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Burden of disease attributable to second-hand smoke exposure: a systematic review

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Abbreviations:

SHS: second-hand smoke

PAF: population attributable fractions

WHO: World Health Organization

FCTC: Framework Convention on Tobacco Control

EU: European Union

IHD: ischaemic heart disease

LRI: lower respiratory infections

DALY: disability-adjusted life years

PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses

RR: relative risk

GBD: Global Burden of Disease, Injuries and Risk Factors Study

IHME: Institute for Health Metrics and Evaluation

CRA: comparative risk assessment

LC: lung cancer

COPD: chronic obstructive pulmonary

OM: otitis media

SIDS: sudden infant death syndrome

LBW: low birth weight

Abstract

Our aim was to provide a systematic review of studies on the burden of disease due to second-hand smoke (SHS) exposure, reviewing methods, exposure assessment, diseases causally linked to SHS, health outcomes, and estimates available to date.

A literature review of studies on the burden of disease from SHS exposure, available in PubMed and SCOPUS, published 2007-2018 in English language, was carried out following the PRISMA recommendations. Overall, 588 studies were first identified, and 94 were eligible.

Seventy-two studies were included in the systematic review. Most of them were based on the comparative risk assessment approach, assessing SHS exposure using mainly surveys on exposure at home/workplaces. Diseases more frequently studied were: lung cancer, ischemic heart disease, stroke, chronic obstructive pulmonary disease, asthma and breast cancer in adults; lower respiratory tract infection, otitis media, asthma, sudden infant death syndrome and low birth weight in children. The SHS exposure assessment and the reported population attributable fractions (PAF) were largely heterogeneous. As an example, the PAF from lung cancer varied between 0.6% and 20.5%. Moreover, PAF were estimated applying relative risks and SHS exposures with no consistent definitions or with different age classes.

The research gap on the SHS exposure burden is shrinking. However, estimates are not yet available for a number of countries, particularly the Middle Eastern and African countries, and not all diseases with the strongest evidence of causation, such as sudden infant death syndrome, have been explored. Moreover, in some cases the applied methodology revealed relatively low quality of data.

Key-words: systematic review; second-hand smoke; burden of disease; population attributable fraction; tobacco

Introduction

Exposure to second-hand tobacco smoke (SHS) has been classified as a “Group 1” carcinogen (known human carcinogen) by the International Agency for Research on Cancer and has been shown to have several adverse health effects on adults and children, including respiratory outcomes, acute and chronic cardiovascular effects, and lung cancer.[1-2]

Smoking bans have been increasingly applied all over the world after the recommendation of the World Health Organization (WHO) in 2007 to comply with Article 8 of the Framework Convention on Tobacco Control (FCTC).[3] Smoke-free policies has been broadly applied in workplaces, public venues and transportation.[4] Decreases in SHS exposure after the implementation of smoke-free policies was showed in several studies. with reductions up to 80–90% in workplaces and public places [5-7]

As a consequence, the social unacceptability of SHS and consequently the adoption of voluntary smoking bans in homes in the European Union (EU) countries increased.[8] Evidence suggests that there has been an increase in the prevalence of smoke-free homes. For example, smoke-free homes increased from 72% in 2008 to 78% in 2012 in Italy, after 8 years from the ban implementation,[9-10] and from 16% in 1998 to almost 50% in 2008 in smokers’ houses in England.[11] Moreover, the percentage of Spanish households that reported expenditure on tobacco decreased by 2% after the Spanish ban of 2011.[12]

Although population exposure to SHS has declined over the past two decades, many non-smokers are still exposed to SHS in workplaces, public places, homes, and vehicles. Worldwide, 40% of children, 33% and 35% respectively of non-smoking males and females were exposed to SHS in 2004.[13] Non-smokers’ exposure to SHS has declined by 97% in the past 20 years in Scotland, but there are still nearly one in five non-smoking adults who have measurable exposure to SHS on any given day.[14] Moreover, 54% of youths are still exposed to SHS in any setting in Italy,[15] exposure to SHS at home was the main source of exposure for non-smokers in Spain,[16] and in 2016 72% of children under 12 years are exposed in any setting in Spain.[17]

In 2017, globally 1.2 million of deaths were attributable to SHS exposure, of which 63,822 occurred among children younger than 10 year-old.[18] The largest number of estimated deaths attributable to SHS exposure in adults was caused by ischaemic heart disease (IHD), followed by lower respiratory infections (LRI) in children, and asthma in adults, whereas in terms of disability-adjusted life years (DALY) due to exposure to SHS, most DALYs were from LRI in children, followed by those from IHD and then from asthma in adults.[13] Almost half of the total burden attributable to exposure to SHS was in Southeast Asia and in the Western Pacific, with a high burden of disease also estimated in Europe, particularly in the Eastern and Mediterranean countries.[13]

There are several studies that have estimated the SHS-attributable burden at a global, national, or regional level. However, they used different approaches and methodologies, lists of diseases attributable to SHS exposure, SHS exposure assessments, and outcomes for estimating the burden. As a way to provide a systematic information about the different approaches, the main aim of this systematic review is to describe and summarize the estimates available between 01/01/2017 and 31/12/2018 of the SHS exposure and the health impact, in order to map the estimated disease burden and to identify data gaps.

Methods

We performed a systematic revision of the published literature of studies that estimated the burden of disease due to SHS exposure at the population level. Any study type providing estimates of mortality, morbidity or costs derived from direct counting, from special surveys, or from modelling was considered. We followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines (see apprendix).[19] For this purpose, systematic literature searches were conducted in PubMed (United States National Library of Medicine; http://www.pubmed.org) and SCOPUS (Elsevier;).

For SHS exposure we used the keywords "secondhand" or "second-hand" or "passive smok*" or "environmental tobacco", and for its burden we searched for "burden" or "attributable". We repeated the search in PubMed also using the Mesh term "Tobacco smoke pollution". The search was limited to English language studies published between 01/01/2007 and 31/12/2018 on humans. We arbitrarly decided to start from 2007, but such a choice was informed, aimed to review recent data. In addition, we checked reference lists of the retrieved articles. The syntax for PubMed and Scupus searches is reported in the Appendix.

We excluded editorials, statements of experts, reviews and other non-original researches, e.g., studies reporting and commenting data from other studies. Moreover, because they normally do not contain original estimates of attributable burden, we excluded studies that estimated the burden with a cost-effectiveness design or studies that simulate the introduction of a smoking ban. We also excluded cohort or case-control studies assessing the role of SHS exposure in the aetiology of selected diseases. We did not a priori exclude systematic reviews and meta-analyses or case-control studies that were mostly aimed at obtaining estimates of relative mortality or morbidity risks due to SHS exposure, as in some cases the estimated relative risks (RRs) were then used in the same article in order to obtain burden estimates.[20-22]

We identified 844 studies (280 from PubMed and 564 from SCOPUS), 256 of which were duplicates. The PubMed search with the Mesh term for SHS produced similar results (262 papers). Screening of titles left 482 articles on burden due to SHS exposure. The PRISMA flow chart is reported in Figure 1. After reading the titles and abstracts, we rejected 388 papers: 35% of them were reviews, letters, notes or other studies not reporting original results; 21% estimated RRs of death/disease from selected SHS-related diseases due to SHS exposure or RRs for the effects of selected policies; 14% reported results of surveys or cohort studies on the prevalence of SHS exposure or SHS-related diseases or expenditures; 15% were not on SHS or did not estimate the burden; the other were excluded because they were performed in animals or cells, ecologic studies, on methods to measure or model exposure, meta-analyses on RRs, on policies evaluation.

Moreover, we rigorously examined the reference lists of the included articles in order to find missed papers and we added other 4 articles,[23-26] one which was published in 2006 but we considered it too relevant for not including it in the review. [24]

All the articles retrieved were reviewed by two of the authors of this review (GC and AL) and for the studies that were included in the systematic review information on the study characteristics were registered using a data extraction form. Information included geography, methodology and assumptions of the analysis, exposure assessment, diseases under study with the associated RR definitions, type of outcomes and main results. In case of any disagreement, they again reviewed the article together, and achieved a consensus.

Ninety-four studies were identified, and 22 of them were excluded after reading the full text thoroughly because they were not estimating the burden of disease due to SHS exposure.

Results

Study geography: We included 72 studies in the review. Four of them were carried out within the Global Burden of Disease, Injuries and Risk Factors Study (GBD), a project coordinated by the Institute for Health Metrics and Evaluation (IHME) that provides a comprehensive assessment of risk factor exposure and attributable burden of disease.[25-27,80] Besides the GBD studies that estimated the burden for almost all countries worldwide, 21 studies were implemented in EU, 16 in the US and Canada, 18 in China and in other Asian countries (Japan, Korea, Mongolia, Taiwan, and Vietnam), 7 in Oceania Countries (Australia, Indonesia, and New Zealand), and the remaining in Morocco, Israel, Norway and Switzerland (Table 1).

Methodology: Most of the studies used the comparative risk assessment (CRA) methodology (Table 1), a comparable and transparent approach developed by the WHO to estimate the disease burden from several diverse risk factors.[13,28-30] The CRA approach consists in the following steps: (1) estimate of exposure in a population; (2) select the more appropriate relative risk; and (3) estimate the population attributable fraction (PAF). The resulting PAF, estimated by sex, age and disease, or population group is then multiplied by the number of DALYs, deaths, cases or costs in each group and the overall PAF is estimated as a weighted with weights the proportions in each stratum.

The estimates of the burden of disease have been developed using the above method, as well as with variations of it. Some studies applied the CRA approach using RRs or prevalence directly estimated within a survey or cohort [21,22,31-33] or used them to make projections of the burden.[34] In other cases the PAFs published in other studies were applied to the study population-specific statistics.[35-37]

Five studies used approaches different from the CRA method: simulation models,[38-40] future excess fractions approach, [41] and life table approach.[42]

Diseases: The burden was estimated for adults in 61.1% of the studies, for children in 12.5% of the studies and for both in 26.4% of the studies (Table 2). In most cases, only diseases with strongest evidence of causation with SHS were analysed. In fact, the diseases mainly studied for adults were lung cancer (LC) (76.2%), IHD (54.0%), stroke (33.3%), asthma (23.8%), chronic obstructive pulmonary disease (COPD) (17.5%) and breast cancer (11.1%). In the 2017 GBD study also the burden from diabetes was estimated. In children, the burden from LRI was studied in 60.7% of the papers, otitis media (OM) and asthma in 53.6%, sudden infant death syndrome (SIDS) in 25.0%, and low birth weight (LBW) in 17.9% (Table 2).

Some studies analysed the burden of disease with weak or uncertain evidence of a causal relationship with SHS exposure (17 studies). In adults, few studies evaluated the burden from cervical (1 study),[35] larynx and pharynx (1),[41] and nasal sinus cancer (2),[35,42] hypertension (1),[43] peptic ulcer (1),[43] tuberculosis (1),[44] atopic diseases (1),[45] and multiple sclerosis (1).[46] In children, we found studies evaluating the burden from preterm delivery and spontaneous abortion (1),[35] stillbirth(1)[47], burns (1),[35] atopic diseases(1),[45] attention deficit hyperactivity disorder (3),[48-50] learning disability (1),[48] problem behaviours (1)[51], meningitis (1),[23] and respiratory diseases other than asthma (upper respiratory infections (1),[27] respiratory distress syndrome and respiratory conditions of newborns (2),[49,53] respiratory syncytial virus bronchiolitis (2),[35,53] and pneumonia (2) [31,54]).

Population attributable fraction: In Tables 3 and 4 we reported the estimated PAF respectively for adults and children for diseases with the strongest evidence of causation with SHS, i.e. LC, IHD, COPD, stroke, asthma and breast cancer in adults; and OM, SIDS, LRI asthma and LBW in children. When both the PAF for deaths and DALYs were estimated, only that for deaths was reported in the tables. When PAFs were not reported, if possible, we estimated them using the RR and the prevalence estimates reported in the paper. Only RR defined for dichotomous exposure, i.e. SHS exposed/not exposed, were used in the PAF computation, thus the PAF was not estimated when this was not available.[55]

For each disease the PAF were highly heterogeneous among studies. In adults, the PAF from lung cancer for all ages varied from 0.6% for exposure in both genders to SHS at home in the European study by Vineis et al. [32] up to 50.9% for males exposed to SHS in Indonesia.[56] The PAF from IHD varied between 1.4% in New Zealand and 13% in Chinese women; that from COPD varied between 4.1% in the GBD 2017 worldwide estimate and 12.2% in women from Taiwan; that from stroke varied between 1.3% in New Zealand and 5.3% in Korean men; the PAF from asthma varied between 4.6% in USA and 38% in Chinese women; finally, the PAF from breast cancer varied between 1.9% and 27% (Table 3). In children the PAF estimates ranged between 0.9% and 22.4% for otitis media in USA, 6.7%-43.6% for SIDS, 2.0%-31.9% for lower respiratory infections, 0.8%-35% for asthma and 2.1%-23.5% for low birth weight (Table 4).

In most cases, in order to estimate the PAF, the included papers used the same meta-analytical RR along with estimates of prevalence to SHS exposure that did not generally coincide with the definition of exposure to SHS in the studies included in such meta-analyses (Tables 3-4).

Exposure assessment: SHS exposure was mainly assessed through surveys (56 out of 72 studies) asking for self-reported SHS spousal exposure or exposure at home or workplace and, sometimes, in car or hospitality venues; in 5 studies SHS was cotinine-measured and in 8 it was modelled (Table 2).

In the surveys, exposure in the house or in the workplace was assessed by asking if participants were ever [57-63], daily [46,64] or at least once per week [38,43,64-67] exposed to SHS. Household exposure was also assessed by asking whether smoking was allowed in the house [48-49,68] or, in some cases, whether living with a smoker [33,44, 69-70], or, for children, whether parents smoked.[21,45]

In the 2017 GBD study, as well as in the Cao et al (2018) study,[71] SHS exposure within the household was considered to exist when non-smoking members of a household reported being exposed to SHS from a smoking member of the same household. Surveys on both household composition and tobacco habits were used to estimate the joint probability of being a non-smoker and living with a smoker.[72] Country, year, age and sex-specific estimates were then used in a spatiotemporal Gaussian process regression model to estimate exposure for every country.[18]

Assumptions: In computing the SHS attributable burden for adults, smokers are usually excluded from the analyses, since it is supposed that the large impact of active smoking may mask the more subtle health effects due to SHS, and the PAF is therefore applied to the total burden in non-smokers only.[28] The definition of non-smoker was not uniform among studies. In some cases only never smokers, i.e., lifelong non-smokers, were considered,[46,53,66-67,72-73] whereas in other cases both former and never smokers [32,54,61,74-75] were included among non-smokers. The latter group was in some cases defined also as everyone excluding current smokers, i.e. daily or occasional smokers or those declaring to be current smokers,[22,44,70, 52,76-77] or daily smokers.[25-26] Moreover, in some studies non-smokers were more formally defined as anyone whose total amount of smoked cigarettes was less than 100 during their lifetime,[78] or those who had stopped smoking or had not smoked 100 cigarettes in their lifetime.[60]

Data sources: In almost all the studies, the burden was estimated for countries or regions using official statistics. Two studies applied the CRA methodology to data (prevalence, costs) from survey samples ,[43-44] Shin et al. [45] estimated and applied the PAF in a cohort, Simons et al. [79] applied the PAF to the incidence extracted from a review of Canadian studies, whereas the Royal College of Physicians [23] used the incidence data estimated from a cohort of UK children. The GBD studies used estimates of mortality and DALYs from a model in order to provide figures for every country. A Bayesian meta-regression model (DisMod-MR) and a spatiotemporal Gaussian process regression model (ST-GPR) were used to pool raw data from different sources, control and adjust for bias in data, and incorporate other types of information such as country-level covariates.[18]

Outcomes: The SHS–attributable burden of disease was mainly studied in terms of mortality (55.6% of the studies), followed by morbidity (33.3%), DALYs (22.2%) and costs (18.1%). Some studies investigated also the burden from hospital admissions or years of potential life lost (Table 1).

Sensitivity analyses: In several studies, a univariate sensitivity analysis, changing various inputs and assumptions of the main analysis one at time, was performed in order to evaluate the robustness of the estimates. Some studies tested the lower and upper limits of the RRs or SHS prevalence estimates [13,27,40,44,54,57-59,64,49,69,52,76,80]. Waters et al. [37], who used a simplified CRA approach using PAF estimated for other populations, tested the PAF's ranges in a sensitivity analysis. Other sources of exposure to SHS were also explored, including exposure in cars, workplaces or during leisure time,[54,59,66-67] or by evaluating both self-reported and estimated with biomarkers.[39, 52,66-67]

Assumptions about the study population were also explored, by considering different populations at risk from SHS, i.e. never smokers only, never and former smokers, and never, former, and current smokers.[54,59,66-67]

In some sensitivity analyses health outcomes with less robust evidence were included.[54, 66-67] In one paper, also the effect of lag times from exposure to the onset of the disease was tested.[80]

In studies examining the impact of policies on the SHS attributable burden, sensitivity analyses were performed applying the bounds of the effect of policies published in the literature were carried out.[58]

Rehm et al. [81] carried out a sensitivity analysis on cost estimates. In studies using methods different from the CRA approach, other parameters where varied in a sensitivity analysis, i.e. the method for producing projections of cancer incidence rates in Carey et al. [41], or changing the assumptions regarding smoking initiation rates in Cavana et al. [40] or smoking prevalence.[76]

Discussion

Our review shows that many hazards due to SHS exposure are well known and morbidity and mortality attributable to SHS have been studied widely, yet there are many diseases and regions with no information. Beyond the GBD studies, the burden for EU countries was estimated in 29% of the selected studies. However, not all 28 EU Member States were covered, since estimates were available for Belgium, Denmark, Finland, France, Germany, Hungary, Italy, the Netherlands, Poland, Spain, Sweden and the UK, only, most of them only in adults, and not for all diseases, not including some with evidence of a causal relationship with SHS. Several studies were carried out also in Northern America (16 studies, 22%), Asian (18 studies, 25%), and Oceania countries (7 studies, 10%). Moreover, very little research has been done in Middle Eastern or African countries, with the burden from SHS estimated only in single studies carried out in Israel and Morocco.[70,82] A further assessment is therefore still needed.

The CRA methodology was the most widely used and most studies estimated the burden from diseases with a strong causal relationship with SHS exposure. For some diseases, however, despite the evidence of causation with SHS exposure, e.g. SIDS, LBW, and asthma, the burden was not widely evaluated and this could be due to the lack of data. The most frequently studied diseases were LC, IHD, COPD and stroke for adults, and LRI and OM for children. Moreover, recently also breast cancer and diabetes were included among the diseases with a strong evidence of causation with SHS exposure.[18]

Results showed a large heterogeneity in PAF and, as a consequence, in the SHS-attributable burden. This could be due to variations in prevalence across countries which have both different smoking habits and legislations in place (e.g. Europe versus China and other Asian countries). As an example, in Asian compared to EU countries, there is a greater gap in smoking prevalence by gender. In fact, men are more likely to smoke, whereas women are more likely to be exposed to SHS, and therefore SHS-attributable burden is heavier above all in Asian women. There is thus clearly a high burden in Asian countries which need for greater awareness and increased regulatory frameworks.

In less than 10% of studies there was an objective measurement of exposure to SHS, and self-reported exposure was the most widely used estimate, mainly assessed using surveys asking for household or workplace exposure or quantifying daily exposure. However, the definition of exposure was highly heterogeneous among studies. Exposure in cars or during leisure time was rarely explicitly considered, probably because the corresponding RR, necessary for the PAF estimate, were not simply available. Due to high costs in collecting measurements, i.e., cotinine in urine or saliva, future studies are unlikely to adopt objective measurements of SHS exposure. Self-reported SHS exposure is considered a low-cost approach to obtain a sufficiently accurate information on SHS exposure and several studies were carried out to validate the use of SHS exposure assessment questions with cotinine measurements, resulting in moderate to good correlations.[85-86] Recommended questions for studies assessing SHS have been defined, in order to meet reasonable standards for reliability and validity.[85]

Few studies in estimating the PAF, used the same assessment of SHS exposure as that used in the RR definition. In the studies on adults, Park at al.[57] and Rumrich et al.[62] used SHS exposure at home or workplace in both RR and prevalence. Vineis et al. [32] used the same survey for the RR and the prevalence estimate. The study by Pandeya et al.[83] generated a good approximation since it estimated the PAF by applying the RR estimated with exposure from spousal to a prevalence estimated from a survey asking if living with an ever smoker. In children, beyond the SHS assessment, in several studies also the age bands for the prevalence estimation was not the same as the one of the RR definition. The Royal college of Physicians [23] for OM used the same definition of exposure for RR and SHS prevalence

as children exposed to household smoking; Max et al. for SIDS and for LBW used the same definition of SHS prevalence as the one of RR, i.e. children exposed to maternal smoking during pregnancy.[49,52]
In some studies, a model was used to estimate the number of deaths or DALYs or the SHS exposure not available from official statistics or surveys.[25-27,71,73,84] This approach permits to estimate SHS exposure for all countries with lacking information, but has the drawback of producing estimates with a larger uncertainty.
In the burden of disease estimation many sources of uncertainty are used, such as RR and prevalence data, and assumptions, so sensitivity analyses should be used to test the impact of these sources of uncertainty and to obtain an estimation of the size of uncertainty itself.[11] In most of the studies the sensitivity analyses tested the impact of different assumptions in terms of RRs, SHS prevalence and exposure definition.[13,27,39-40,44,49, 52,57-59,54,64,66-67,69,76,80] The inclusion of current smokers and former smokers in the sensitivity analyses for acute coronary syndrome is noteworthy, given that smokers and former smokers experienced nearly as much a reduction as non-smokers in disease-specific admissions after the smoking ban in public places and workplaces.[84]
Limit of this study is that papers not in English language, proceedings of conferences, and grey literature were not included in the systematic review. However, our study has the strength that, to our knowledge, it is the first comprehensive review with systematic approach on the burden due to SHS exposure.

Conclusion

This systematic review highlighted that the burden of disease due to SHS exposure has been extensively studied worldwide, with a great variability in the burden of SHS-associated diseases across countries/regions, probably due to the different level of exposures, but many areas remain with insufficient evidence. Important, not all diseases with the strongest evidence of causation were assessed, and the CRA methodology has been applied to several but not all countries consistently. Furthermore, we identified relevant gaps in the quality of data, that should be addressed in future studies.

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Figure labels:

Figure 1 – PRISMA flow chart of publications (01/01/2007-31/12/2018) included in the systematic review.

Table 1 – Results of the literature review on studies from PubMed and SCOPUS on the burden of disease from SHS exposure, published between 01/01/2007 and 31/12/2018 in English language.

Study	Assessment method	Country	Disease	Method	Burden indicator
Adults					
Ádám et al., 2013 [58]	survey	Hungary	LC, IHD, COPD, stroke	CRA	deaths, DALYs
Becher et al., 2018 [64]	survey	Germany	LC	CRA with modified formula for the never smokers estimation	deaths
Cai et al., 2014 [43]	survey	China	COPD, asthma, IHD, stroke, hypertension, peptic ulcer	CRA	healthcare costs[§*]
Cao et al., 2018 [71]	model	France	LC	CRA	cases
Carey et al., 2017 [41]	survey	Australia	LC, larynx cancer, pharynx cancer	projections using future excess fraction (FEF)	deaths
Cavana et al., 2008 [40]	-	New Zeeland	Overall	simulated based approaches	deaths
Cui et al., 2016 [87]	survey	China (Hubei Province)	LC, IHD, stroke, LRI	CRA	deaths, DALYs
Feigin et al., 2016 [88]	model	Worldwide (188 countries)	Stroke	CRA	DALYs
Fischer et al., 2016 [38]	survey	Germany	IHD, stroke, COPD	simulated based approaches	cases
Gan et al., 2007 [65]	survey	China	LC, IHD	CRA	deaths, DALYs
García-Esquinas et al., 2018 [55]	survey	US	all cancers; LC; colon, rectum and anum; pancreas	mediation approaches for survival data (changes in mortality mediated by changes in SHS exposure)	deaths
Ginsberg et al., 2014 [82]	-	Israel	overall	naive: proportion of PAF from USA	deaths, hospitalization days, costs
GBD 2015 Risk Factors Collaborators, and others, 2016 [25]	model	Worldwide	LC, IHD, stroke, LRI	CRA	deaths, DALYs
GBD 2016 Risk Factors Collaborators, and others, 2017 [26]	model	Worldwide	LC, IHD, COPD, stroke, LRI, breast cancer, diabetes	CRA	deaths, DALYs
Gram et al., 2016 [22]	survey	Norway	breast cancer	cohort CRA	cases
Ha et al., 2011 [78]	survey	Korea	IHD	CRA	deaths
Hänninen et al., 2014 [80]	survey	EU (Belgium, Finland, France, Germany, Italy,	LC, IHD, asthma	CRA	DALY

		the Netherlands)			
Hauri et al., 2011 [42]	survey	Switzerland	LC, IHD, stroke, nasal sinus cancer, COPD, asthma	difference expected - observed number of hospital days, life table method for YLL	hospital days, YLL
Hedström et al., 2016 [46]	survey	Sweden	multiple sclerosis	excess proportion of cases	cases
Heidrich et al., 2007 [59]	survey	Germany	IHD	CRA	deaths, cases
Heo et al., 2015 [60]	survey	Korea	LC, IHD, asthma, COPD, stroke	CRA	deaths
Heuschmann et al., 2007 [61]	survey	Germany	stroke	CRA	deaths, cases
Hill et al., 2017 [34]	model	Mongolia	LC, IHD, stroke, COPD	CRA projections	deaths
Islami et al., 2017 [73]	survey	China	LC	CRA	deaths
Islami et al., 2018 [74]	cotinine-measured	US	LC	CRA	deaths, cases
Järvholm et al., 2013 [89]	survey	Sweden	LC, acute myocardial infarction	CRA	deaths
Lightwood et al., 2009 [39]	cotinine-measured	US	IHD	simulated based approaches	deaths, cases, healthcare costs§
Lim et al., 2012 [27]	model	worldwide	LC, IHD, stroke	CRA	deaths, DALYs
Liu et al., 2014 [75]	survey	US (Minnesota and the US)	LC, IHD, asthma	CRA, Lifetime excess risk	deaths, asthma initiation
López et al., 2007 [66]	survey	Spain	LC, IHD	CRA	deaths
López et al., 2016 [67]	survey	Spain	LC, IHD	CRA	deaths
Mason et al., 2016 [54]	survey	New Zealand	LC, IHD, stroke	CRA	deaths, DALYS
Mason et al., 2015 [53]	cotinine-measured	US (public housing in US)	LC, IHD, asthma	CRA	cases, deaths, costs
Max et al., 2012 [52]	survey & cotinine-measured	US	LC, IHD	CRA	deaths, YPLL, productivity
Max et al., 2015 [49]	survey	US	LC, IHD, breast cancer, asthma	CRA	YPLL, deaths, costs
Öberg et al., 2011 [13]	survey	worldwide	LC, IHD, asthma	CRA	deaths, DALYs
Pandeya et al., 2015 [83]	model	Australia	LC	CRA	cases
Park et al., 2014 [57]	survey	Korea	LC	CRA	deaths, cases
Parkin, 2011 [72]	model	UK	LC	CRA	cases
Permitasari et al., 2018 [56]	survey	Indonesia	LC	CRA	DALYs
Plescia et al., 2011 [36]	-	US (North Carolina)	LC, stroke	simplified CRA‡	treated prevalence, costs

Rehm et al., 2007 [81]	survey	Canada	cancer, cardiovascular disease	CRA	deaths, PLL, costs
Rumrich et al., 2015 [62]	survey	Finland	asthma	CRA	prevalent cases, YLD, DALY
Rushton et al., 2010 [90]	survey	UK	LC	CRA	cases
Rushton et al., 2008 [91]	survey	UK	LC	CRA	deaths
Rushton et al., 2012 [92]	survey	UK	LC	CRA	cases
Saywell et al., 2013 [35]	-	US (Indiana)	LC, IHD, stroke, nasal sinus cancer, breast cancer, cervical cancer, asthma	simplified CRA‡	loss-of-life and healthcare costs§
Schram-Bijkerk et al., 2013 [63]	survey	The Netherlands	LC, IHD, asthma	CRA	cases, DALYs
Shin et al., 2017 [45]	survey	New Zealand	atopic diseases	PAF in cohort	PAF
Sung et al., 2014 [76]	survey	Taiwan	LC, IHD, cerebrovascular disease,, asthma	CRA	deaths, YPLL, healthcare costs§
Tachfouti et al., 2016 [70]	survey	Morocco	LC, IHD	CRA	deaths
The Smoke Free Partnership, 2006 [24]	survey	EU (25 countries)	LC, IHD, stroke, COPD	CRA	deaths
Vineis et al., 2007 [32]	survey	EU (France, Italy, Denmark, Sweden, The Netherlands and Potsdam, Germany)	LC	survey CRA	cases
Wang et al., 2011 [93]	survey	China	LC	CRA	deaths, cases
Waters et al., 2009 [37]	-	US (Minnesota)	LC, stroke	simplified CRA‡	cases, treated prevalence, costs
Wilson et al., 2018 [69]	survey	Australia	cancer		deaths
Wu et al., 2010 [33]	survey	Taiwan (Kaohsiung City)	COPD, chronic bronchitis	survey CRA	
Xia et al., 2018 [94]	survey	China	LC	CRA	deaths
Yao et al., 2015 [44]	survey	China	asthma, breast cancer, IHD, LC, tuberculosis	CRA	healthcare costs§
Yao et al., 2018 [95]	survey	home	US	healthcare utilization	Poisson model
Zahra et al., 2016 [77]	survey	Korea	LC, IHD, stroke	CRA	DALYs
Zahra et al., 2018 [96]	survey	Korea	LC, IHD, stroke	CRA	DALYs
Children					
Behm et al., 2012 [20]	survey	US	SIDS	CRA	deaths
Cui et al., 2016 [87]	survey	China (Hubei Province)	LRI, OM	CRA	deaths, DALYs

Ginsberg et al., 2014 [82]	-	Israel	overall	naive: proportion of PAF from USA	deaths, hospitalization days, costs
GBD 2015 Risk Factors Collaborators, and others, 2016 [25]	model	Worldwide	LRI, OM	CRA	deaths, DALYs
GBD 2016 Risk Factors Collaborators, and others, 2017 [26]	model	Worldwide	LRI, OM	CRA	deaths, DALYs
Hänninen et al., 2014 [80]	survey	EU (Belgium, Finland, France, Germany, Italy, the Netherlands)	LRI, OM, asthma	CRA	DALY
Hill et al., 2017 [34]	model	Mongolia	LRI	CRA projections	deaths
Jarosińska et al., 2014 [97]	survey	Poland	LBW, SIDS, LRI, OM, asthma	CRA	cases, DALYs
Kabir et al., 2011 [48]	survey	US	learning disability, attention-deficit disorder, attention-deficit/hyperactivity disorder, conductor behavioral disorders	CRA	cases
Lim et al., 2012 [27]	model	worldwide	LRI, upper respiratory infections, OM	CRA	deaths, DALYs
Mason et al., 2016 [54]	survey	New Zealand	LBW, SIDS, LRI, OM, pneumonia, asthma	CRA	deaths, DALYs
Mason et al., 2015 [53]	cotinine-measured	US (public housing in US)	LBW, SIDS, LRI, respiratory syncytial virus bronchiolitis, OM, asthma	CRA	cases, deaths, costs
Max et al., 2014 [50]	survey & cotinine-measured	US (California)	attention deficit hyperactivity disorder	CRA	education and healthcare costs§
Max et al., 2012 [52]	survey & cotinine-measured	US	SIDS, LBW, respiratory distress syndrome, other respiratory conditions of newborns	CRA	deaths, YPLL, productivity
Max et al., 2015 [49]	survey	US	SIDS, LBW, LRI, OM, chronic respiratory symptoms, attention deficit hyperactivity disorder, asthma, respiratory distress syndrome, respiratory conditions of newborn	CRA	YPLL, deaths, costs
Öberg et al., 2011 [13]	survey	worldwide	LRI, OM, asthma	CRA	deaths, DALYs
Plescia et al., 2011 [36]	-	US (North Carolina)	LBW, LRI, OM, asthma and wheeze	simplified CRA‡	treated prevalence, costs
Reece et al., 2018 [47]	survey	30 low-income and middle- income countries	steelbirth	CRA	deaths
Royal College of Physicians, 2010 [23]	survey	UK	LRI, wheeze, OM, asthma, meningitis	CRA	deaths, cases
Rumrich et al., 2015 [62]	survey	Finland	asthma	CRA	prevalent cases, YLD, DALY
Saywell et al., 2013 [35]	-	US (Indiana)	SIDS, asthma, respiratory syncytial virus bronchiolitis, OM, LRI, burns,	simplified CRA‡	loss-of-life and healthcare costs§

			LBW, spontaneous abortion		
Schram-Bijkerk et al., 2013 [63]	survey	The Netherlands	SIDS, LRI, OM, asthma	CRA	cases, DALYs
Shin et al., 2017 [45]	survey	New Zeland	atopic diseases	PAF in cohort	PAF
Simons et al., 2011 [79]	survey	Canada	asthma	CRA	cases
Suzuki et al., 2009 [31]	survey	Vietnam (Khanh Hoa Province)	pneumonia	survey CRA	hospital admissions
Tabuchi et al., 2015 [21]	survey	Japan	asthma	CRA with estimated RR	hospitalization
Waters et al., 2009 [37]	-	US (Minnesota)	LRI, LBW, OM, asthma and wheeze	simplified CRA‡	cases, treated prevalence, costs
Yang et al., 2018 [51]	survey	Korea	problem behaviors	CRA	cases

LC: lung cancer; IHD: ischemic heart disease; LBW: low birth weight; SIDS: sudden infant death syndrome; LRI: lower respiratory tract infection; OM: otitis media; COPD: chronic obstructive pulmonary disease; CRA: comparative risk assessment; YPLL: years of potential life lost; DALY: disability adjusted life year; YLD: years lived with disability.

§ Healthcare costs: expenditures for inpatient hospital stays and outpatient visits.

* based on survey information on prevalence, costs, rural southwest in China.

‡ PAF form published studies.

Table 2 - Summary of the literature review on studies from PubMed and SCOPUS on the burden of disease from SHS exposure, published between 01/01/2007 and 31/12/2018 in English language.

Summary of measure	Number of studies (total N=72) N (%)
Outcomes	
mortality	40 (55.6)
morbidity	24 (33.3)
costs	13 (18.1)
DALYs	16 (22.2)
YPLL/hospitalization days/admissions	9 (12.5)
Population	
adults	44 (61.1)
children	9 (12.5)
both	19 (26.4)
Diseases	
Adults (total N=63)	
LC	48 (76.2)
IHD	34 (54.0)
COPD	11 (17.5)
stroke	21 (33.3)
asthma	15 (23.8)
breast cancer	7 (11.1)
diabetes	1 (1.6)
Children (total N=28)	
LRI	17 (60.7)
OM	15 (53.6)
SIDS	7 (25.0)
asthma	15 (53.6)
LBW	5 (17.9)
Exposure assessment	
survey questionnaire	54 (75.0)
cotinine-measurement	3 (4.2)

survey questionnaire & cotinine-measurement	2 (2.8)
model	8 (11.1)
not reported	5 (6.9)

DALY: disability adjusted life year; YPLL: years of potential life lost; LC: lung cancer; IHD: ischemic heart disease; COPD: chronic obstructive pulmonary disease; LRI: lower respiratory tract infection; OM: otitis media; SIDS: sudden infant death syndrome; LBW: low birth weigh

Table 3 – Proportion attributable fraction (PAF) estimates due to second-hand smoke (SHS) among adults never (or non-) smokers for selected diseases, sorted by disease, continent (world, North America, Oceania, Europe, Asia and Africa), year of publication and author name.

Study **Country**	**RR**				**SHS exposure**		
	Definition	**Endpoint***	**Source**	**RR^**	**Definition**	**Source**	
Lung cancer							
World							
Öberg et al., 2011 [13] World	NA	Inc/Mort	[2]	H: 1·21 Wo: 1·22	At home or at work		
GBD, 2016 [25] World	NA	NA	Integrated exposure response curves (IER) were used to estimate country-specific RR.	NA	SHS exposure in non-smokers. Exposure by a household member.	Various national and international surveys.	NA
GBD, 2017 [26] World	NA	NA	IER for PM2.5 air pollution were used to estimate country-specific RR.	NA	SHS exposure in non-smokers. Exposure by a household member.	NA	NA
North America							
Waters et al., 2009 [37] USA	NA	NA	[2]	NA	NA	National survey from Minnesota Department of Health	NA
Liu et al., 2014 [75] USA	NA	NA	[2]	1.22	SHS exposure in non-smokers. Serum cotinine level ≥0.05 ng/mL.	National Health and Nutrition Examination Survey (NHANES)[100]	Men: Women:
Mason et al., 2015 [53] USA	Exposure to SHS from the spouse	Inc	[2]	1.21	SHS exposure in non-smokers. Scenario 1: serum cotinine level ≥0.05 ng/mL. Scenario 2: serum cotinine level ≥0.015 ng/mL.	NHANES	Scenario 18-50 y: 51-64 y: 65-84 y: ≥85 y: Scenario 18-50 y: 51-64 y: 65-84 y: ≥85 y:
Max et al., 2015 [49] USA	Spousal ever smoking	Inc/Mort	[101]	1.29	SHS exposure in non-smokers. Living in a house where someone smokes inside at least 1 day per week.	California Health Interview Survey (CHIS)	5.0
Islami et al., 2018 [74] USA	Spousal ever smoking	Inc	[52,102]	1.29	SHS exposure in non-smokers. Serum cotinine level ≥0.05 ng/mL.	NHANES [103]	Men: Women:

Oceania							
Pandeya et al., 2015 [83] Australia	Spousal smoking	Inc/Mort	[104]	M: 1.37 W: 1.24	SHS exposure in never. Living with an ever smoker.	Data from population census [105]	Men: Women:
Mason et al., 2016 [54] New Zealand	Exposure to SHS from the spouse	Inc	[2]	1.21	SHS exposure in non-smokers. People smoking inside the respondent's home and/or in the car they travelled in.	New Zealand Health Surveys	5.4
Permitasari et al., 2018 [56] Indonesia	NA	NA	[105]	M: 2.28 W: 1.31	NA	NA	Men: Women:
Europe							
López et al., 2007 [66] Spain	Spousal smoking	Inc/Mort	[106]	HM: 1.34 HW: 1.24 Wo: 1.39 H&Wo: 1.39	SHS exposure in never smokers. At least one hour per week at home and/or at work.	Regional surveys in Spain [107-109]	At home Men 35-64 y: ≥65 y: Women 35-64 y: ≥65 y: At work c Men 35-64 y: Women 35-64 y: At home Men 35-64 y: Women 35-64 y:
Vineis et al., 2007 [32] Europe	Present exposure at home and/or woprkplace.	Inc/Mort	EPIC study [110-111]	H: 1.03 Wo: 1.65 H&Wo: 1.34	SHS exposure among non-smokers. Present exposure at home and/or woprkplace.	EPIC study [110-111]	Home: Work: Home an 58
Parkin, 2011 [72] UK	SHS exposure from spouse/at workplace	NA	[104]	M: 1.37 W: 1.24			Men: Women:
Järvholm et al., 2013 [89] Sweden	NA	NA	NA	1.25	SHS exposure in non-smoking women.	[112]	Women:
Schram-Bijkerk et al., 2013 [63] The Netherlands	NA	NA	[102]	1.21	SHS exposure in non-smokers. Daily exposure.	[113]	18-40 (m
López et al., 2016 [67] Spain	Spousal smoking; workplace exposure	Inc/Mort	[106]	HM: 1.34 HW: 1.24 Wo: 1.39 H&Wo: 1.39	SHS exposure in never smokers. One or more people usually smoking inside the home; a workpartner usually smoke	Representative national survey	At home Men 35-64 y: ≥65 y: Women 35-64 y: ≥65 y: At work c

					close enough to smell the SHS.		Men 35-64 y: Women 35-64 y: At home Men 35-64 y: Women 35-64 y:
Becher et al., 2018 [64] Germany	SHS exposure at home; spousal smoking	Inc/Mort	Pooled estimate from [2,114]	1.21	SHS exposure in never smokers. At any place, once per week or daily	Own estimate from available data [115]	Men: Women:
Cao et al. 2018 [71] France	never smokers who were exposed to tobacco smoke from a smoking partner	incidence	[104]	M: 1.37 W: 1.24	SHS exposure in never on-smokers. Exposure by a household member ^	National Surveys (INSEE on for marital status, Baromètre santé on for smoking status)	Men 30-34 y: 35-39 y: 40-44 y: 45-49 y: 50-54 y: 55-59 y: 60-64 y: 65-69 y: 70-74 y: 75-79 y: 80-84 y: ≥85y: Women 30-34 y: 35-39 y: 40-44 y: 45-49 y: 50-54 y: 55-59 y: 60-64 y: 65-69 y: 70-74y: 75-79 y: 80-84 y: ≥85 y:
Asia							
Wang et al., 2011 [93] China	Ever exposure from spouse or ever workplace exposure	Mort	[116]	H: 1.15 Wo: 1.79	SHS exposure in never smokers. At home and workplace.	National survey	Women Home: Workpla
Heo et al., 2015 [60] Korea	Spousal ever smoking	Inc	[101-102,104]	1.29	SHS exposure in non-smokers. KNHANES Household member smoking at home and/or smell of tobacco smoke at workplace. KCHS At least 1 hour of exposure at home and/or smell of smoke for at least 1 hour per day at workplace.	Korean National Health and Nutrition Examination Survey (KNHANES) 2005-2010 [117]; Korean Community Health Survey (KCHS) [118]	Men: Women:
Park et al.,	SHS exposure at	Inc/Mort	Meta-analysis	INC	SHS exposure in	KNHANES	At home

2014 [57] Korea	home/at workplace		conducted by the authors	HM: 1.00 HW: 1.32 WoM: 1.15 WoW: 1.37 MORT HM: 1.34 HW: 1.32 WoM: 1.15 WoW: 1.37	non-smokers. At home or workplace.	[117]	Men: Women: At workp Men: Women:
Sung et al., 2014 [76] Taiwan	Spousal ever smoking	Inc	[101]	1.29	SHS exposure in non-smokers. Exposure at home or at workplace during the past week.	National survey (Adult Smoking Behavior Survey)	Total: Men: Woman:
Yao et al., 2015 [44] China	NA	NA	[119]	1.13	Participants living with a current smoker.	National Rural Household Survey (NRHS)	Men: Women:
Zahra et al., 2016 [77] Korea	NA	NA	[120]	1.51	SHS exposure in non-smokers. At home or workplace.	KNHANES [117]	Men 25-29 y: 30-34 y: 35-39 y: 40-44 y: 45-49 y: 50-54 y: 55-59 y: 60-64 y: 65-69 y: 70-74 y: 75-79 y: ≥80 y: Women 25-29 y: 30-34 y: 35-39 y: 40-44 y: 45-49 y: 50-54 y: 55-59 y: 60-64 y: 65-69 y: 70-74 y: 75-79 y: ≥80 y:
Islami et al., 2017 [73] China	NA	NA	[121]	M: 1.58 W: 1.34	SHS exposure in never smokers. At least weekly either at home or at work.	Global Adult Tobacco Survey [100]	NA

Zahra and Park, 2018 [96] Korea	NA	NA	[120]	1.51	SHS exposure in nonsmokers at work or home	KCHS[118]	6-35
Xia et al., 2018 [94] China	NA	NA	NA	NA	SHS exposure in non-smokers for at least 15 min on 1 day per week	2002 Chinese National Nutrition and Health Survey (NNHS)	Men: Women:
Africa							
Tachfouti et al., 2016 [70] Morocco	Spousal smoking	Inc/Mort	[106]	HM: 1.34 HW: 1.24 Wo: 1.39 H&Wo: 1.39	SHS exposure in never smokers. At home or at workplace.	National survey [122]	At home Men 35-64 y: ≥65 y: Women 35-64 y: ≥65 y: At work o Men 35-64 y: Women 35-64 y: At home Men 35-64 y: Women 35-64 y:
Ischemic heart disease (IHD)							
World							
Öberg et al., 2011 [13] World		Inc	[2]	1.27	SHS exposure in non-smokers. Exposure at home or at work.		
GBD, 2016 [25] World	NA	NA	IER curves were used to estimate country-specific RRs.	NA	SHS exposure in non-smokers. Exposure by a household member.	Various national and international surveys.	NA
GBD, 2017 [26] World	NA	NA	IER curves for PM2.5 air pollution were used to estimate country-specific RRs.	NA	SHS exposure in non-smokers. Exposure by a household member.	NA	NA
North America							
Liu et al., 2014 [75] USA	NA	NA	[2]	1.27	SHS exposure in non-smokers. Serum cotinine level ≥0.05 ng/mL.	NHANES [100]	Men: Women:
Mason et al., 2015 [53] USA	SHS exposure at home by a spouse or cohabitant or at workplace	Inc/Mort	[2,13]	1.27	SHS exposure in non-smokers. Scenario 1: serum cotinine level ≥0.05 ng/mL. Scenario 2: serum cotinine	NHANES	Scenario 51-64 y: 65-84 y: ≥85 y: Scenario 51-64 y: 65-84 y: ≥85 y:

					level ≥0.015 ng/mL.		
Max et al., 2015 [49] USA	NA	Inc	[2]	1.50	SHS exposure in non-smokers. Living in a house where someone smokes inside at least 1 day per week.	CHIS	5.01
Oceania							
Mason et al., 2016 [54] New Zealand	SHS exposure at home by a spouse or cohabitant or at workplace	Inc/Mort	[2]	1.27	SHS exposure in non-smokers. People smoking inside the respondent's home and/or in the car they travelled in.	New Zealand Health Surveys	5.4
Europe							
López et al., 2007 [66] Spain	NA	NA	[123-124]	H: 1.30 Wo: 1.21 H&Wo: 1.30	SHS exposure in never smokers. At least one hour per week at home and/or at work.	Regional surveys in Spain [107-109]	At home Men 35-64 y: ≥65 y: Women 35-64 y: ≥65 y: At work Men 35-64 y: Women 35-64 y: At home Men 35-64 y: Women 35-64 y:
Schram-Bijkerk et al., 2013 [63] The Netherlands	SHS exposure at home by a spouse or cohabitant or at workplace	Inc/Mort	[2]	1.27	SHS exposure in non-smokers. Daily exposure.	[113]	18-40 (m
Fischer et al., 2016 [38] Germany	Mixed definitions (regular SHS exposure; e.g., spousal smoking or exposure to 20 cigs/day)	Inc/Mort	[125]	M: 1.06 W: 1.50	SHS exposure likely in non-smokers. At any place, once per week or daily	Own estimate from available data [126]	Men 18-29 y: 30-39 y: 40-49 y: 50-59 y: 60-69 y: ≥70 y: Women 18-29 y: 30-39 y: 40-49 y: 50-59 y: 60-69 y: ≥70 y:
López et al., 2016 [67] Spain	NA	NA	[123-124]	H: 1.30 Wo: 1.21 H&Wo: 1.30	SHS exposure in never smokers. One or more people usually smoking inside the home; a workpartner usually smoke	Representative national survey	At home Men 35-64 y: ≥65 y: Women 35-64 y: ≥65 y: At work

					close enough to smell the SHS.		Men 35-64 y: Women 35-64 y: At home Men 35-64 y: Women 35-64 y:
Asia							
Ha et al., 2011 [78] Korea	SHS exposure at workplace	Inc/Mort	Meta-analysis conducted by the authors	M: 1.19 W: 1.22	SHS exposure in never smokers. At work for more than ¼ of working time (2 hours a day)	National survey on working conditions [127]	Men: Women:
Heo et al., 2015 [60] Korea	Mixed definitions (e.g., spousal smoking or SHS exposure at home or workplace)	Inc/Mort	[128]	M: 1.22 W: 1.24	SHS exposure in non-smokers. KNHANES Household member smoking at home and/or smell of tobacco smoke at workplace. KCHS At least 1 hour of exposure at home and/or smell of smoke for at least 1 hour per day at workplace.	KNHANES 2005, 2007-2010 [117]; KCHS[118]	Men Total: 20-29 y: 30-39 y: 40-49 y: 50-59 y: 60-69 y: 70+ y: Women Total: 20-29 y: 30-39 y: 40-49 y: 50-59 y: 60-69 y: 70+ y:
Sung et al., 2014 [76] Taiwan	NA	Mort	[101]	1.23	SHS exposure in non-smokers. Exposure at home or at workplace during the past week.	National survey (Adult Smoking Behavior Survey)	Total: Men: Woman:
Yao et al., 2015 [44] China	NA	NA	[128-129]	M: 1.24 W: 1.22	Participants living with a current smoker.	National Rural Household Survey (NRHS)	Men: Women:
Zahra et al., 2016 [77] Korea	NA	NA	[120]	20-29 y: 1.47 30-34 y: 1.43 35-39 y: 1.40 40-44 y: 1.37 45-49 y: 1.34 50-54 y: 1.31 55-59 y: 1.28 60-64 y: 1.25 65-69 y: 1.22 70-74 y: 1.19 75-79 y: 1.17 ≥80 y: 1.14	SHS exposure in non-smokers. At home or workplace.	KNHANES [117]	Men 25-29 y: 30-34 y: 35-39 y: 40-44 y: 45-49 y: 50-54 y: 55-59 y: 60-64 y: 65-69 y: 70-74 y: 75-79 y: ≥80 y: Women 25-29 y: 30-34 y: 35-39 y: 40-44 y: 45-49 y: 50-54 y:

							55-59 y: 60-64 y: 65-69 y: 70-74 y: 75-79 y: ≥80 y:
Zahra and Park, 2018 [96] Korea	NA	NA	[120]	25-29 y: 1.47 30-34 y: 1.43 35-39 y: 1.40 40-44 y: 1.37 45–49 y: 1.34 50–54 y: 1.31 55–59 y: 1.28 60–64 y: 1.25 65–69 y: 1.219 70–74 y: 1.191 75–79 y: 1.165 80+ y: 1.139	SHS exposure in nonsmokers at work or home	KCHS[118]	6-35
Africa							
Tachfouti et al., 2016 [70] Morocco	NA	NA	[123]	H: 1.30 Wo: 1.21 H&Wo: 1.30	SHS exposure in never smokers. At home or at workplace.	National survey [122]	At home Men 35-64 y: ≥65 y: Women 35-64 y: ≥65 y: At work o Men 35-64 y: Women 35-64 y: At home Men 35-64 y: Women 35-64 y:
COPD							
World							
GBD, 2017 [26] World	NA	NA	IER curves for PM2.5 air pollution were used to estimate country-specific RRs.	NA	SHS exposure in non-smokers. Exposure by a household member.	NA	NA
Europe							
Fischer et al., 2016 [38] Germany	Mixed definitions (regular SHS exposure; e.g., spousal smoking or exposure to 20 cigs/day)	Inc/Mort	[125]	M: 1.50 W: 2.17	SHS exposure likely in non-smokers. At any place, once per week or daily	Own estimate from available data [126]	Men 18-29 y: 30-39 y: 40-49 y: 50-59 y: 60-69 y: ≥70 y: Women 18-29 y: 30-39 y: 40-49 y: 50-59 y: 60-69 y: ≥70 y:
Asia							

Heo et al., 2015 [60] Korea	Lifetime home SHS exposure ≥42 years	Inc	[130]	1.55	SHS exposure in non-smokers. KNHANES Household member smoking at home and/or smell of tobacco smoke at workplace. KCHS At least 1 hour of exposure at home and/or smell of smoke for at least 1 hour per day at workplace.	KNHANES 2005, 2007-2010 [117]; KCHS [118]	Men: Women:
Sung et al., 2014 [76] Taiwan	NA	Inc	[101]	1.55	SHS exposure in non-smokers. Exposure at home or at workplace during the past week.	National survey (Adult Smoking Behavior Survey)	Total: Men: Woman:
Stroke							
World							
Feigin et al., 2016 [88] World			Meta-analysis of published studies.				
GBD, 2016 [25] World	NA	NA	IER curves were used to estimate country-specific RRs.	NA	SHS exposure in non-smokers. Exposure by a household member.	Various national and international surveys.	NA
GBD, 2017 [26] World	NA	NA	IER curves for PM2.5 air pollution were used to estimate country-specific RRs.	NA	SHS exposure in non-smokers. Exposure by a household member.	NA	NA
Oceania							
Mason et al., 2016 [54] New Zealand	Spousal smoking or SHS exposure at home or at workplace	Inc/Mort	[131]	1.25	SHS exposure in non-smokers. People smoking inside the respondent's home and/or in the car they travelled in.	New Zealand Health Surveys	5.4
Europe							
Heuschmann et al., 2007 [61] Germany	NA	Inc/Mort	Pooled estimate from [132-133]	1.18	SHS exposure likely in non-smokers.	[134]	Men: Women:

Fischer et al., 2016 [38] Germany	Mixed definitions (regular SHS exposure; e.g., spousal smoking or exposure to 20 cigs/day)	Inc/Mort	[125]	M: 1.40 W: 1.43	SHS exposure likely in non-smokers. At any place, once per week or daily	Own estimate from available data [126]	Men 18-29 y: 30-39 y: 40-49 y: 50-59 y: 60-69 y: ≥70 y: Women 18-29 y: 30-39 y: 40-49 y: 50-59 y: 60-69 y: ≥70 y:
Asia							
Heo et al., 2015 [60] Korea	Spousal smoking or SHS exposure at home or at workplace	Inc/Mort	[131]	1.25	SHS exposure in non-smokers. KNHANES Household member smoking at home and/or smell of tobacco smoke at workplace. KCHS At least 1 hour of exposure at home and/or smell of smoke for at least 1 hour per day at workplace.	KNHANES 2005, 2007-2010 [117]; KCHS[118]	Men: Women:
Zahra et al., 2016 [77] Korea	NA	NA	[120]	20-29 y: 1.59 30-34 y: 1.54 35-39 y: 1.49 40-44 y: 1.45 45-49 y: 1.41 50-54 y: 1.36 55-59 y: 1.32 60-64 y: 1.28 65-69 y: 1.25 70-74 y: 1.21 75-79 y: 1.18 ≥80 y: 1.15	SHS exposure in non-smokers. At home or workplace.	KNHANES [117]	Men 25-29 y: 30-34 y: 35-39 y: 40-44 y: 45-49 y: 50-54 y: 55-59 y: 60-64 y: 65-69 y: 70-74 y: 75-79 y: ≥80 y: Women 25-29 y: 30-34 y: 35-39 y: 40-44 y: 45-49 y: 50-54 y: 55-59 y: 60-64 y: 65-69 y: 70-74 y: 75-79 y: ≥80 y:

Zahra and Park, 2018 [96] Korea	NA	NA	[120]	25–29 y: 1.59 30–34 y: 1.541 35–39 y: 1.493 40–44 y: 1.448 45–49 y: 1.405 50–54 y: 1.362 55–59 y: 1.322 60–64 y: 1.283 65–69 y: 1.246 70–74 y: 1.211 75–79 y: 1.177 ≥80 y: 1.145	SHS exposure in nonsmokers at work or home	KCHS [118]	6-35
Asthma							
World							
Oberg et al., 2011 [13] World	SHS exposure at home and workplace in the previous 12 months	Inc	[135]	1.97	At home and/or at work.		
North America							
Liu et al., 2014 [75] USA	SHS exposure at workplace in the previous 12 months	Inc	[135]	2.16	Percentage of servers not covered by smoke-free restaurants and/or bars.	[136]	Restaurar Bars:
Mason et al., 2015 [53] USA	SHS exposure at home and workplace in the previous 12 months	Inc	[135]	1.97	SHS exposure in non-smokers. Scenario 1: serum cotinine level ≥0.05 ng/mL. Scenario 2: serum cotinine level ≥0.015 ng/mL.	NHANES	Scenario 18-50 y: 51-64 y: 65-84 y: ≥85 y: Scenario 18-50 y: 51-64 y: 65-84 y: ≥85 y:
Max et al., 2015 [49] USA	NA	Inc	[135]	1.97	SHS exposure in non-smokers. Living in a house where someone smokes inside at least 1 day per week.	CHIS	5.01
Europe							
Schram-Bijekerk et al., 2013 [63] The Netherlands	SHS exposure at home and workplace in the previous 12 months	Inc	[135]	1.97	SHS exposure in non-smokers. Daily exposure.	[113]	18-40 (m
Rumrich et al., 2015 [62] Finland	SHS exposure at home and workplace in the previous 12 months	Inc	[135]	1.97	Exposure to SHS in never smokers. Exposure during past 12 months at home or at workplace.	[135]	10
Asia							
Heo et al., 2015 [60] Korea	SHS exposure at home and workplace in the	Inc	[135]	1.97	SHS exposure in non-smokers. KNHANES	KNHANES 2005, 2007-2010 [117];	Men: Women:

	previous 12 months				Household member smoking at home and/or smell of tobacco smoke at workplace. KCHS At least 1 hour of exposure at home and/or smell of smoke for at least 1 hour per day at workplace.	KCHS[118]	
Sung et al., 2014 [76] Taiwan	SHS exposure at home and workplace in the previous 12 months	Inc	[135]	1.97	SHS exposure in non-smokers. Exposure at home or at workplace during the past week.	National survey (Adult Smoking Behavior Survey)	Total: Men: Woman:
Yao et al., 2015 [61] China	SHS exposure at home and workplace in the previous 12 months	Inc	[135]	1.97	Participants living with a current smoker.	National Rural Household Survey (NRHS)	Men: Women:
Breast cancer							
World							
GBD, 2017 [26] World	NA	NA	From published meta-analyses.	1.07	SHS exposure in non-smokers. Exposure by a household member.	NA	NA
North America							
Max et al., 2015 [49] USA	NA	Inc	[101]	1.68	SHS exposure in non-smokers. Living in a house where someone smokes inside at least 1 day per week.	CHIS	3.1
Europe							
Gram et al., 2016 [22] Norway	NA	Incidence	Original	1.18	SHS exposure in never smokers. NA	Original	64.8
Asia							
Yao et al., 2015 [44] China	NA	NA	[138]	1.60	Participants living with a current smoker.	National Rural Household Survey (NRHS)	62.2
Diabetes							
World							
GBD, 2017 [26] World	NA	NA	From published meta-analyses.	1.34	SHS exposure in non-smokers. Exposure by a household member.	NA	NA

* Inc: Incidence; Mort: mortality; DALY: DALYs; NA: not available
^ M: men; W: women; H: home; Wo: work

Table 4 – Proportion attributable fraction (PAF) estimates due to second-hand smoke (SHS) among children for selected diseases, sorted by disease, continent (world, North America, Oceania, Europe, Asia and Africa), year of publication and author name.

RR				SHS exposure			PAF (%)
Definition	**Endpoint***	**Source**	**RR**	**Definition**	**Source**	**%**	
Children aged <3 years with serum cotinine concentration greater than or equal to 2.5 ng/mL (otitis media with effusion)	Inc	[101,139]	1.38	Children having one or both parents who smoke or being exposed to tobacco smoke or to a person who smokes indoors	Various national and multinational Surveys (mainly Global Youth Tobacco Smoking (GYTS):13-15 years)	NA	1.7 (DALYs)
Children exposed to household smoking (middle ear infection and surgery for middle ear disease)	Inc	[140]	1.37	Children aged < 5 years exposed to any tobacco smoke inside the home	Various national and international surveys	NA	5.4
Children exposed to household smoking (middle ear infection and surgery for middle ear disease)	Inc	[140]	1.37	Children aged <14 years exposed to tobacco smoke by a household member, (household composition as proxy for exposure/ assumption that all persons living with a smoker are exposed to smoke)	Various national and international surveys	NA	3.5
			Not used			Not used	14.0
Children aged < 4 years exposed to SHS fro either parent (middle ear effusion)	Inc	[2]	1.33	Cotinine level greater than 0.05 / 0.015 ng/mL measured in children aged 3-11 (assumed also for children aged < 3 years)	National NHANES	0.05 ng/mL: 61 0.015 ng/mL: 85	0.05 ng/mL: 17.2 0.015 ng/mL: 22.4
Children aged <3 years with serum cotinine concentration greater than or equal to 2.5 ng/mL (otitis media with effusion)	Inc	[101,139]	1.38	Children aged <3 years who live in households that allow smoking and where smoking is reported to occur some days or every day	CHIS to children (<12 years) and adolescents (12-17 years)	2.44 (1.64,3.25)	0.9
Children exposed to household smoking (middle ear	Inc	[140]	1.32	Children exposed to SHS in home and car: surveyed adults declaring that anyone smokes inside their home and/or in the	New Zealand Health Surveys	8.7	2.7

RR				SHS exposure			PAF (%)
Definition	Endpoint*	Source	RR	Definition	Source	%	
infection)				car their child travelled in			
Children exposed to household smoking (middle ear disease)	Inc	Meta-analysis in [23]	1.35	Children aged 4-15 years not living in a smoke-free home	Health Survey for England (HSE)	22	7.1
Children aged <3 years with serum cotinine concentration greater than or equal to 2.5 ng/mL (otitis media with effusion)	Inc	[101,139]	1.38	Children aged 0-4 years being exposed to tobacco smoke at home	[112]	28	9.6 (4.0,16.8)
Children aged <3 years with serum cotinine concentration greater than or equal to 2.5 ng/mL (otitis media with effusion)	Inc	[101,139]	1.38	Children exposed to any tobacco smoke: Scenario 1: surveyed adults admitted to smoking/having smoked in the presence of their children Scenario 2: children aged 13-15 years exposed in households and public place	Scenario 1: national survey Scenario 2: GYTS	Scenario 1: 48 Scenario 2: 60	Scenario 1: 15.4 Scenario 2: 18.6
Children aged <1 year exposed to postnatal maternal smoking	Mort	[23]	3.15	Households with at least one infant and a rule disallowing smoking anywhere in the home	Tobacco use Supplement to the Current Population Survey	1995: 35.9 2006: 11.7	1995: 43.6 2006: 20.1
Children exposed to maternal smoking during pregnancy	Mort	[141]	2.29	Infant exposure to maternal smoking in utero	Data from birth certificates [142]	13.2	14.6
Children aged <1 year exposed to postnatal maternal smoking	Mort	[143]	1.94	Cotinine level >0.05 / 0.015 ng/mL measured in children aged 3-11 (assumed for children aged < 3 years)	NHANES	0.05 ng/mL: 48 0.015 ng/mL: 81	0.05 ng/mL: 31.1 0.015 ng/mL: 43.2
Children exposed to maternal smoking during pregnancy	Mort	[141]	2.29	Infant exposure to maternal smoking in utero	Maternal and Infant Health Assessment survey	5.6	6.7
Children aged <1 year exposed to	Mort	[143]	1.94	Mothers with newborns smoking at two weeks after birth	Nationwide Well Child/Tamarik	13	10.9

RR				SHS exposure			PAF (%)
Definition	Endpoint*	Source	RR	Definition	Source	%	
postnatal maternal smoking					iOra health checks programme for infants		
Children aged <1 year exposed to postnatal maternal smoking	Mort	[143]	1.94	Smoking women aged 20–39 years	Global Adult Tobacco Smoking (GATS)	26	19.6
Children aged <1 year exposed to household exposure	Mort	Meta-analysis in [23]	2.31	Children aged 4-15 years not living in a smoke-free home	Health Survey for England (HSE)	22	22.4
Children aged <1 year exposed to postnatal maternal smoking	Mort	[143]	1.94	Children aged 0-4 years being exposed to tobacco smoke at home	[113]	28	20.8 (9.9,34.0)
Children aged 0-3 years exposed to SHS from either parent	Inc	[2]	1.55	Children having one or both parents who smoke or being exposed to tobacco smoke or to a person who smokes indoors	Various national and multinational surveys (mainly GYTS: 13-15 years)	NA	6.3 (DALYs)
NA	NA	IER curves were used to estimate country-specific RRs.	NA	Children aged < 5 years exposed to any tobacco smoke inside the home	Various national and international surveys	NA	6.7
NA	NA	IER curves were used to estimate country-specific RRs.	NA	People of all ages years exposed to tobacco smoke by a household member, (household composition as proxy for exposure/ assumption that all persons living with a smoker are exposed to smoke)	Various national and international surveys	NA	5.8
Children aged 0-3 years exposed to SHS from either parent	Inc	[2]	1.55	Cotinine level >0.05 / 0.015 ng/mL measured in children aged 3-11 (assumed for children aged < 3 years)	NHANES	0.05 ng/mL: 61 0.015 ng/mL: 85	0.05 ng/mL: 25.1 0.015 ng/mL: 31.9
Children aged 0-2 years exposed to parental smoking	Inc	[101]	1.75	Children aged <2 years who live in households that allow smoking and where smoking is reported to occur some days or every day	CHIS to children (<12 years) and adolescents (12-17 years)	2.70 (1.77,3.62)	2.0

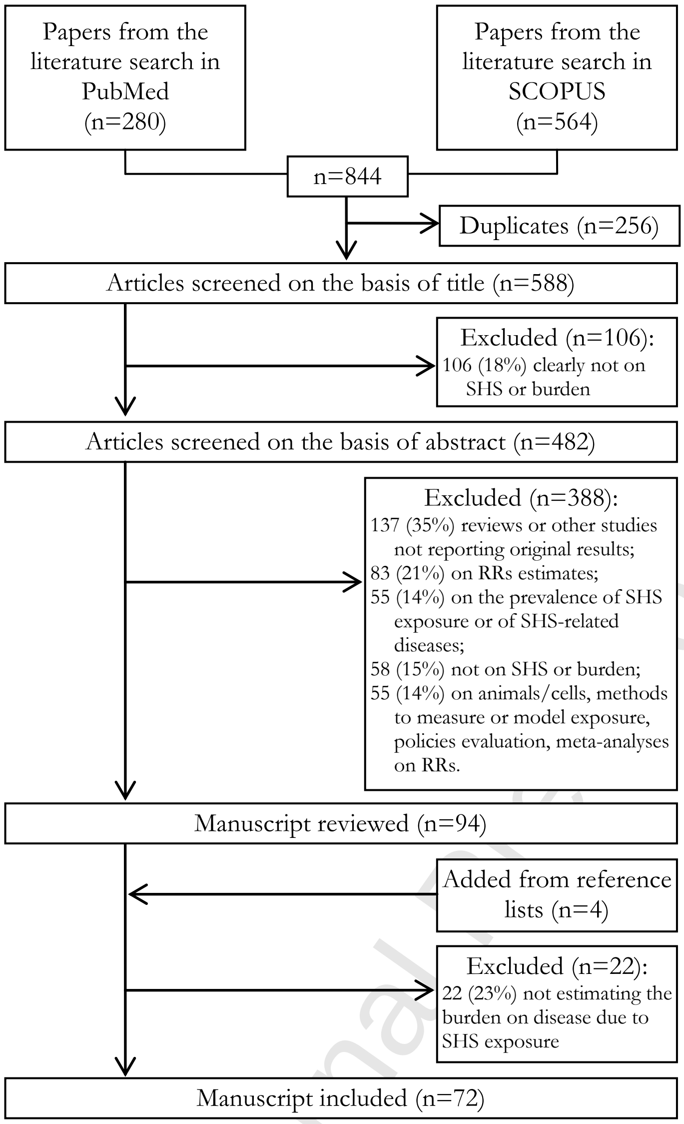
RR				SHS exposure			PAF (%)
Definition	Endpoint*	Source	RR	Definition	Source	%	
Children aged 0-2 years exposed to SHS by any household member	NA	[140]	1.54	Children exposed to SHS in home and car: surveyed adults declaring that anyone smokes inside their home and/or in the car their child travelled in	New Zealand Health Surveys	8.7	4.5
Children exposed to household smoking	Inc	Meta-analysis in [23]	1.54	Children aged 4-15 years not living in a smoke-free home	Health Survey for England (HSE)	22	10.6
Children aged 0-2 years exposed to SHS from either parent	NA	[2]	1.55	Children aged 0-4 years being exposed to tobacco smoke at home	[113]	28	13.3 (7.8,19.9)
Children aged 0-3 years exposed to SHS from either parent	Inc	[2]	1.55	Children exposed to any tobacco smoke: Scenario 1: surveyed adults admitted to smoking/having smoked in the presence of their children Scenario 2: children aged 13-15 years exposed in households and public place	Scenario 1: national survey Scenario 2: GYTS	Scenario 1: 48 Scenario 2: 60 exposed in households/public place	Scenario 1: 20.9 Scenario 2: 24.8
Children aged 0-14 years exposed to SHS from either parent	Inc	[101]	1.32	Children having one or both parents who smoke or being exposed to tobacco smoke or to a person who smokes indoor	Various national and multinational surveys (mainly GYTS:13-15 years)	NA	1.6 (DALYs)
		[2]	1.23	NA	Minnesota Department of Health	not known	35
Children aged 0-5 years exposed to maternal smoking during pregnancy	Inc	[144-145]	1.40	NA	Websites of government agencies and published studies	9.0	3.5
Children aged 1-17 years exposed to SHS by parental report or by cotinine measurement	Inc	[146]	1.32	- Children aged 1-11 years: cotinine level >0.05 / 0.015 ng/mL (measured in children aged 3-11 assumed also for children aged < 3 years) - Children 12-19 years: reporting no smoking in the previous 30 days, no use of any nicotine-	NHANES	0.05 ng/mL: 61 0.015ng/mL: 85	0.05 ng/mL: 16.3 0.015ng/mL: 21.4

RR				SHS exposure			PAF (%)
Definition	Endpoint*	Source	RR	Definition	Source	%	
				containing product within the previous 5 days and a serum cotinine level > 0.05 /0.015 ng/mL.			
Children aged 0-14 years exposed to SHS from either parent	Inc	[101]	1.32	Children who live in households that allow smoking and where smoking is reported to occur some days or every day	CHIS to children (<12 years) and adolescents (12-17 years)	0-11 years: 2.63 (2.24,3.02) 12-17 years: 3.81 (3.21,4.42)	0-11 years: 0.8 12-17 years: 1.2
Children aged 1-17 years exposed to SHS by parental report or by cotinine measurement	Inc	[146]	1.32	Children exposed to SHS in home and car: surveyed adults declaring that anyone smokes inside their home and/or in the car their child travelled in	New Zealand Health Surveys	8.7	2.7
Children aged 3-4 and 5-16 years exposed to household smoking	Inc	Meta-analysis in [23]	3-4 years: 1.21 5-16 years: 1.50	Children aged 4-15 years not living in a smoke-free home	Health Survey for England (HSE)	22	3-4 years: 4.4 5-16 years: 9.9
Children aged 0-14 years exposed to SHS from either parent	Inc	[101]	1.32	Children aged 0-4 years being exposed to tobacco smoke at home	[113]	28	8.2 (4.6, 12.9)
Children aged 0-14 years exposed to SHS from either parent	Inc	[101]	1.32	Children exposed to any tobacco smoke: Scenario 1: surveyed adults admitted to smoking/having smoked in the presence of their children Scenario 2: children aged 13-15 years exposed in households and public place	Scenario 1: national survey Scenario 2: GYTS	Scenario 1: 48 Scenario 2: 60	Scenario 1: 13.3 Scenario 2: 16.1
Children aged 0-14 years exposed to SHS from either parent	Inc	[101]	1.32	Children aged 15 years and over regularly exposed to SHS or having at least one smoking parent	[147]	4	1.3
Children aged 0-8 years exposed to parental indoor smoking	Inc	Estimated in nationally a representativ e population-based birth cohort	0-2.5 years: 1.54 2.5–4.5 years: 1.43 4.5–8 years: 1.72	Children aged 0-5 years exposed to parental indoor smoking	Estimated in nationally a representative population-based birth cohort	10.9	0-2.5 years: 5.6 2.5-4.5 years: 4.5 4.5-8 years: 7.3

RR				SHS exposure			PAF (%)
Definition	Endpoint*	Source	RR	Definition	Source	%	
Children exposed to maternal smoking during pregnancy	Mort	[141]	1.83	Infant exposure to maternal smoking In utero	Data from birth certificates [142]	13.2	9.9
Children aged 0 years with non-smoking mother ever exposed to SHS at work or at home	Inc	[148]	1.38	Non-smoking women with cotinine level >0.05 / 0.015 ng/mL	NHANES	0.05 ng/mL: 48 0.015 ng/mL: 81	0.05 ng/mL: 15.4 0.015 ng/mL: 23.5
Children aged 0 years with non-smoking mother ever exposed to SHS at work or at home	Inc	[148]	1.38	Smoking pregnant women	Maternal and Infant Health Assessment survey	5.6 (4.90,6.40)	2.1
Children aged 0 years with non-smoking mother ever exposed to SHS at work or at home	Inc	[148]	1.38	Non-smoking pregnant women who had a partner who smoked	Antenatal interview in the "Growing Up in New Zealand" longitudinal study	7.0 (6.3,7.6)	2.6
Children aged 0 years with non-smoking mother ever exposed to SHS at work or at home	Inc	[148]	1.38	Adults admitting to smoke in the presence of pregnant women and non-smoking women aged 20-45 years exposed to SHS at home	[149]	27	9.3

* Inc: Incidence; Mort: mortality; DALY: DALYs; NA: not available

Figure 1 – PRISMA flow chart of publications (01/01/2007-31/12/2018) included in the systematic review.



Highlights

- Burden of disease from second-hand smoke was not studied for all worldwide areas
- Not all diseases with the strongest evidence of causation were assessed
- Burden is estimated applying risks and exposures with not consistent definitions
- The population attributable fractions are largely variable among studies