 28 (48)	What are the key success factors that could lead to the successful implementation of the new model? Please tick ONLY 3.		
Top position	**Items**	**Freq (#)**	**Freq (%)**
1	Realistic aspiration: incremental change based on shifting incentives	7	47
2	Open innovation based on results	7	47
3	Tolerance to failure	7	47
4	Private sector interested in MEAs and need the population to try their innovations	4	27
5	Solution-based model in moonshot missions and increased applicability of solutions	4	27
6	Pilot the model at EU IMI level	4	27
7	EU Next Generation Europe funds (European Recovery Plan)	3	20
8	Other (open text)	3	20
9	Scale	2	13

Frequency: Freq (#) indicates the number of panellists who have selected the item and Freq (%) indicates the corresponding percentage of the total number of panel respondants.
IMI, Innovative Medicines Initiative (now Innovative Health Initiative).
MEAs, managed entry agreements.

ANNEX D. R3 ADDITIONAL RESULTS

65 **Table D1** R3 Kendall's W for Causes and PSM Governance, Barriers and Enablers

Kendall's Coefficients of Concordance W

	causes	governance	barriers	facilitators
# of options	5	4	9	9
# of raters	22	22	22	22
Chi-squared	18.9455	6.4909	8.9333	7.2
df	4	3	8	8
p-value *	0.0008	0.0900	0.3480	0.5152
Kendall's W **	0.2153	0.0983	0.0508	0.0409

* Alternative hypothesis: W is greater than 0
** Corrected for tied ranks
Kendall's W were calculated using the package DescTools in R version 4.1.2

66 **Table D2** R3 Kendall's W for main Causes of the problem by expert segment

Kendall's Coefficients of Concordance W

Causes of the problem	Payers	Performers	Users	Shapers
#options	5	5	5	5
# raters	3	7	3	9
Chi-square	7,733	4,571	6,667	9,156
df	4	4	4	4
p-value*	0,102	0,334	0,155	0,057
Kendall's W **	0,6444	0,1633	0,5556	0,2543

* Alternative hypothesis: W is greater than 0
** Corrected for tied ranks

67 **Table D3** R3 Kendall's W for PSM Governance by expert segment

Kendall's Coefficients of Concordance W

PSM Governance	Payers	Performers	Users	Shapers
#options	5	5	5	5
# raters	3	7	3	9
Chi-square	1,800	0,771	4,200	5,400
df	3	3	3	3
p-value*	0,615	0,856	0,241	0,145
Kendall's W **	0,2000	0,0367	0,467	0,2000

* Alternative hypothesis: W is greater than 0
** Corrected for tied ranks

68 **Table D4** R3 Kendall's W for PSM Barriers by expert segment

Kendall's Coefficients of Concordance W

PSM Barriers	Payers	Performers	Users	Shapers
#options	9	9	9	9
# raters	3	7	3	9
Chi-square	6,400	4,267	11,733	7,733
df	8	8	8	8
p-value*	0,6025	0,8323	0,1635	0,4599
Kendall's W **	0,2667	0,0762	0,4889	0,1074

* Alternative hypothesis: W is greater than 0
** Corrected for tied ranks

69 **Table D5** R3 Kendall's W for PSM Enablers by expert segment

Kendall's Coefficients of Concordance W

PSM Enablers	Payers	Performers	Users	Shapers
#options	9	9	9	9
# raters	3	7	3	9
Chi-square	10,311	6,438	7,200	9,037
df	8	8	8	8
p-value*	0,244	0,598	0,515	0,339
Kendall's W **	0,4296	0,1150	0,3000	0,1255

* Alternative hypothesis: W is greater than 0
** Corrected for tied ranks

70 **Table D6** R3 consensus PSM: Normative Preferences & Problem Definition by segment

R3 Delphi survey (n=27, RR= 81%)

Normative Preferences (social values)		CA(%)	Payer	Performer	User	Shaper
STMT 1.1	**Norm 1: Equity** "Generally speaking, health systems should secure equal access to affordable, preventive, curative and good quality healthcare according to the need regardless of ethnicity, gender, age, social status or ability to pay".	100%	●●	●●	●●	●●
STMT 1.2	**Norm 2: Efficiency / Cost-effectiveness** "Generally speaking, health systems should reward efficiency, normally quantified by cost-effectiveness analysis, so innovation really improving the patient journey for a certain cost (value for money), contributing to the health systems sustainability".	86%	●●	●●	●●	●●
STMT 1.3	**Ethical dilemma.** In market economies, when incentives (risks & rewards) are not fully aligned with public health needs, these norms may imply an ethical dilemma because complying with rewarding efficiency frequently prevents from complying with equity.	77%	●	●●	●●	●●
STMT 1.4	**Efficiency dominates equity.** In industry decision-making, when the equity norm conflicts with the efficiency norm, efficiency (rewards) is superior to equity, resulting in a profit-oriented R&I model rather than public health equity-driven approach.	68%	●	●●	●●	●●
STMT 1.5	**Public-Private mistrust**. Mutual mistrust between public and private actors about the risk and reward management along the R&I cycle due to, among others, lack of transparency of public-private investments, but also unpredictability of market access conditions, keeping the R&D focus on most profitable diseases.	91%	●●	●●	●●	●●
STMT 1.6	**Health equity as a R&I priority.** Improving health equity should be a priority for the biomedical R&I model.	100%	●●	●●	●●	●●
STMT 1.7	**Health equity as a priority in decision-making in your organisation.** Improving health equity is a priority in the decision-making of your organization.	90%	●	●●	●●	●●
Problem Definition						
STMT 1.8	**Equity and speed as main problem.** The main problem with the biomedical R&I system is equity and speed, given that health innovation is not reaching citizens around the world fast enough in an equitable and sustainable manner.	81%	●	●●	●●	●●

Level of consensus (CON) based on the percentage of combined agreement (CA, agree and somewhat agree).(●●) Level 1 supermajority agreement (67-100%), (●●) level 2 simple majority agreement (50%-66%), (empty) level 3 no consensus (0-49%).

71 **Table D7** R3 Causes with no consensus or less agreement

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	CD(%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
Causes - Governance											
STMT 2.3	**Social contract trap**. The current paradigm is that the government (particularly in high-income countries) funds basic R&D in universities and research institutions, and then the industry develops and manufactures new products incentivised by patent protection.	New	2	55	32	36	18	14	18	14	0
STMT 2.5	**Supply oligopoly.** Concentration on few huge biomedical multinational companies since the last 30 years.	New	2	62	34	43	19	10	24	5	5
STMT 2.6	**Lack of inter-sectorial coordination.** The healthcare sector is often reluctant to engage as fully and broadly as would be desirable with non-health actors because "health is different".	New	1	70	30	35	35	5	25	0	9
STMT 2.8	**Poor health innovation management** among managers in both the provider and producer realms.	New	1	69	32	37	32	16	16	0	14
Causes - Needs											
STMT 2.12	**Excess of "me-too" products.** R&D is mainly focused on alternative me-too treatments rather than unmet needs, because it implies less R&D risk and investment, and large markets (i.e. USA, EU).	New	2	52	33	33	19	14	19	14	5
STMT 2.13	**Pharmaceutical Policies predominantly ruled by private sector interests,** with the economic angle dominating the public health angle, resulting in a "technology push" R&D agenda that maximizes the industry return on investment (ROI).	Rev	1	68	27	36	32	14	14	5	0
STMT 2.14	**Lack of alignment between Academia–Government–Pharma**. Mismatch between academia research lines (determined by Principal Investigators) and the governments and big corporates agenda, because no one is clearly telling the academia what are the public health priorities and incentives.	Rev	2	64	27	41	23	14	14	9	0

Table D7. R3 Causes with no consensus or less agreement (cont.)

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	CD(%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
Causes - Results											
STMT 2.19	**Non-inclusive RCT**. Randomised clinical trials (RCT) design are mainly made for "beautified patients", highly-selected patient population with the best prognosis, so the drug is approved for patients without complications.	New	2	60	30	25	35	20	10	10	9
Causes - Risks & Rewards											
A- R&I Gap											
STMT 2.27	**Private funding gap in start-ups/SMEs for early-stage projects.** Most of the venture capital and private equity firms do not target early-stage project companies due to the high risk and long development cycles.	New	2	58	26	32	26	5	21	16	14
STMT 2.31	**Unintended consequences of incentives.** For instance, regulatory incentives for rare diseases that make industry concentrate in few rare diseases with similar solutions or in oncology for niche patients.	New	1	74	27	37	37	16	11	0	14
B- High prices based on Patents and Value-based Pricing (VBP) as main innovation drivers											
STMT 2.35	**Price-Value paradox.** Low expected profits from medications that provide the most health benefit and converse. (i.e. generic antibiotics can still treat the majority of infections versus innovative cancer treatments with low impact on survival).	Rev	2	57	38	24	33	19	19	5	5
STMT 2.38	**High price US-driven business model as investment in public health.** The global pharmaceutical development is largely funded by American patients who accept to overpay for pharmaceuticals, recognizing that the removal or relaxing of price controls is an investment in public health.	New	2	52	37	26	26	16	21	10	14
STMT 2.39	**VBP means low net benefit for the public system.** Value-based pricing (VBP, as cost per QALY gained) allows health payers to pay more for a technology that either generates more clinical benefit or saves costs to the system. Payers have a maximum price per QALY gained as a threshold. In practice, companies price their products an amount that sits close to that threshold. The net benefit for the public sector is close to zero, because much of that benefit is company profit.	Rev	3	42	42	10	32	16	26	16	16
STMT 2.40	**Risk-sharing practices incentivise high prices.** Risk-sharing agreements such as the Managed Access Funds in the UK is a conditional approval and reimbursement after clinical trial phase II. By paying industry before completing the trials, the health payer should have a lower price because it is de-risking pharma. In reality, the company ask a high price upfront and, if the evidence is finally not worth that value, they commit to give a rebate, which is not normally done. This happens because health systems have pressure to get the product to patients.	New	3	47	42	18	29	18	24	12	23

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; O, other responses (open text); NQ, participants who indicated that they were not qualified to respond.

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of agreement/disagreement.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Combined disagreement (CD, somewhat disagree + disagree).

72 **Table D8** R3 PSM statements with no consensus or less agreement

R3 Delphi survey (n=27, RR= 81%)

Statement		VAR	CON	CA (%)	CD (%)	A (%)	SA (%)	SD (%)	D (%)	O (%)	NQ (%)
C- CO-CREATED PREFERRED SUPPLIER MODEL DEFINITION											
STMT 3.8	**De-risk role of public sector by increasing the R&I funding.** The more public funding dedicated to priority R&I, the more efficiently it could be used by academia, startups and SMEs (assuming professional competence and impact-oriented R&D), requiring less private investment, and resulting in lower prices.	New	2	64	27	18	46	23	5	9	0
D- ACCREDITATION REQUIREMENTS: 4 "SHARE" PRINCIPLES											
STMT 3.16	**Share RISK & REWARDS. Voluntary disclosure of the private R&I investment**. Companies could decide to voluntary disclose the R&I private investment, as they will be naturally incentivized to do so, especially if the private investment share is large.	New	**2**	55	36	36	18	9	27	9	0
STMT 3.20	**Share RISK & REWARDS. Price-Volume negotiations.** Price modulation for global access could consider Price-Volume agreements with countries with a budget cap (more volume implies lower price per patient).	New	1	74	26	42	32	21	5	0	14

N, total number of responses; RR, response rate.

Variation (VAR) of R3 Delphi survey statements with respect to R1 Delphi survey. Equal, revised (rev), new statement. Revised and new statements include new ideas generated during R2 interviews.

Responses to each statement (STMT) are represented as percentages of the total responses. A, agree; SA, somewhat agree; SD, somewhat disagree; D, disagree; O, other responses (open text); NQ, participants who indicated that they were not qualified to respond.

Results show frequencies of each statement. The proportion of participants who selected 'not qualified to respond' is reported in the data table but removed from the denominator to calculate the level of agreement/disagreement.

Level of consensus (CON) based on the percentage of combined agreement (CA, agree + somewhat agree). Level 1 supermajority agreement (CA 67-100%), level 2 simple majority agreement (CA 50%-66%), level 3 no consensus (CA 0-49%).

Combined disagreement (CD, somewhat disagree + disagree).

ANNEX E. R3 INFORMATIONAL INPUT: R1 AND R2 CONSENSUS STATEMENTS

CONSENSUS STATEMENTS R1 & R2

The following statements are the **23 consensus points** and main **facilitators** of the new model pointed out by the key informants participating in round 2 Delphi scoring survey (cohort B) assessing the consensus points of round 1 (cohort A).

Consensus criteria: at least 80% scored neutral/agree/strongly agree statements and, among them, at least 50% agree/strongly agree.

NORMATIVE PREFERENCES *(What do we, as society, want to achieve with the biomedical R&I model?)*

1. **Norm 1**: "Generally speaking, health systems should secure universal **access** to affordable, preventive, curative and good quality healthcare **regardless** of ethnicity, gender, age, social status or ability to pay"
2. **Norm 2:** "Generally speaking, health systems should reward **efficiency**, meaning solutions tackling the root of the problem based on disruptive innovation, really improving the patient journey and the sustainability of the health systems"

PROBLEM DEFINITION *(What is the main problem of the current biomedical R&I system?)* **Scoping equity facts and values:**

3. As little as **1%** of all global funding for health R&D is allocated to diseases mostly noted in LMIC countries (such as malaria and TB) even though they account for more than **12.5%** of the global burden of disease" (WHO, 2016).
4. Improving **equity** in terms of health access and outcomes should be a **priority** for the **R&I model.**
5. Improving **equity** in terms of health access and outcomes is a **priority** for **my organization.**
6. The **R&I model** should be **redefined**.

BACKGROUND THEORY I *(What are the main causes that prevent the current biomedical R&I model from fulfilling health equity goals?)*

7. **Health needs are not discussed in advance** between the main stakeholders because there is not the culture. Research has been mainly "**investigator-led**" with only a progressive tiny increase in evidence-based research led by HTA agencies oriented to public health needs.
8. The **mismatch** between financial **incentives** (commercial value) for biomedical innovation and the **public health needs**.
9. **Global Health** priorities are already set in the **UN Sustainable Development Goals**, but they **aren't** really impactful in **engaging** pharmaceutical organizations.
10. **Public purchasers** failing to use their **market power** to set a clear and robust priority **agenda** and financial **incentives** strategy, including smart procurement.
11. There is a lot of **misunderstanding** about what is **value in health** between private and public sector with current private-public negotiations focused on **price** rather than value proposition.
12. **Pricing** and reimbursement based on **value** means promoting **excellence** and deliver **results.** That is **high return on investment** resulting from high impact innovation that really changes the way patients are managed and their health outcomes. You have to look at the total cost of healthcare, not only at the costs of a new drug, so consider the savings in healthcare costs and increase in productivity as a result of the innovation.
13. **Insufficient real-world evidence** sharing and **data integration** by national governments.

BACKGROUND THEORY II *(How can we reach a universal access/equitable and efficient biomedical R&I model?)*

14. Selected 5 priority elements of the R&I model that should be redefined:
    - **Orientation to public health priorities covering unmet needs**
    - **Reward outcomes (in terms of health/environment/financial/social outcomes)**
    - **Pricing mechanism (i.e. risk sharing, MEA, subscription model)**

- **Transparency in scientific data**
- **Transparency in financial data** (publication of public investment received, etc)

15. Gains for the industry: "**Responsible capitalism**" by **truly thinking about the patient**. The way big biotech companies are starting to perform in stock market is not just about benefit, it's also about being responsible, giving value to the society as an efficient actor, and that goes beyond pricing and profit.

CO-CREATION OF A NEW R&I MODEL based on the Preferred Supplier model *(What can be a feasible and effective biomedical R&I model to increase health equity?)*

NEEDS

16. Priorisation of the **unmet public health needs** to be **incentivised** should be based on **epidemiology** (burden of disease, etc) and situations in which **impact is not rewarded naturally**, for instance when **difficult to show results** (i.e. mental health), **small populations** (i.e. rare diseases), **low availability to pay** (i.e. LMIC, disregarded socio-economic groups), **restricted use** (i.e. new antibiotics), etc.

RISKS & REWARDS

17. **Price** should be linked to **impact** (related to science that brings value to the patients) **modulated** by the **tracked R&I cost and investment** record.
18. **Reimbursement** agreements between payers and manufacturers for innovative therapies could be **Managed Entry Agreements**, **Advanced Market Commitments**, **Subscription model** (i.e. for new antibiotics), among others.
19. Governments should promote **population-based purchasing** agreements, **bundling payments** based on solutions increasing the health care outcomes of the whole population (big indicators).

RESULTS

20. Mobilise **scientific data** so the development of new treatments can be improved and speed up, accepting and sharing failure results as an important part of the R&I process.
21. **Real-world evidence** related to healthcare outcomes is mainly owned by the government who should facilitate access to this aggregate data to improve the design and implementation of solutions.

OUTCOMES

22. Evaluate health interventions with full **HTA (C/E)** including legal, ethical and social aspects.
23. Apply the **HTA** results including ethical, legal and social aspects to better define and quantify value-based pricing in order to promote an equitable, efficient and high-quality health system.

ENABLERS

Selected main enablers that could lead to a successful implementation of the new R&I model

- **Realistic aspiration: incremental change based on shifting incentives**
- **Open innovation** based on **results**
- Tolerance to **failure**
- **Pilot** the model at **EU IMI** (currently Innovative Health Initiative)

ANNEX F. R3 INFORMATIONAL INPUT: SUMMARY OF THE PROPOSED PSM

PREFERRED SUPPLIER INNOVATION MODEL FOR HEALTH EQUITY

Summary of the **revised Preferred Supplier model** co-created with the **new ideas** generated in round 2 interviews with key informants (cohort B) during March-October 2022. It will help you to answer the section 3 of the final survey (Co-creation of the Preferred Supplier model).

WHY

PROBLEM DEFINITION
The main **problem** of the current biomedical R&I system is that innovation is not reaching citizens around the world fast enough in an equitable and sustainable manner.

BACKGROUND THEORY
This health equity problem responds to the fact that:

- The market **incentives** are **not** completely **aligned** with **unmet public health needs (market failure).**
- **Mutual mistrust** between public and private actors on **R&I risks and rewards management** that are considered high and not well leveraged, due to several reasons, such as lack of transparency of R&I investments, but also unpredictability of market access (regulatory delays, product diversion, lack of delivery and treatment infrastructure) that makes difficult to align them to priority challenges.

This situation keeps the focus on profitable diseases as a result of a **moral dilemma**:

NORMATIVE PREFERENCES
Main **social values** to define an R&I model are:

- **Norm 1: Equity:** "Generally speaking, health systems should secure equal access to affordable, preventive, curative and good quality healthcare according to the need regardless of ethnicity, gender, age, social status or ability to pay.
- **Norm 2: Efficiency / Cost-effectiveness (HTA):** "Generally speaking, health systems should reward efficiency, normally quantified by cost-effectiveness analysis, so effective innovation really improving the patient journey for a certain cost (value for money), contributing to the sustainability of the health systems".

Given the **capitalist market rules**, when **incentives (risks and rewards) are not completely aligned with public health needs**, these two norms may imply an ethical **dilemma** because **complying** with rewarding **efficiency** (norm 2, in which high impact should mean high ROI) frequently **prevents** from complying with **equity** (norm 1)**.**

In industry decision making when the equity norm **conflicts** with the efficiency norm, **efficiency (rewards)** is **superior** to **equity**, resulting in a profit-oriented R&I model rather than public health equity-driven approach. As a reaction to this problem it is proposed the co-creation of a more equitable biomedical R&I model.

Main hypothesis: It is desired and feasible to co-create a new biomedical R&I model based on the common social values of the different stakeholders, given the public purchasers' market power, by providing the appropriate incentives and risk leveraging practices resulting in a new fair play for more equitable, agile and sustainable outcomes.

Equitable outcomes refer to reduce the biomedical R&G gap and modulate prices for global access.

Summary Co-created Preferred Supplier model (PSM)

WHAT
As a response, it is proposed the **Preferred Supplier** model as a new **social enterprise model** in which pharma and biotech companies **engaged** with **environmental** and **social practices** (such as **equity** and **data sharing) get credit** as **preferred providers** of the public sector for priority health challenges.

HOW
The co-created Preferred Supplier model proposes an **accreditation** of the biomedical corporates for **health payers and funders** to have a level of **guarantee** that the social and environmental requirements are met by the providers as a baseline, non-debatable. In **exchange** the public sector provides significant push **incentives** (mainly for academia/SMEs) and pull incentives (for accredited corporates) for the **priority health challenges** identified by **governments** and normally comprised in the **UN SDGs.** For large corporates, only those accredited as **Preferred Suppliers** developing effective innovative solutions can benefit from the market incentives. The incentives for public health priorities are **conditional** on a commitment to **global access** and **universal data sharing practices** that lead to more equitable and faster outcomes. In this way, suppliers improve their level of accreditation.

WHO
The model can act as a "**social safety net" mechanism** to be activated by governments and multilateral organizations (i.e. WHO) and supported by other stakeholders (i.e. investors, philanthropists, civil society organizations). Preferred supplier accreditation could **initially** apply to **listed and large pharma and biotech companies** (>500 employees or >500m€ turnover) and may progressively incorporate SMEs. So, **push incentives** for priority challenges would mainly benefit **academia/startups/SMEs** discovering potential solutions, and **pull incentives** would mainly benefit accredited Preferred Supplier **pharma and biotech corporates** developing and marketing the final product.

The Preferred Supplier model builds on **accreditation requirements** and **incentives.**

I. **Accreditation REQUIREMENTS**

The Preferred Supplier **accreditation** is based on these **4 SHARE principles**:

1. **Share NEEDS**. **Balanced R&I portfolio**. To ensure that the biomedical research agenda prioritizes public health and social needs, preferred suppliers should invest a tangible part of their R&I portfolio to these needs. The priority health challenges could be defined by the UN SDGs as well as regional and national governments priorities considering epidemiology (i.e. burden of disease) and /or situations in which impact is not rewarded naturally, for instance when difficult to show results (i.e. mental health), small populations (i.e. rare diseases), low availability to pay (i.e. LMIC, disregarded socio-economic groups), restricted use (i.e. new antibiotics), etc.

2. **Share RESULTS. Health data spaces**. Given the enormous social value of health knowledge, preferred suppliers should share scientific data, from R&I projects, to raw data, clinical trial results and real-world evidence, including failure (unsuccessful medical products candidates) to reduce waste of resources and increase speed.

3. **Share RISK & REWARDS**: **Risk-Impact hybrid pricing model**. Rewards for innovative products should balance **impact** (outcomes/value-based) modulated by the **risk** assumed along the development pipeline defined by the R&I **funding mix** (public-private capital). **Impact** will be rewarded applying new **value-based pricing** (i.e. de-link Netflix/subscription model according to the population net health gain, risk-sharing agreements as the Managed Entry Agreements, etc) and outcomes will be evaluated with HTA. To assess the R&I **risk**, preferred suppliers should **declare** all the **public funding received** during the R&I cycle. Companies could decide to disclose the private investment of the funding mix. **Price modulation** favoring **global access** commitment should, for instance, consider **price segmentation** by the ability to pay (i.e. according to GDP per capita) and **price-volume** negotiation (with a budget cap, so more volume implies lower price

per patient. In return, **push incentives** have been given for priority challenges, as well as preferred suppliers should have access to significant **pull incentives**, such as regulatory incentives, innovative pricing, and large purchase commitments if the product efficacy is proven.

4. **Share OUTCOMES.** Additionally to HTA outcome assessment, in order to ensure sustainable practices, preferential access to funds should be granted to companies that demonstrate compliance with best corporate practices: **environmenta**l (i.e. in R&I manufacturing and distribution), **social** (i.e. equitable access, sharing data), as well as corporate **finance practices** (i.e. reduce share buybacks and reinvest part of the profit in R&I) that will determine the Preferred Supplier accreditation level.

The Preferred Supplier **accreditation criteria** could be defined by these 2 pillars and indicators:

Pillar 1. **Corporate Impact**

- **Sustainable Impact:** disclosure by industry of **Environmental, Social and Governance (ESG)** KPIs, alongside the financial information. In some countries, such as the EU and the USA, the ESG regulation is already in place for large and public companies and represents the need for the industry to understand and address their externalities to maintain their social license (the perception that a business is acting in a fair, appropriate way, deserving trust) and deliver meaningful impact over the long term. This regulation is being reinforced, for instance, with the EU Corporate Sustainability Reporting Directive (CSRD) regulation approved by the European Parliament the 10th November 2022; and in the USA the Securities and Exchange Commission (SEC) proposed in March 2022 climate-risk disclosure requirements in addition to the requirement to all public companies to disclose ESG-related risks.
- **Access to Medicine Index like Index like**. For the biomedical sector, the consideration of an Access to Medicine index could stimulate industry to improve access in low-resource countries by getting credit for it as preferred suppliers. For instance, the **Access to Medicine Index** (ATMi) **ranks** the world's largest 20 pharma companies according to their ability to expand access in low- and middle-income countries. The biennial index assesses the Governance (strategy, compliance), the R&I portfolio and the Implementation (pricing and product delivery). Since 2008, the index is published by the Access to Medicine Foundation in Netherlands, an international not-for-profit organization. The ATMi rank could be converted into a key performance indicator (KPI) allowing pharma and biotech firms to measure it and be audited.

Pillar 2. **Data disclosure**
Open source disclosure of scientific and financial data should be regulated for **all the R&I projects receiving public funding** (<u>not</u> only for Preferred Suppliers) as follows:

- **Disclosure of Scientific data** at three levels**: R&I project pipeline**, **raw data** and **results**, with the publication of clinical trials phase III and real-world evidence results, including failure. For results, it could be given a certain period of time and/or a license, except in case of Global Public Health Emergency.
- **Disclosure of Financial data:** disclose of public **R&I funding** tracked during the cycle by academy and industry. It could be linked to the potential commercial assets (i.e. patents, registered software), applying blockchain technology.

In summary, the Preferred Supplier **regulation** is proposed as the following:

For all the priority products submitted by the Preferred Suppliers to **Regulatory Agencies** (i.e. EMA, FDA) for marketing approval there should be the transparency obligation at the moment of the submission of the dossier to present **annually audited indicators:**

- **ESG KPI**: already <u>mandatory</u> in different countries along with the financial reports. Required for Preferred Suppliers.
- **Access to Medicine Index-like KPI**: <u>proposed as voluntary.</u> Required for Preferred Suppliers.

- **Disclosure of Funding Data**: proposed as mandatory for all public-funded projects to disclose the R&I public funding received. Required for Preferred Suppliers.
- **Disclosure of Scientific Data**: proposed as mandatory for all public-funded projects. Required for Preferred Suppliers.

Additionally, companies should commit to collect outcomes of the new product submitted for marketing approval (Social, Environmental, Financial outcomes) that will have an impact on the next exercise ESG and ATMi indicators, so to the Preferred Supplier accreditation for additional incentives.

II. Accreditation INCENTIVES

The Preferred Supplier accreditation is a recognition of good practices, **not** a binding condition, so there is no initial contract with the preferred suppliers. Preferred supplier rewards are based on significant push and pull Incentives for priority public health challenges such as:

- **PUSH Incentives (funding)**: intensified R&I funding in **early phases** (especially with grants and investment to academia/research centers and start-ups/SMEs) and for **growth-stage clinical trials phase II-III** (with long-term public-private matching venture capital investment, especially for SMEs).
- **PULL Incentives (market access**): significant pull incentives options to reward industry R&I success ranging from **regulatory policies** (i.e. fast track, exclusivity extension), to **new value-based pricing models** (i.e. de-link subscription/Netflix model) and **purchasing commitments** (i.e. advanced market commitment, centralized purchasing), among others.

ANNEX G. INFORMED CONSENT AND COMMITMENT OF CONFIDENTIALITY FORMS

Informed consent and commitment of confidentiality for cohort A

UNIVERSITAT DE BARCELONA

Sociology Department
Avinguda Diagonal 696, 4th floor
08034 Barcelona

INFORMED CONSENT FORM AND COMMITMENT OF CONFIDENTIALITY

RESEARCH PROJECT: SOCIAL INNOVATION FOR HEALTH EQUITY: A DESIRED R&D MODEL[4]

This Informed Consent and Confidentiality Commitment Form is aimed at **key informants** who are invited to participate in the **PhD research** ***"Social Innovation for Health Equity: A desired R&D model"*** led by Marina Espriu Simon at the University of Barcelona Economics and Business Faculty Sociology Department and funded by the Barcelona Institute for Global Health (ISGlobal).

The PhD research is focused on the **desirability** and **feasibility** of a new **biomedical R&D model** in improving health **equity co-created** by different stakeholders in light of a set of **values**. The participants in this research are considered **key informants** and have been chosen according to their knowledge and experience, as well as representative of the biomedical ecosystem to provide information about their views and perspectives on the research topic.

In order to facilitate the consensus R&D model, the research work will apply an interactive Health Technology Assessment (HTA) technique with the key informants including the following 3 steps:

- Answering a self-administered online **survey** (estimated 15 minutes)
- Participating in a semi-structured online **interview** (estimated 55 minutes)
- **Rating** your level of agreement/disagreement with a selection of statements about the proposed R&D model (estimated 15 minutes)

COMMITMENTS

As a key informant in the area of study, I have been invited to participate in the research "Social Innovation for Health Equity: A desired R&D model". By means of signing this document:

(i) I voluntarily consent to participate in this research and to answer questions related to the biomedical R&D process and outcomes, understanding that I can withdraw at any time if I wish to do so.

(ii) I give my consent for the interview to be recorded and for its content to be used only for the purpose of this research, always preserving the confidentiality of the information and my privacy.

(iii) I give my consent for my name appearing on the list of people interviewed as key informants (expected to be around 20 people) as long as the content of the interview is not related in any case to my name.

[4] *The final PhD thesis title has been edited with respect to the one mentioned in the informed consent.*

(iv) I am aware of the name of the researcher who is directing the study with whom I can contact at any time to clarify any questions that I need in this regard, and have access to the results of the research if I request it:

Marina Espriu Simon
Marina.espriu@isglobal.org
+34. 648. 725. 361
Department of Sociology
Economics and Business Faculty
University of Barcelona

(v) I receive a copy of this document signed by the researcher of the project as proof and guarantee of her commitment to confidentiality and privacy.

.....

Name and signature of the participant **Name and signature of the researcher**
Date and place: **Date and place:**

.....

PERSONAL DATA PROTECTION

Related to the personal data protection according to the EU regulation 2016/679 of April 27 and 3/2018 of December 5, we inform you that:

a) In accordance with what is established in the aforementioned regulation, the UNIVERSITAT DE BARCELONA, (with fiscal identity number Q0818001J and address at Gran Via de les Corts Catalanes, 585 -08007 Barcelona) as responsible for the processing of personal data, informs that you can contact the Data Protection Delegate by writing to the postal address (Travessera de les Corts, 131-159, Pavelló Rosa, 08028 - Barcelona), or by sending an email to **protecciodedades@ub.edu.**

b) You have the right to access your data, request the rectification of inaccurate data or, if applicable, request its deletion, as well as limit its processing, oppose and withdraw the consent to its use for certain purposes. You can exercise these rights by writing to the postal address or by sending an email to the address mentioned in the previous paragraph. Likewise, we inform you of your right to file a claim with the Catalan Data Protection Agency in the case of any action by the University of Barcelona that you consider to violate your rights.

Informed consent and commitment of confidentiality for cohort B

UNIVERSITAT DE BARCELONA

Sociology Department
Avinguda Diagonal 696, 4th floor
08034 Barcelona

INFORMED CONSENT FORM AND COMMITMENT OF CONFIDENTIALITY

RESEARCH PROJECT: POLICY CONSIDERATIONS FOR A DESIRED EQUITABLE BIOMEDICAL R&D MODEL[5]

This Informed Consent and Confidentiality Commitment Form is aimed at **key informants** who are invited to participate in the **PhD research *"Policy considerations for a Desired Equitable Biomedical R&D model"*** led by Marina Espriu Simon at the University of Barcelona Economics and Business Faculty Sociology Department and funded by the Barcelona Institute for Global Health (ISGlobal).

The PhD research is focused on the **desirability** and **feasibility** of a new **biomedical R&D model** in improving health **equity co-created** by different stakeholders in light of a set of **values**. The participants in this research are considered **key informants** and have been chosen according to their knowledge and experience, as well as representative of the biomedical ecosystem to provide information about their views and perspectives on the research topic.

In order to facilitate the consensus R&D model, this research work will apply an interactive Health Technology Assessment (HTA) technique with **key informants** in two cohorts (A and B) and a total of three rounds. The cohort B in which you are involved includes the following 3 steps:

- Read the **Policy brief** paper and answer a self-administered online **initial scoring survey** with some scoping questions and your level of agreement/disagreement with the consensus points of the first group of key informants about the proposed new biomedical R&D model (15 min)
- Participate in a semi-structured online **interview** (55 min)
- Answer a **final scoring survey** with your level of agreement/disagreement with a selection of new statements about the proposed new R&D model (15 min)

COMMITMENTS

As a key informant in the area of study, I have been invited to participate in the research "***Policy considerations for a Desired Equitable Biomedical R&D model***". By means of signing this document:

(vi) I voluntarily consent to participate in this research and to answer questions related to the biomedical R&D process and outcomes, understanding that I can withdraw at any time if I wish to do so.

(vii) I give my consent for the interview to be recorded and for its content, as well as the content of the surveys, to be used only for the purpose of this research, always preserving the **confidentiality** of the information and my **privacy**.

(viii) I give my consent for my name appearing on the list of key informants (expected to be around 20-25 people) as long as the content of the interview and the surveys is not related in any case to my name.

[5] *The final PhD thesis title has been edited with respect to the one mentioned in the informed consent.*

(ix) I am aware of the name of the researcher who is directing the study with whom I can contact at any time to clarify any questions that I need in this regard, and have access to the results of the research if I request it:

Marina Espriu Simon
Marina.espriu@isglobal.org
+34. 648. 725. 361
Department of Sociology
Economics and Business Faculty
University of Barcelona

(x) I receive a copy of this document signed by the researcher of the project as proof and guarantee of her commitment to confidentiality and privacy.

.....

Name and signature of the participant **Name and signature of the researcher**
Date and place: **Date and place:**

.....

PERSONAL DATA PROTECTION

Related to the personal data protection according to the EU regulation 2016/679 of April 27 and 3/2018 of December 5, we inform you that:

a) In accordance with what is established in the aforementioned regulation, the UNIVERSITAT DE BARCELONA, (with fiscal identity number Q0818001J and address at Gran Via de les Corts Catalanes, 585 -08007 Barcelona) as responsible for the processing of personal data, informs that you can contact the Data Protection Delegate by writing to the postal address (Travessera de les Corts, 131-159, Pavelló Rosa, 08028 - Barcelona), or by sending an email to **protecciodedades@ub.edu.**

b) You have the right to access your data, request the rectification of inaccurate data or, if applicable, request its deletion, as well as limit its processing, oppose and withdraw the consent to its use for certain purposes. You can exercise these rights by writing to the postal address or by sending an email to the address mentioned in the previous paragraph. Likewise, we inform you of your right to file a claim with the Catalan Data Protection Agency in the case of any action by the University of Barcelona that you consider to violate your rights.