



## Short Communication

## Worldwide use of HPV self-sampling for cervical cancer screening

B. Serrano<sup>a,b,\*</sup>, R. Ibáñez<sup>a,b</sup>, C. Robles<sup>a</sup>, P. Peremiquel-Trillas<sup>a,b</sup>, S. de Sanjosé<sup>c,d</sup>, L. Bruni<sup>a,b</sup><sup>a</sup> Cancer Epidemiology Research Program, Catalan Institute of Oncology, IDIBELL, L'Hospitalet de Llobregat, Barcelona, Spain<sup>b</sup> Centro de Investigación Biomédica en Red de Epidemiología y Salud Pública (CIBERESP CB06/02/0073), Madrid, Spain<sup>c</sup> National Cancer Institute, Rockville, MD, USA<sup>d</sup> ISGlobal, Barcelona, Spain

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## ABSTRACT

An increasing body of evidence supports the validity of self-sampling as an alternative to clinician collection for primary Human Papillomavirus (HPV) screening. Self-sampling effectively reaches underscreened women and can be a powerful strategy in low- and high-resource settings for all target ages. This work aims to summarize the current use of HPV self-sampling worldwide. It is part of a larger project that describes cervical cancer screening programmes and produces standardized coverage estimates worldwide. A systematic review of the literature and official documents supplemented with a formal World Health Organisation country consultation was conducted. Findings show that the global use of HPV self-sampling is still limited. Only 17 (12%) of countries with identified screening programs recommend its use, nine as the primary collection method, and eight to reach underscreened populations. We identified 10 pilots evaluating the switch to self-sampling in well-established screening programs. The global use of self-sampling is likely to increase in the coming years. COVID-19's pandemic has prompted efforts to accelerate HPV self-sampling introduction globally, and it is now considered a key element in scaling up screening coverage. The information generated by the early experiences can be beneficial for decision-making in both new and existing programs.

## 1. Introduction

Cervical cancer is a largely preventable disease but remains the fourth most common cancer and the fourth leading cause of cancer death in women worldwide (Ferlay et al., 2020). Most of these cases occur in countries where women are not routinely screened or whose programs do not reach quality standards. In well-established successful programs, cases mainly result from women who do not participate in screening (Benard et al., 2021; Ibáñez et al., 2015).

Given the highly effective and cost-effective cervical cancer prevention strategies available, in 2020, the World Health Organisation (WHO) launched a global initiative to eliminate cervical cancer as a public health problem during the 21st century (*Global strategy to accelerate the elimination of cervical cancer as a public health problem, 2020*). Human Papillomavirus (HPV) tests have proven more sensitive, reproducible and to allow for safer extended screening intervals than conventional cytology or visual inspection with acetic acid (VIA) (Ronco et al., 2014; Arbyn et al., 2012). HPV testing is less dependent on operator expertise than cytology or VIA, making it more suitable for

resource-constrained settings. Furthermore, HPV testing can be performed on vaginal samples collected by the woman herself, known as self-sampling. Self-sampling is a safe and easy approach increasing the opportunities of reaching women that otherwise would not participate in a clinician-based screening or facilitate their access to a screening test (*WHO Guideline on self-care interventions for health and well-being, 2021*). Systematic reviews and meta-analysis confirm that self-sampling is a highly acceptable method for cervical cancer screening in terms of ease of use, convenience, privacy, and physical and emotional comfort, in both high- and low and middle-income countries (LMIC). In addition, comparable diagnostic accuracy has also been confirmed for cervical intraepithelial neoplasia grade two or worse (CIN2+) of self-collected and clinician collected samples if amplification approaches such as polymerase chain reaction (PCR) based tests are used (Nishimura et al., 2021; Arbyn et al., 2018; Kamath Mulki and Withers, 2021).

Despite its potential benefits, the implementation of vaginal self-sampling has challenges, including healthcare workers training to explain the self-sampling procedure adequately to participating women, transportation of the collected specimens, laboratory technical

\* Corresponding author at: Cancer Epidemiology Research Program, Catalan Institute of Oncology, IDIBELL, Avda. Granvia de L'Hospitalet, 199–203 08908 L'Hospitalet de Llobregat, Barcelona, Spain.

E-mail address: [bscarro@iconcologia.net](mailto:bscarro@iconcologia.net) (B. Serrano).

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differences between cervical and vaginal samples processing, and finally, skilled clinicians to manage and follow-up positive women (Hawkes et al., 2020). It is important to include clinical management algorithms and follow-up systems for HPV positive women, as well as to confirm the long-term protection afforded by an HPV negative self-sampling result. Though more evidence on this point is needed, it seems that the current 5-year interval for women with an HPV negative clinician collected result could also be feasible with a negative self-sample (Zhang et al., 2018).

Consequently, the WHO now recommends primary HPV based screening and includes self-sampling among the recently published guidelines on self-intervention for health and as part of the cervical cancer screening guidelines (WHO Guideline on self-care interventions for health and well-being, 2021), and the International Agency for Research on Cancer update of the efficacy and effectiveness of cervical cancer screening methods also supports this statement (Bouvard et al., 2021). Furthermore, the COVID-19 pandemic has accelerated the introduction of HPV self-sampling because it reduces the risk of exposure to the virus and expands health services, helping to address delays in screening. We aim to summarize for the first time the global use of the self-sampling approach in countries recommending primary HPV-based screening.

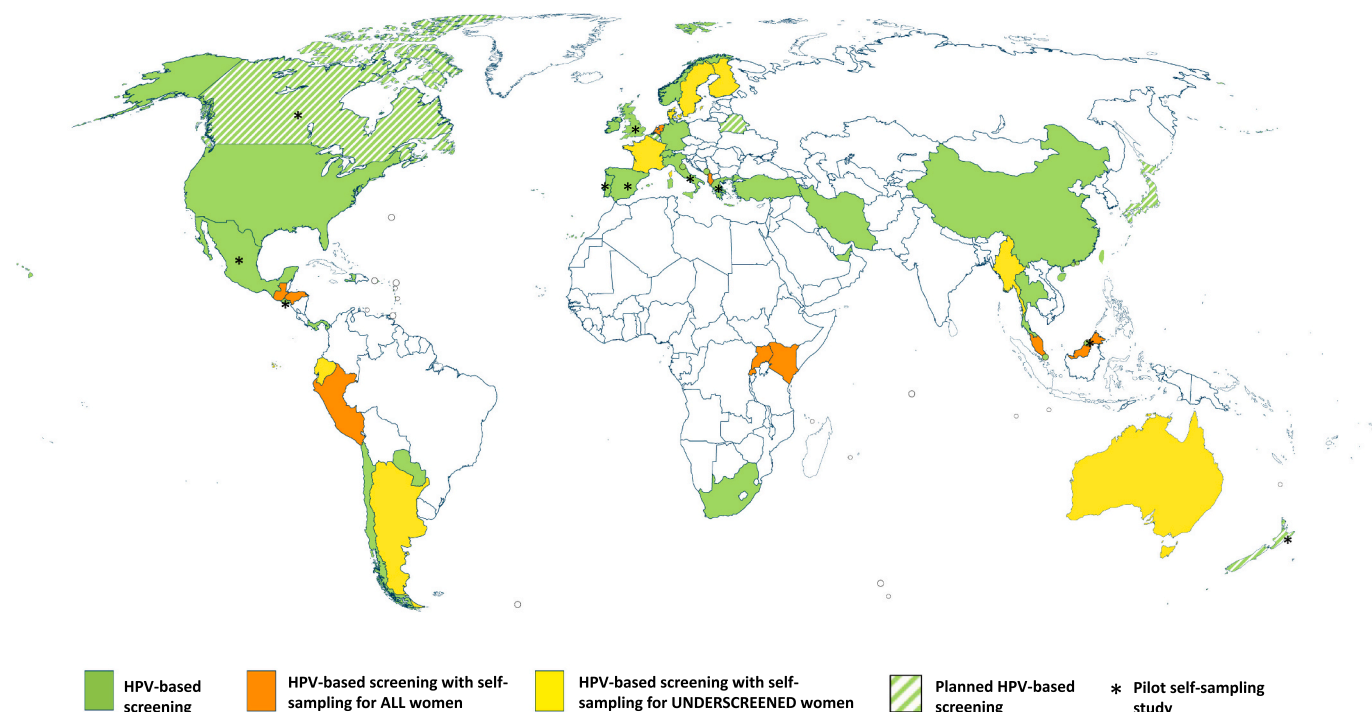
## 2. Methodology

This work is part of a larger project that describes cervical cancer screening programmes worldwide and produces standardized cervical cancer screening coverage estimates (Bruni, Serrano et al. Submitted). In brief, the project methodology included a systematic review of the scientific literature and official documents, conducted up to October 2020, to identify all available data on official national recommendations and cervical cancer screening coverage worldwide for the 194 WHO member states and eight associated countries and territories (American Samoa, Bermuda, China-Hong Kong special administrative region, French

Polynesia, Greenland, Palestine, Puerto Rico, and Tokelau). The search algorithm included an initial search in official websites (e.g., health departments and national epidemiological institutions), followed by a global review with internet search engines. A systematic search in PubMed was also performed, using a combination of terms relevant to “cervical cancer”, “screening”, and “coverage” for each specific country. Reference lists of included documents were also reviewed for additional information. Professional translators assisted investigators in searching for information and interpreting the data in countries with official languages such as Arabic, Russian, or Chinese. All retrieved information on official national recommendations was cross-checked and supplemented with official responses to the WHO Non-Communicable Diseases Country Capacity Survey 2019. The global data search was finally supplemented with a formal WHO country consultation, conducted from Nov 27th, 2020, to Feb 12th, 2021. Countries were grouped into five geographical regions using the United Nations classification system, and by income level using the 2019 World Bank’s classification. The data produced through this work represents the first edition of the WHO cervical cancer screening estimates (Bruni, Serrano et al. Submitted). Future updates of these WHO indicators to monitor the worldwide uptake of self-sampling over time is planned.

## 3. Results

Official recommendations for cervical cancer screening were identified in 139 (69%) countries and territories. Up to February 2021, 48 (24%) countries recommended primary HPV-based screening. HPV testing was recommended alone or in combination with other screening tests. Most countries recommending primary HPV screening are transitioning from cytology. Six countries (Canada, New Zealand, Belgium, Belarus, Japan and Trinidad & Tobago) reported plans in 2020 for HPV-based screening introduction in the coming one or two years (Fig. 1). Among the 140 LMIC, 17% had introduced such screening (three low-,



**Fig. 1.** Self-sampling approach in countries officially recommending HPV-based screening. The solid pattern indicates that the country recommends HPV-based screening (either alone or combined with cytology and/or VIA), the striped pattern indicates that the country plans the introduction of primary HPV screening in the coming years. The boundaries shown and the designations used on this map do not imply the expression of any opinion whatsoever concerning the legal status of any country, territory, city or area or its authorities, or concerning the delimitation of its frontiers or boundaries.

**Table 1**  
Self-sampling approach in countries officially recommending HPV-based screening.

| Country         | Income        | Recommended*                | Year intro HPV-based screening/ Self-sampling | Target population             | Notes  |
|-----------------|---------------|-----------------------------|---|-------------------------------|--|
| <b>EUROPE</b>   |               |                             |   |                               |  |
| Albania         | Upper middle- | In national program         | 2019/2019                                     | All women                     | Before the implementation of the national HPV-based screening programme with self-sampling, a pilot study was conducted in the Fier region in southern Albania (year 2017).<br>The national program started in 2019, in Tirana district and gradually expands over 3 years through the country.  |
| Denmark         | High-         | In national program         | 2012/2018                                     | Underscreened women           | HPV-based screening with the option of self-sampling is implemented in some municipalities while other municipalities use cytology as primary test   |
| Finland         | High-         | In national guidelines      | 2017/2017                                     | Underscreened women           |  |
| France          | High-         | In national guidelines      | 2020/2020                                     | Underscreened women           | By Nov 2020, HPV-based screening was introduced by 16/21 regions. Seven regions had fully introduced self-sampling for underscreened women, and one additional region had partially introduced self-sampling.  |
| The Netherlands | High-         | In national program         | 2017/2017                                     | All women                     |  |
| Sweden          | High-         | In national program         | 2015/2015                                     | Underscreened women           | Pilot study in women residing in underserved rural areas of Northern Greece (year 2015).   |
| Greece          | High-         | Pilot study                 |   | Underscreened women           | Pilot study in women residing in a specific area in Verona (Veneto region) (year 2019).  |
| Italy           | High-         | Pilot study                 |   | All women                     | Pilot study in underscreened women living in Regional Health Administration of Portugal Centro (year 2018).  |
| Portugal        | High-         | Pilot study                 |   | Underscreened women           | Pilot study in women living in Galicia (year 2019), and in Cataluña (year 2021).   |
| Spain           | High-         | Pilot study                 |   | All women                     | Pilot study in underscreened women living in selected areas in London (year 2017).   |
| United Kingdom  | High-         | Pilot study                 |   | Underscreened women           |  |
| <b>AFRICA</b>   |               |                             |   |                               |  |
| Kenya           | Lower middle- | In national guidelines      | 2018/2018                                     | All women                     | HPV-test (with self-sampling) is not generally available in the country. Most facilities use VIA/VILI, followed by cytology.   |
| Rwanda          | Lower-        | In national program         | 2013/2021                                     | All women                     | HPV-based screening (with self-sampling) is being used at different hospitals in three districts of the country with a goal of scaling it up countrywide.  |
| Uganda          | Lower-        | In the strategic plan       | 2020/2020                                     | All women                     | Before the implementation of the national HPV-based screening programme with self-sampling, a pilot study was conducted (year 2019) in women living with HIV at 16 selected health facilities in the country. The pilot results were used to generate recommendations for effective implementation of HPV testing for cervical cancer screening with the aim of increasing uptake of cervical cancer screening in women living with HIV and other groups in Uganda.<br>The Pilot recommendations were considered to scale up the screen-triage- and-treat using HPV and VIA to 640 health facilities with HIV clinics across Uganda from October 2020–2025 with support from partners. |
| <b>AMERICA</b>  |               |                             |   |                               |  |
| Argentina       | Upper middle- | In national guidelines      | 2014/2014                                     | Underscreened women           | Before the implementation of the national HPV-based screening programme with self-sampling, a pilot study was conducted (year 2011).<br>Progressive implementation of the HPV test nationwide. Self-sampling started in Jujuy and Tucumán provinces.   |
| Ecuador         | Upper middle- | In national cancer strategy | 2017/2017                                     | Special populations           | For population with socio-cultural & geographic barriers.  |
| Guatemala       | Lower middle- | In national guidelines      | 2020/2020                                     | All women                     | Before the implementation of the national HPV-based screening programme with self-sampling, a pilot study was conducted in Chimaltenango, Guatemala y Sacatepéquez (year 2014)   |
| Perú            | Lower middle- | In national guidelines      | 2017/2017                                     | All women                     | Progressive implementation of the HPV test nationwide. HPV-based screening started in Tumbes, Loreti and Junín   |
| Honduras        |               | In national guidelines.     | 2015/2015                                     | Special populations/All women | Women with difficulties to access health services or all women who asks for (regions Francisco Morazán, El Paraíso y Copan).   |

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Table 1 (continued)

| Country   | Income        | Recommended*                        | Year intro HPV-based screening/ Self-sampling | Target population                               | Notes  |
|---|---------------|-------------------------------------|---|---|--|
| El Salvador   | Lower middle- | Pilot study                         |   | Underscreened women                             | Pilot study in underscreened women living in the departments of San Vicente, La Paz, Cabañas, and Cuscatlán, Paracentral region El Salvador (within CAPE -Cervical Cancer Prevention in El Salvador, managed by the Ministry of Health) (year 2011 and 2016).  |
| Mexico  | Upper middle- | Pilot study                         |   | Special populations/All women                   | Pilot study in women living in high-risk and marginalized areas in Veracruz (year 2010) and in all women living in Morelos State (year 2007).  |
| <b>OCEANIA</b>                                      |               |                                     |   |   |  |
| Australia   | High-         | In national program                 | 2018/2018                                     | Underscreened women                             | Should be done in a health care setting and at a health professional's request.  |
| <b>ASIA</b>   |               |                                     |   |   |  |
| Malaysia  | Upper middle- | Into nsational program              | 2019/2019                                     | All women                                       | The country is currently in transition towards a generalized use of HPV test as the primary screening test. The rollout of the HPV screening test started in 2019 and will be nationwide by 2024. Malaysia adopts the Australia cervical screening guidelines.   |
| Myanmar   | Lower middle- | Into national program.              | 2018/2018                                     | Special populations                             | HPV-based screening for women living in rural areas  |
| Brunei  | High-         | Pilot                               |   |   | In 2019, Brunei has embarked on research study to look at acceptability of self-sampling HPV test. The Ministry of Health is considering the implementation of the HPV test.   |
| <b>PLANNING INTRODUCTION OF HPV-BASED SCREENING</b> |               |                                     |   |   |  |
| Canada  | High-         | Pilot study                         |   | Underscreened/All women/<br>Special populations | Pilot studies in some regions: in Manitoba in underscreened women, in Newfoundland and Labrador in rural and urban settings, and in Ontario in aboriginal First Nation community in Northwest Ontario.   |
| New Zealand   | High-         | Public consultation + pilot studies |   | Underscreened                                   | Planned introduction HPV test in national program. The Parliamentary Review Committee strongly recommends the introduction of self-sampling, starting with a pilot study. Public consultation for the introduction of self-sampling. There are currently two pilot studies in progress in Maori women. |

**Sources:**

**Albania:** a) Institute of Public Health Albania. How to use the self-administered HPV testing kit [Si duhet të përdorni kitin për testimin HPV me vetëmarrje]. Available at: <http://www.ishp.gov.al/>; b) World Health Organization. Albania upgrades its cervical cancer screening programme with WHO's support. Available at: <https://www.euro.who.int/en>

**Denmark:** Danish Health Authority. Recommendations for cervical cancer screening - 2018 [Screening for livmoderhalskræft - anbefalinger 2018]. Available at: <https://www.sst.dk/da>

**Finland:** The Finnish Medical Society. Current Care Guidelines. Learn more about new sampling techniques [Lisätietoja uusista näytteenottotekniikoista]. Available at: <https://www.kaypahoito.fi/en/>

**France:** Haute Autorité de Santé - France. Public Health Guidelines Summary. Evaluation of human papillomavirus (HPV) tests for primary screening of precancerous and cancerous lesions of the cervix and the role of p16/Ki67 dual immunostaining (July 2019). Available at: [https://www.has-sante.fr/jcms/pprd\\_2986129/en/home](https://www.has-sante.fr/jcms/pprd_2986129/en/home)

**The Netherlands:** a) National Institute for Public Health and the Environment - The Netherlands. Self-sampling kit [Zelfafnameset]. Available at: <https://www.rivm.nl/>; b) Aitken CA, van Agt HME, Siebers AG, et al. Introduction of primary screening using high-risk HPV DNA detection in the Dutch cervical cancer screening programme: a population-based cohort study. *BMC Med.* 2019 Dec 11;17(1):228.

**Sweden:** a) Regional Cancer Centre. Cervical cancer prevention. National care program [Regionala Cancercentrum i Samverkan. Cervixcancerprevention. Nationellt vårdprogram]. In Swedish. 2021-04-13 Version. Available at: <https://cancercentrum.se/samverkan/>; b) Status of the introduction of the cervical cancer prevention program [Status för införandet av vårdprogrammet för livmoderhalscancerprevention]. Available at: <https://cancercentrum.se/samverkan/>

**Greece:** Chatzistamatiou K, Chatzaki E, Constantinidis T, et al. Self-collected cervicovaginal sampling for site-of-care primary HPV-based cervical cancer screening: a pilot study in a rural underserved Greek population. *J Obstet Gynaecol.* 2017 Nov;37(8):1059-1064.

**Italy:** Veneto region. Use of self-sampling in the cervical cancer screening program with HPV tests in AULSS 9 Scaligera [Utilizzo dell'auto-prelievo nel programma di screening per la prevenzione del carcinoma della cervice uterina con test per Papilloma Virus (HPV) nell'AULSS 9 Scaligera - Allegato a DRG nr. 1100 del 30 luglio 2019]

**Portugal:** RTP Noticias Portugal. Press: Regional Health Administration of Portugal Centro launches a project of cervical cancer screening using self-sampling at home [Saúde do Centro lança projeto de rastreio do cancro

do colo do útero em casa. 23/10/2018]. Available at: <https://www.rtp.pt/noticias/>

**Spain:** a) Health department. Galicia. Program for early detection of cervical cancer in Galicia [Xunta de Galicia. Servizo Galego de Saúde (SERGAS). Programa galego de detección precoz do cancro de cérvix]. Available at: <https://www.sergas.es>; b) La Voz de Galicia. Press: Sergas will send a device at home for cervical cancer screening (El Sergas enviará un dispositivo a casa para hacer el cribado de cáncer de cérvix 23/11/2019). Available at: <https://www.lavozdeg Galicia.es/>; c) Health Department. Government of Catalonia. Protocol for cervical cancer screening activities in Catalonia. [Protocol de les activitats de cribatge de càncer de coll uterí a Catalunya. Protocol d'adaptació al model 2015. Generalitat de Catalunya. Departament de Salut. 2019]

**United Kingdom:** a) ISRCTN registry. A London HPV self-sampling pilot (ISRCTN23940319); b) Lim AW, Hollingworth A, Kalwij S, et al. Offering self-sampling to cervical screening non-attenders in primary care. *J Med Screen.* 2017 Mar;24(1):43-49.

**Kenya:** Ministry of Health, Kenya. Kenya National Cancer Screening Guidelines Nairobi, November 2018

**Rwanda:** a) Press: Rwanda scaling up fight against cancer (05/02/2021). Available at: <https://www.aa.com.tr>; b) Binagwaho A, Ngabo F, Wagner CM, Mugeni C, Gatera M, Nutt CT, Nsanzimanac S. Integration of comprehensive women's health programmes into health systems: cervical cancer prevention, care and control in Rwanda. *Bull World Health Organ.* 2013 Sep 1; 91(9): 697-703.

**Uganda:** Republic of Uganda. Ministry of Health. The national cervical cancer prevention and control strategic cancer plan 2020-2025 (September 2020)

**Argentina:** Ministry of Health. National cancer institute. Argentina. Cervical Cancer Prevention. Recommendations for screening, follow-up and treatment of women in the framework of screening programs based on the HPV test (2015). [Prevención del cáncer cervicouterino. Recomendaciones para el tamizaje, seguimiento y tratamiento de mujeres en el marco de programas de tamizaje basados en el test de VPH. Actualización 2015]

**Ecuador:** Protocolos para la Detección Oportuna del Cáncer de Cuello Uterino. Quito: Ministerio de Salud Pública, Dirección Nacional de Estrategias de Prevención y Control-MSP; 2015.

**Guatemala:** Health ministry Guatemala. Comprehensive Care Guide for the Prevention, Detection and Treatment of Precursor Lesions of Cervical Cancer in Guatemala (2020) [Guía de Atención Integral para la Prevención, Detección y Tratamiento de lesiones precursoras de Cáncer Cervicouterino en Guatemala]

**Peru:** a) Ministry of Health Peru. Clinical practice guide for the prevention and management of cervical cancer (2017) [Guía de práctica clínica para la prevención y manejo del cáncer de cuello uterino 2017]; b) Ministry of Health Perú. Resolución ministerial 576-2019.

**Honduras:** Secretary of Health, Government of the Republic of Honduras. Protocol for the screening and treatment of premalignant lesions for cervical cancer prevention (November, 2015) [Protocolo para el tamizaje y tratamiento de lesiones premalignas para la prevención del cáncer cervicouterino - Noviembre 2015]

**El Salvador:** a) Cremer ML, Maza M, Alfaro KM, et al. Introducing a High-Risk HPV DNA Test Into a Public Sector Screening Program in El Salvador. *J Low Genit Tract Dis.* 2016 Apr;20(2):145-50; b) Maza M, Melendez M, Masch R, et al. Acceptability of self-sampling and human papillomavirus testing among non-attenders of cervical cancer screening programs in El Salvador. *Prev Med.* 2018 Sep;114:149-155.

**Mexico:** a) Mendoza González Z. Screening program for cervical cancer: public policies and experiences of actors who implement the program in the state of Veracruz, Mexico [Programa de detección del cáncer cervicouterino: políticas públicas y experiencias de los actores que implementan el programa en el estado de Veracruz, México]. *Salud Colectiva.* 2017;13(3):521-535; b) Lazcano-Ponce E, Lórinz AT, Torres L, et al. Specimen self-collection and HPV DNA screening in a pilot study of 100,242 women. *Int J Cancer.* 2014 Jul 1;135(1):109-16.

**Australia:** Department of Health. Australian government. National Cervical Screening Program – How to take your own sample for an HPV test. Available at: <https://www.health.gov.au/>

**Malaysia:** Ministry of Health Malaysia. Rose Foundation. Program Rose: Removing Obstacles to Cervical Screening. 2019. Available at: <https://www.programrose.org/>

**Myanmar:** WHO country consultation

**Brunei:** a) personal communication WHO country consultation; b) Chaw L, Lee SHF, Hazwani Ja'afar NI, et al. Reasons for non-attendance to cervical cancer screening and acceptability of HPV self-sampling among Bruneian women: A cross-sectional study. medRxiv 2021.03.30.21254670; doi: <https://doi.org/10.1101/2021.03.30.21254670>

**Canada:** a) Jalili F, O'Connell C, Templeton K, et al. Assessing the impact of mailing self-sampling kits for human papillomavirus testing to underscreened non-responder women in Manitoba. *Current Oncology.* 2019;26(3); b) Cervical cancer screening in Canada. *Environmental Scan:* 2019-2020; c) Zehbe I, Moeller H, Severini A, et al. Feasibility of self-sampling and human papillomavirus testing for cervical cancer screening in First Nation women from Northwest Ontario, Canada: a pilot study. *BMJ Open.* 2011 Feb 26;1(1):e000030.

**New Zealand:** a) New Zealand. National screening unit. National Cervical Screening Programme: HPV Primary Screening Clinical Pathway to Introduce Self-Testing for Public Consultation 2021. Available at: <https://www.nsu.govt.nz/>; b) Ministry of Health. New Zealand government. Report of the Parliamentary Review Committee Regarding the National Cervical Screening Programme April 2019

\* Source from which the information was retrieved (national guidelines, screening program website, strategic plan...)



five lower-middle- and 16 upper-middle-income countries), compared to 39% countries among the 62 high-income countries (Bruni, Serrano et al. Submitted).

Among the 48 countries with HPV-based programs, 17 (35%) report having introduced self-sampling in their national programs or guidelines, either for underscreened populations in eight countries (Argentina, Australia, Denmark, Ecuador, Finland, France, Myanmar and Sweden) or as the primary screening option for all women in nine countries (Albania, Kenya, Guatemala, Honduras, Malaysia, Netherlands, Peru, Rwanda and Uganda). Most of these countries have simultaneously introduced the use of HPV-based screening and the self-sampling approach (Fig. 1, Table 1). Among the 17 countries recommending HPV self-sampling, two (12%) are low-, five (29%) are lower-middle-, four (24%) are upper-middle- and six (35%) are high-income countries. Eight additional countries are also piloting self-sampling to decide whether to include this option in their screening guidelines, either targeting all women (Brunei, Mexico, Italy, Spain) or targeting underscreened populations (El Salvador, Greece, Mexico, Portugal and United Kingdom). Most countries recommending HPV-based screening are located in Europe and America, 17 and 16 countries respectively, and among them, one in three countries have also introduced self-sampling in their screening recommendations, and seven more countries are piloting this approach. Among the six countries planning to introduce HPV-based screening, New Zealand and Canada are also piloting self-sampling (Fig. 1, Table 1).

#### 4. Discussion

The present work summarizes for the first time the current implementation of screening with HPV self-sampling worldwide, in a context in which an increasing number of countries are switching to virological testing. Currently, 35% of the 139 countries with identified official screening recommendations promote the use of primary HPV-based screening. The use of HPV self-sampling is only recommended in 17 countries at the time of this review, 35% among countries recommending HPV-based screening. In eight of them, it is recommended for reaching underscreened populations and in nine as the primary collection method. In ten more countries, self-sampling is in a piloting phase.

A minimum screening coverage of 70% among screening targeted women has long been recommended to observe an impact in mortality from the disease. The WHO's elimination initiative is reinforcing this 70% target of women aged 35–45 years screened at least twice with a high-performance test and 90% treatment of women with identified lesions (*Global strategy to accelerate the elimination of cervical cancer as a public health problem, 2020*). Currently, screening and treating identified cervical lesions is the main strategy to reduce cervical cancer in the short-term. However, recent estimates confirm that program performance is suboptimal in most countries. Two out of three women aged 30–49 years have never been screened, with significant disparities between high- and LMICs (83% vs 27% ever coverage, respectively). In addition, 55 (39%) LMIC still lack cervical cancer screening programmes, most of them from Africa and Asia (Bruni, Serrano et al. Submitted).

The use of self-sampling for HPV primary screening provides a key opportunity to increase coverage, particularly in low-resource settings, where infrastructure and specialized workforce is very limited. Although only eleven LMIC have introduced such screening in their official recommendations at the time of this review, it is essential to emphasize that the increased awareness aiming to eliminate cervical cancer may facilitate its introduction in the coming years. However, economic factors and varying healthcare priorities can limit the implementation of HPV-based screening. The cost of HPV testing is perceived as a significant barrier to primary HPV testing, but modeling studies have already demonstrated the benefits of even a single high-precision screen over lifetime (Canfell et al., 2020). Importantly, several new, more affordable assays designed explicitly for LMIC, allowing point-of-care HPV testing

are currently under development (Arbyn et al., 2020). HPV-based screening with self-sampling is a highly cost-effective approach. It overcomes the human constraints faced by many LMICs, as only women that screen positive will require gynecological exams, and therefore reducing the specialized workforce (de Sanjose and Holme, 2019). Another advantage of self-sampling devices is that they do not require a cold chain and are stable after collection, minimizing the infrastructure and logistics required for transport to a central HPV testing facility (Cho et al., 2021). However, it is critical to ensure an adequate follow-up and management of screen positives. If not, gains on increased participation are of no use (Zhang et al., 2018; Verdoodt et al., 2015; Paolino et al., 2020). Further, the increased risk of cervical cancer in women living with human immunodeficiency virus (HIV) and the limited data on the use of self-sampling in this population may require additional accuracy studies in settings where HIV prevalence is high (Wong et al., 2018).

Our findings show that HPV self-sampling is mainly used to reach underscreened populations. In many countries, the COVID-19 disease has disrupted cervical cancer screening programs, changing the perspectives of self-sampling as a primary screening method for all women. Recently, a thorough evaluation of the impact of the pandemic and the key learnings to strengthen cancer screening activities worldwide have been reported. Wentzensen et al. discuss the opportunity to renew and make cervical cancer screening more resilient, highlighting the advantages of risk-based management, HPV-based screening, and in particular, the use of HPV-self sampling (Wentzensen et al., 2021).

HPV self-sampling is a promising strategy to overcome the multiple barriers to cervical cancer screening in low-resource settings and increasing attendance in underscreened women in countries with well-established screening programs. The HPV self-sampling approach may be the only way to improve access to and uptake of screening, especially in those regions of the world with the highest burden of disease, and is now considered a key pillar to reach the WHO elimination target (*WHO Guideline on self-care interventions for health and well-being, 2021*; de Sanjose and Holme, 2019). The information generated by the early experiences can be beneficial for decision-making in both new and existing programs.

#### Funding credits and disclosure of potential and real conflicts of interest

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#### CRediT author statement

Laia Bruni conceptualized the project. Beatriz Serrano designed the data-extraction form, did the literature search, and collected the data. Beatriz Serrano prepared the tables and figures and wrote the

manuscript. All authors contributed to data interpretation, critically revised subsequent drafts, and read and approved the submitted version.

## References

- Arbyn, M., Ronco, G., Anttila, A., Meijer, C.J.L.M., Poljak, M., Ogilvie, G., et al., 2012 Nov 20. Evidence regarding human papillomavirus testing in secondary prevention of cervical cancer. *Vaccine*. 30 (Suppl. 5), F88–F99.
- Arbyn, M., Smith, S.B., Temin, S., Sultana, F., Castle, P., 2018 Dec 5. Detecting cervical precancer and reaching underscreened women by using HPV testing on self samples: updated meta-analyses. *BMJ*. 363, k4823.
- Arbyn, M., Weiderpass, E., Bruni, L., de Sanjosé, S., Saraiya, M., Ferlay, J., et al., 2020 Feb. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis. *Lancet Glob. Health* 8 (2), e191–e203.
- Benard, V.B., Jackson, J.E., Greek, A., Senkomago, V., Huh, W.K., Thomas, C.C., et al., 2021 May 21. A population study of screening history and diagnostic outcomes of women with invasive cervical cancer. *Cancer Med.* 10 (12), 4127–4137.
- Bouvard, V., Wentzensen, N., Mackie, A., Berkhof, J., Brotherton, J., Giorgi-Rossi, P., et al., 2021 Nov 10. The IARC Perspective on Cervical Cancer Screening. *N Engl J Med*. 385 (20), 1908–1918.
- Canfell, K., Kim, J.J., Brisson, M., Keane, A., Simms, K.T., Caruana, M., et al., 2020. Mortality impact of achieving WHO cervical cancer elimination targets: a comparative modelling analysis in 78 low-income and lower-middle-income countries. *Lancet* 395 (10224), 591–603.
- Cho, H.-W., Hong, J.-H., Lee, J.K., 2021 Jan. Detection of high-risk human papillomavirus infection and treatment of high-grade vaginal intraepithelial neoplasia: A single-institution study. *Int. J. Gynaecol. Obstet.* 154 (2), 227–232.
- de Sanjosé, S., Holme, F., 2019 Apr 16. What is needed now for successful scale-up of screening? *Papillomavirus Res.* 7, 173–175.
- Ferlay, J., Ervik, M., Lam, F., Colombet, M., Mery, L., Piñeros, M., Znaor, A., Soerjomataram, I., Bray, F., 2020. Global Cancer Observatory: Cancer Today. International Agency for Research on Cancer, Lyon, France. <https://gco.iarc.fr/today> (accessed July 8, 2021).
- Global strategy to accelerate the elimination of cervical cancer as a public health problem [Internet]. [cited 2021 Jul 7]. Available from: <https://www.who.int/publications-detail-redirect/9789240014107>.
- Hawkes, D., Keung, M.H.T., Huang, Y., McDermott, T.L., Romano, J., Saville, M., et al., 2020 Apr 24. Self-Collection for Cervical Screening Programs: From Research to Reality. *Cancers*. 12 (4), E1053.
- Ibáñez, R., Alejo, M., Combalia, N., Tarroch, X., Autonell, J., Codina, L., et al., 2015 Jun 9. Underscreened women remain overrepresented in the pool of cervical cancer cases in Spain: A need to rethink the screening interventions. *Biomed. Res. Int.* 2015, 605375.
- Kamath Mulki, A., Withers, M., 2021 Jan 6. Human Papilloma Virus self-sampling performance in low- and middle-income countries. *BMC Womens Health* 21 (1), 12.
- Nishimura, H., Yeh, P.T., Oguntade, H., Kennedy, C.E., Narasimhan, M., 2021 May. HPV self-sampling for cervical cancer screening: a systematic review of values and preferences. *BMJ Glob. Health* 6 (5), e003743.
- Paolino, M., Gago, J., Pera, A.L., Cinto, O., Thouyaret, L., Arrossi, S., 2020. Adherence to triage among women with HPV-positive self-collection: a study in a middle-low income population in Argentina. *Ecancermedicalscience*. 14, 1138.
- Ronco, G., Dillner, J., Elfström, K.M., Tunesi, S., Snijders, P.J.F., Arbyn, M., et al., 2014 Feb 8. Efficacy of HPV-based screening for prevention of invasive cervical cancer: follow-up of four European randomised controlled trials. *Lancet*. 383 (9916), 524–532.
- Verdoodt, F., Jentschke, M., Hillemanns, P., Racey, C.S., Snijders, P.J.F., Arbyn, M., 2015 Nov 1. Reaching women who do not participate in the regular cervical cancer screening programme by offering self-sampling kits: A systematic review and meta-analysis of randomised trials. *Eur. J. Cancer* 51 (16), 2375–2385.
- Wentzensen, N., Clarke, M.A., Perkins, R.B., 2021 Oct 1. Impact of COVID-19 on cervical cancer screening: Challenges and opportunities to improving resilience and reduce disparities. *Prev. Med.* 151, 106596.
- WHO Guideline on self-care interventions for health and well-being [Internet]. [cited 2021 Jul 29]. Available from: <https://www.who.int/publications-detail-redirect/9789240030909>.
- Wong, J.P.H., Vahabi, M., Miholjic, J., Tan, V., Owino, M., Li, A.T.W., et al., 2018 Feb. Knowledge of HPV/cervical cancer and acceptability of HPV self-sampling among women living with HIV: A scoping review. *Curr. Oncol.* 25 (1), e73–e82.
- Zhang, L., Xu, X.-Q., Hu, S.-Y., Chen, F., Zhang, X., Pan, Q.-J., et al., 2018 Nov. Durability of clinical performance afforded by self-collected HPV testing: A 15-year cohort study in China. *Gynecol. Oncol.* 151 (2), 221–228.