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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 attributable 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, and published from 2007 to 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, low birth weight and asthma, 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]

Smoke-free policies have been expanding worldwide since the World Health Organization (WHO) encouraged in 2007 countries to follow Article 8 of the Framework Convention on Tobacco Control (FCTC) to protect people from SHS.[3] Legislation has been widely implemented in indoor public places, workplaces, and public transportation. [4] Since the implementation of indoor smoke-free environments, several studies have demonstrated important reductions of SHS exposure, including an 80–90% decrease in settings with previously high-exposure levels, such as workplaces and hospitality venues like bars and restaurants. [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 male and female non-smokers 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 systematically reviewed the published literature of studies estimating 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; http://www.scopus.com/).

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. The decision to start from 2007 was arbitrary but informed, based on the concept of reviewing 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 recommendations, expert statements, reviews and other non-original papers, 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 aimed to assess 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.

Additionally, we thoroughly looked through the reference lists of the articles for missed papers and we added 4 papers,[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.[27] 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 disease, age, gender, or population group is then multiplied by the number of deaths, cases, DALYs 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] steelbirth(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 the 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 use the same meta-analytical RR along with estimates of prevalence to SHS exposure that doesn't 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, because it is suspected 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]

Some sensitivity analyses also examined the impact of including health outcomes with less robust evidence.[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 of the SHS attributable burden, sensitivity analyses on the estimate of the policy effect on exposure using the lowest and highest values 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, Italy, Hungary, Poland, Spain, Sweden, the Netherlands 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 a study carried out Israel and a study in Morocco among the selected studies.[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 the variation in prevalence across countries which have both different smoking habits and legislation in place (e.g. Europe versus China and other Asian countries). As an example, in Asian countries, 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 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 measures 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 obtaining from moderate to good correlations.[85-86] Recommended questions for studies assessing SHS were defined that 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 of 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.
Estimates of attributable burden have many sources of uncertainty, including data inputs (such as RR and prevalence estimates) 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 admissions for such disease due to 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.

References

1. IARC. Tobacco smoke and involuntary smoking. Handbooks on tobacco control. Lyon, International Agency for Research on Cancer 2004.
2. US Department of Health and Human Services. The health consequences of involuntary exposure to tobacco smoke: a report of the Surgeon General. Atlanta, GA: US Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2006.
3. WHO. Word Health Organization Framework Convention on Tobacco Control (WHO FCTC). Geneve: World Health Organization 2003.
4. WHO. World Health Organization Report of the Global Tobacco Epidemic. Implementing smoke-free environments. Geneve: World Health Organization, 2009.
5. Gorini G, Moshammer H, Sbrogiò L et al. Italy and Austria before and after study: second - hand smoke exposure in hospitality premises before and after 2 years from the introduction of the Italian smoking ban. *Indoor Air* 2008;18:328-34.
6. IARC. Methods for evaluating tobacco control policies. Handbooks on tobacco control. Lyon, International Agency for Research on Cancer 2008.
7. López MJ, Fernández E, Pérez-Rios M et al. Impact of the 2011 Spanish smoking ban in hospitality venues: indoor secondhand smoke exposure and influence of outdoor smoking. *Nicotine Tob Res* 2013;15:992-6
8. Martínez-Sánchez JM, Blanch C, Fu M, Gallus S, La Vecchia C, Fernández E. Do smoke-free policies in work and public places increase smoking in private venues? *Tob Control* 2014;23:204-7.
9. Minardi V, Gorini G, Carreras G, et al. Compliance with the smoking ban in Italy 8 years after its application. *Int J Public Health* 2014;59:549-54.
10. Gallus S, Lugo A, Gorini G, Colombo P, Pacifici R, Fernandez E. Voluntary home smoking ban: prevalence, trend and determinants in Italy. *Eur J Public Health* 2016;26:841-44.
11. Jarvis MJ, Sims M, Gilmore A, Mindell J. Impact of smoke-free legislation on children's exposure to secondhand smoke: cotinine data from the Health Survey for England. *Tob Control* 2012;21:18-23
12. García Villar J, López-Nicolás A. Who is afraid of smoking bans? An evaluation of the effects of the Spanish clean air law on expenditure at hospitality venues. *Eur J Health Econ*.2015;16:813-34
13. Öberg M, Jaakkola MS, Woodward A, Peruga A, Prüss-Ustün A. Worldwide burden of disease from exposure to second-hand smoke: a retrospective analysis of data from 192 countries. *Lancet* 2011;377:139-46
14. Semple S, Mueller W, Leyland AH, Gray L, Cherrie JW. Assessing progress in protecting non-smokers from secondhand smoke. *Tob Control* 2018. pii: tobaccocontrol-2018-054599.
15. Martínez-Sánchez JM, Gallus S, Zuccaro P, et al. Exposure to secondhand smoke in Italian non-smokers 5 years after the Italian smoking ban. *Eur J Public Health* 2012;22:707-12.
16. Martínez-Sánchez JM, Sureda X, Fu M, et al. Secondhand smoke exposure at home: assessment by biomarkers and airborne markers. *Environ Res* 2014;133:111-6.
17. López MJ, Arechavala T, Continente X, et al. Social inequalities in secondhand smoke exposure in children in Spain. *Tob Induc Dis* 2018;16:14.
18. GBD 2017 Risk Factors Collaborators, and others. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018;392:1923-1994.
19. Liberati A, Altman DG, Tetzlaff J, et al. ThePRISMA statement for reporting systematic reviews and meta-analyses of studies thatevaluate health care interventions: explanation and elaboration. *PLoS Med* 2009;6:e1000100.
20. Behm I, Kabir Z, Connolly GN, Alpert HR. Increasing prevalence of smoke-free homes and decreasing rates of sudden infant death syndrome in the United States: an ecological association study. *Tob Control* 2012;21:6-11.

21. Tabuchi T, Fujiwara T, Nakayama T, et al. Maternal and paternal indoor or outdoor smoking and the risk of asthma in their children: a nationwide prospective birth cohort study. *Drug Alcohol Depend* 2015;147:103-8.
22. Gram IT, Little MA, Lund E, Braaten T. The fraction of breast cancer attributable to smoking: The Norwegian women and cancer study 1991-2012. *Br J Cancer* 2016;115:616-23.
23. Royal College of Physicians. Passive smoking and children. A report by the Tobacco Advisory Group. London: RCP, 2010.
24. The Smoke Free Partnership. Lifting the Smokescreen : 10 reasons for a smoke free Europe. Report of the European Respiratory Society, Brussels, 2006.
25. GBD 2015 Risk Factors Collaborators, and others, Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet* 2016;388:1659-1724.
26. GBD 2016 Risk Factors Collaborators, and others. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017;390:1345-1422.
27. Lim SS, Vos T, Flaxman AD, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2012;380:2224-60.
28. Öberg M, Jaakkola MS, Prüss-Üstün A, et al. Second-hand smoke: Assessing the environmental burden of disease at national and local levels. Geneva, World Health Organization. WHO Environmental Burden of Disease Series, No. 18, 2010.
29. Ezzati M, López AD, Rodgers A, Vander Hoorn S, Murray CJ; Comparative Risk Assessment Collaborating Group. Selected major risk factors and global and regional burden of disease. *Lancet* 2002; 360: 1347–60.
30. World Health Organization. Comparative quantification of health risks. Ezzati M, López AD, Rodgers A, Murray CJL, eds. Geneva: World Health Organization, 2004. http://www.who.int/healthinfo/global_burden_disease/cra/en/index.html (accessed Sep 1, 2016).
31. Suzuki M, Thiem VD, Yanai H, et al. Association of environmental tobacco smoking exposure with an increased risk of hospital admissions for pneumonia in children under 5 years of age in Vietnam. *Thorax* 2009;64:484-9.
32. Vineis P, Hoek G, Krzyzanowski M, et al. Lung cancers attributable to environmental tobacco smoke and air pollution in non-smokers in different European countries: a prospective study. *Environ Health* 2007 15;6:7.
33. Wu CF, Feng NH, Chong IW, et al. Second-hand smoke and chronic bronchitis in Taiwanese women: a health-care based study. *BMC Public Health* 2010 28;10:44.
34. Hill LD, Edwards R, Turner JR, et al. Health assessment of future PM2.5 exposures from indoor, outdoor, and secondhand tobacco smoke concentrations under alternative policy pathways in Ulaanbaatar, Mongolia. *PLoS One* 2017;12:e0186834.
35. Saywell RM Jr, Zollinger TW, Lewis CK, Jay SJ, Spitznagle MH. A model for estimating the economic impact of secondhand smoke exposure: a study in Indiana. *J Public Health Manag Pract* 2013; 19:E10-9.
36. Plescia M, Wansink D, Waters HR, Herndon S. Medical costs of secondhand-smoke exposure in North Carolina. *N C Med J* 2011;72:7-12.
37. Waters HR, Foldes SS, Alesci NL, Samet J. The Economic Impact of Exposure to Secondhand Smoke in Minnesota. *Am J Public Health* 2009; 99: 754–759.
38. Fischer F, Kraemer A. Health Impact Assessment for Second-Hand Smoke Exposure in Germany--Quantifying Estimates for Ischaemic Heart Diseases, COPD, and Stroke. *Int J Environ Res Public Health* 2016;13:198.
39. Lightwood JM, Coxson PG, Bibbins-Domingo K, Williams LW, Goldman L. Coronary heart disease attributable to passive smoking: CHD Policy Model. *Am J Prev Med* 2009; 36:13-20.

40. Cavana RY, Tobias M. Integrative system dynamics: Analysis of policy options for tobacco control in New Zealand. *Systems Research and Behavioral Science* 2008;25:675-94
41. Carey RN, Reid A, Darcey E, et al. The future excess fraction of occupational cancer among those exposed to carcinogens at work in Australia in 2012. *Cancer Epidemiol.* 2017;47:1-6.
42. Hauri DD, Lieb CM, Rajkumar S, Kooijman C, Sommer HL, Röösli M. Direct health costs of environmental tobacco smoke exposure and indirect health benefits due to smoking ban introduction. *Eur J Public Health*. 2011;21:316-22.
43. Cai L, Cui W, He J, Wu X. The economic burden of smoking and secondhand smoke exposure in rural South-West China. *J Asthma* 2014;51:515-21.
44. Yao T, Sung HY, Mao Z, Hu TW, Max W. The healthcare costs of secondhand smoke exposure in rural China. *Tob Control* 2015;24:e221-6.
45. Shin HH, Lynch SJ, Gray AR, Sears MR, Hancox RJ. How much atopy is attributable to common childhood environmental exposures? A population-based birth cohort study followed to adulthood. *Int J Epidemiol.* 2017 ;46:2009-2016.
46. Hedström AK, Olsson T, Alfredsson L. Smoking is a major preventable risk factor for multiple sclerosis. *Mult Scler* 2016;22:1021-6.
47. Reece S, Morgan C, Parascandola M, Siddiqi K. Secondhand smoke exposure during pregnancy: a cross-sectional analysis of data from Demographic and Health Survey from 30 low-income and middle-income countries. *Tob Control* 2018;28 -054288 -054288
48. Kabir Z, Connolly GN, Alpert HR. Secondhand smoke exposure and neurobehavioral disorders among children in the United States. *Pediatrics* 2011;128:263-70.
49. Max W, Sung HY, Shi Y. The cost of secondhand smoke exposure at home in California. *Tob Control* 2015;24:205-10.
50. Max W, Sung HY, Shi Y. Childhood secondhand smoke exposure and ADHD-attributable costs to the health and education system. *J Sch Health* 2014; 84:683-6.
51. Yang HS, Lim H, Choi JH et al. Environmental Tobacco Smoke Exposure at Home and Attributable Problem Behaviors in Korean Children and Adolescents for 2012–2014 in a Nationally Representative Survey. J Korean Med Sci. 2018; 33: e229.
52. Max W, Sung HY, Shi Y. Deaths from secondhand smoke exposure in the United States: economic implications. *Am J Public Health* 2012;102:2173-80.
53. Mason J, Wheeler W, Brown MJ. The economic burden of exposure to secondhand smoke for child and adult never smokers residing in U.S. public housing. *Public Health Rep* 2015;130:230-44.
54. Mason K. Burden of disease from second-hand smoke exposure in New Zealand. N *Z Med J* 2016;129:16-25.
55. García-Esquinas E, Jiménez A, Pastor-Barriuso R, et al. Impact of declining exposure to secondhand tobacco smoke in public places to decreasing smoking-related cancer mortality in the US population. *Environ Int.* 2018;117:260-267. doi: 10.1016/j.envint.2018.05.008. 16.
56. Permitasari NPAL, Satibi S, Kristina SA. National Burden of Cancers Attributable to Secondhand Smoking in Indonesia. *Asian Pac J Cancer Prev*. 2018;19:1951-1955.
57. Park S, Jee SH, Shin HR, et al. Attributable fraction of tobacco smoking on cancer using population-based nationwide cancer incidence and mortality data in Korea. *BMC Cancer* 2014;14:406.
58. Ádám B, Molnár Á, Gulis G, Ádány R. Integrating a quantitative risk appraisal in a health impact assessment: analysis of the novel smoke-free policy in Hungary. *Eur J Public Health* 2013;23:211-7.
59. Heidrich J, Wellmann J, Heuschmann PU, Kraywinkel K, Keil U. Mortality and morbidity from coronary heart disease attributable to passive smoking. *Eur Heart J* 2007;28:2498-502.
60. Heo S, Lee JT. Disease burdens from environmental tobacco smoke in Korean adults. Int J *Environ Health Res* 2015;25:330-48.
61. Heuschmann PU, Heidrich J, Wellmann J, Kraywinkel K, Keil U. Stroke mortality and morbidity attributable to passive smoking in Germany. *Eur J Cardiovasc Prev Rehabil* 2007;14:793-5.

62. Rumrich IK, Hänninen O. Environmental Asthma Reduction Potential Estimates for Selected Mitigation Actions in Finland Using a Life Table Approach. *Int J Environ Res Public Health* 2015;12:6506-22.
63. Schram-Bijkerk D, van Kempen EE, Knol AB. The burden of disease related to indoor air in the Netherlands: do different methods lead to different results? *Occup Environ Med* 2013;70:126-32.
64. Becher H, Belau M, Winkler V, Aigner A. Estimating lung cancer mortality attributable to second hand smoke exposure in Germany. *Int J Public Health* 2018;63:367-375.
65. Gan Q, Smith KR, Hammond SK, Hu TW. Disease burden of adult lung cancer and ischaemic heart disease from passive tobacco smoking in China. *Tob Control* 2007;16:417-22.
66. López MJ, Pérez-Ríos M, Schiaffino A, et al. Mortality attributable to passive smoking in Spain, 2002. *Tob Control* 2007;16:373-7.
67. López MJ, Pérez-Ríos M, Schiaffino A, Fernández E. Mortality Attributable to Secondhand Smoke Exposure in Spain (2011). *Nicotine Tob Res 2016*;18:1307-10.
68. Behm I, Kabir Z, Connolly GN, Alpert HR. Increasing prevalence of smoke-free homes and decreasing rates of sudden infant death syndrome in the United States: an ecological association study. *Tob Control* 2012;21:6-11.
69. Wilson LF, Antonsson A, Green AC, et al. How many cancer cases and deaths are potentially preventable? Estimates for Australia in 2013. *Int J Cancer* 2018;142:691-701.
70. Tachfouti N, Najdi A, Lyoussi B, Nejjari C. Mortality Attributable to Second Hand Smoking in Morocco: 2012 Results of a National Prevalence Based Study. *Asian Pac J Cancer Prev.* 2016;17:2827-32.
71. Cao B, Hill C, Bonaldi C, et al. Cancers attributable to tobacco smoking in France in 2015. *Eur J Public Health*. 2018;28:707-712. doi: 10.1093/eurpub/cky077.
72. Parkin DM. Tobacco-attributable cancer burden in the UK in 2010. *Br J Cancer* 2011;105:S6–13.
73. Islami F, Chen W, Yu XQ, et al. Cancer deaths and cases attributable to lifestyle factors and infections in China, 2013. *Ann Oncol.* 2017;28:2567-2574.
74. Islami F, Goding Sauer A, Miller KD, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. *CA Cancer J Clin* 2018;68:31-54.
75. Liu R, Bohac DL, Gundel LA, Hewett MJ, Apte MG, Hammond SK. Assessment of risk for asthma initiation and cancer and heart disease deaths among patrons and servers due to secondhand smoke exposure in restaurants and bars. *Tob Control* 2014;23:332-8.
76. Sung HY, Chang LC, Wen YW, Tsai YW. The costs of smoking and secondhand smoke exposure in Taiwan: a prevalence-based annual cost approach. *BMJ Open* 2014;4:e005199.
77. Zahra A, Cheong HK, Lee EW, Park JH. Burden of Disease Attributable to Secondhand Smoking in Korea. *Asia Pac J Public Health* 2016;28:737-750.
78. Ha J, Kim S-G, Paek D, Park J. The magnitude of mortality from ischemic heart disease attributed to occupational factors in Korea. Attributable fraction estimation using meta-analysis. *Saf Health Work* 2011;2:70-82.
79. Simons E, To T, Dell S. The population attributable fraction of asthma among Canadian children. *Can J Public Health* 2011;102:35-41.
80. Hänninen O, Knol AB, Jantunen M, et al. Environmental burden of disease in Europe: assessing nine risk factors in six countries. *Environ Health Perspect* 2014;122:439-46.
81. Rehm J, Gnam W, Popova S, et al. The costs of alcohol, illegal drugs, and tobacco in Canada, 2002. *J Stud Alcohol Drugs* 2007;68:886-95.
82. Ginsberg GM, Geva H. The burden of smoking in Israel-attributable mortality and costs (2014). *Isr J Health Policy Res* 2014;3:28.
83. Pandeya N, Wilson LF, Bain CJ, Martin KL, Webb PM, Whiteman DC. Cancers in Australia in 2010 attributable to tobacco smoke. *Aust N Z J Public Health* 2015;39:464-70.
84. Pell JP, Haw S, Cobbe S, et al. Smoke-free legislation and hospitalizations for acute coronary syndrome. N Engl J Med 2008;359:482-91.

85. Avila-Tang E, Elf JL, Cummings KM, Fong GT, Hovell MF, Klein JD, McMillen R, Winickoff JP, Samet JM. Assessing secondhand smoke exposure with reported measures. *Tob Control.* 2013;22:156-63. doi: 10.1136/tobaccocontrol-2011-050296.
86. Prochaska JJ, Grossman W, Young-Wolff KC, Benowitz NL. Validity of self-reported adult secondhand smoke exposure. *Tob Control.* 2015;24:48-53. doi: 10.1136/tobaccocontrol-2013-051174.
87. Cui F, Zhang L, Yu C, Hu S, Zhang Y. Estimation of the disease burden attributable to 11 risk factors in Hubei Province, China: A comparative risk assessment. *Int J Environ Res Public Health* 2016;13(10). pii: E944
88. Feigin VL, Roth GA, Naghavi M, et al. Global burden of stroke and risk factors in 188 countries, during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet Neurol* 2016;15:913-924.
89. Järvholm B, Reuterwall C, Bystedt J. Mortality attributable to occupational exposure in Sweden. *Scand J Work Environ Health* 2013;39:106-11.
90. Rushton L, Bagga S, Bevan R, et al. Occupation and cancer in Britain. *Br J Cancer* 2010;102:1428-37.
91. Rushton L, Hutchings S, Brown T. The burden of cancer at work: estimation as the first step to prevention. *Occup Environ Med* 2008;65:789-800.
92. Rushton L, Hutchings SJ, Fortunato L, et al. Occupational cancer burden in Great Britain. *Br J Cancer* 2012 ;107 Suppl 1:S3-7.
93. Wang JB, Fan YG, Jiang Y, Kinney PL, Li T. Attributable causes of lung cancer incidence and mortality in China. *Thorac Cancer* 2011;2:156-163.
94. Xia C, Zheng R, Zeng H, et al. Provincial-level cancer burden attributable to active and second-hand smoking in China. *Tob Control* 2018; 0:1-7 doi: 10.1136/tobaccocontrol-2018-054583
95. Yao T, Sung HY, Wang Y, Lightwood J, Max W. Healthcare costs attributable to secondhand smoke exposure at home for U.S. adults. *Prev Med.* 2018;108:41-46. doi:10.1016/j.ypmed.2017.12.028.
96. Zahra A, Park JH. Burden of Disease Due to Secondhand Smoke among Korean Adults at Sub-National Level. *J Korean Med Sci.* 2018;33:e256. doi: 10.3346/jkms.2018.33.e256.
97. Jarosińska D, Polańska K, Wojtyniak B, Kinney PL, Li T. Towards estimating the burden of disease attributable to second-hand smoke exposure in Polish children. *Int J Occup Med Environ Health* 2014;27:38-49.
98. Zollinger TW, Saywell RM Jr, Overgaard AD, Jay SJ, Holloway AM, Cummings SF. Estimating the economic impact of secondhand smoke on the health of a community. *Am J Health Promot.* 2004;18:232–238.
99. Woodward A, Laugesen M. How many deaths are caused by second hand cigarette smoke? *Tob Control.* 2001;10:383–388.
100. Centers for Disease Control and Prevention (CDC). Vital signs: nonsmokers' exposure to secondhand smoke-United States, 1999-2008. *MMWR* 2010;59:1141-6
101. California Environmental Protection Agency: Air Resources Board. Proposed Identification of Environmental Tobacco Smoke as a Toxic Air Contaminant. UCSF: Center for Tobacco Control Research and Education, 2005.
102. Fontham ET, Correa P, Reynolds P, et al. Environmental tobacco smoke and lung cancer in nonsmoking women. A multicenter study. *JAMA* 1994;271:1752-9.
103. National Health and Nutrition Examination Survey: Questionnaires, Datasets, and Related Documentation. Atlanta, GA: Centers for Disease Control and Prevention, National Center for Health Statistics. Available from: https://wwwn.cdc.gov/nchs/nhanes/Default.aspx.
104. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Tobacco Smoke and Involuntary Smoking. IARC Monogr Eval Carcinog Risks Hum. 2004;83:1-1438.
105. WHO. International Agency for Research on Cancer Monographs on the evaluation of carcinogenic risks to humans - second-hand tobacco smoke. Paris: WHO Publications; 2015

106. Hackshaw AK, Law MR, Wald NJ. The accumulated evidence on lung cancer and environmental tobacco smoke. *BMJ* 1997;315:980-8.
107. Pérez-Ríos M, Santiago-Pérez MI, Alonso B, Malvar A, Hervada X Exposure to second-hand smoke: a population-based survey in Spain. *Eur Respir J*. 2007;29:818-9.
108. Borrell C., Baranda I., Rodríguez M. Enquesta de Salut de Barcelona 2000-2001, Ajuntament de Barcelona, Institut Municipal de Salut Public, 2001
109. Departament de Salut Publica Ajuntament de Cornellà. Enquesta de Salut. Cornellà de Llobregat, 1993-1994. Ajuntament de Cornellà de Llobregat, 1995.
110. Riboli E, Hunt KJ, Slimani N, et al. European Prospective Investigation into Cancer and Nutrition (EPIC): study populations and data collection. *Public Health Nutr* 2002;5:1113-24.
111. Vineis P, Airoldi L, Veglia F, et al. Environmental tobacco smoke and risk of respiratory cancer and chronic obstructive pulmonary disease in former smokers and never smokers in the EPIC prospective study. *BMJ* 2005 5;330:277.
112. The work environment 2009. Stockholm: Sweidish Work Envionment Authority; 2009.
113. Gelder BMv, Blokstra A. Environmental tobacco smoke in the Netherlands. First estimates of exposures, review of main health effects and overview of available interventions. Bilthoven: National Institute for Public Health and the Environment, 2008. Report No.: 260601005.
114. Kim CH, Lee YC, Hung RJ, et al. Exposure to secondhand tobacco smoke and lung cancer by histological type: a pooled analysis of the International Lung Cancer Consortium (ILCCO). *Int J Cancer* 2014;135:1918-30.
115. Robert Koch Institute, Department of Epidemiology and Health Monitoring (2015): German Health Interview and Examination Survey for Adults (DEGS1). Public Use File 1. Version. doi: 10.7797/16-200812-1-1-1
116. Wen W, Shu XO, Gao YT, Yang G, Li Q, Li H, Zheng W. Environmental tobacco smoke and mortality in Chinese women who have never smoked: prospective cohort study. *BMJ* 2006;333(7564):376.
117. The National Health and Nutrition Examination Survey. Korean Ministry of Health and Welfare. Available from: http://knhanes.cdc.go.kr/knhanes/index.do
118. Korea centers for disease control and prevention. Korean Community Health Survey. Available from: https://chs.cdc.go.kr/
119. Zhao H, Gu J, Xu H, et al. Meta-analysis of the relationship between passive smoking population in China and lung cancer. *Zhongguo Fei Ai Za Zhi* 2010;13(6):617-23.
120. GBD 2013 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2015;386(10010):2287-323.
121. Fu X, Feng T, Wu M, Zhang L, Jiang C. Relationship between environmental tobacco smoke and lung cancer risk among nonsmokers in China: A meta-analysis. *Zhonghua Yu Fang Yi Xue Za Zhi* 2015;49:644-8.
122. Berraho M, Serhier Z, Tachfouti N, Elfakir S, El Rhazi K et al. Burden of smoking in Moroccan rural areas. *EMHJ* 2010;16:677-683.
123. Steenland K. Risk assessment for heart disease and workplace ETS exposure among nonsmokers. *Environ Health Perspect* 1999;107(Suppl 6):859–863.
124. Law MR, Morris JK, Wald NJ. Environmental tobacco smoke exposure and ischaemic heart disease: an evaluation of the evidence. *BMJ* 1997;315:973-80.
125. Fischer F, Kraemer A. Meta-analysis of the association between second-hand smoke exposure and ischaemic heart diseases, COPD and stroke. *BMC Public Health* 2015;15:1202.
126. Lampert T, List SM. Gesundheitsrisiko Passivrauchen; Robert Koch-Institut: Berlin, Germany, 2010.
127. Park J, Lee N. 2006 Korean Working Conditions Survey. Incheon (Korea): Occupational Safety and Health Research Institute; 2006. Report No.: OSHRI2006-69-755. 125 p. Korean.

128. He Y, Lam TH. A review on studies of smoking and coronary heart disease in China and Hong Kong. *Chin Med J* 1999;112:3-8.
129. He Y. Women's passive smoking and coronary heart disease. *Zhonghua Yu Fang Yi Xue Za Zhi* 1989;23:19-22.
130. Eisner MD, Balmes J, Katz PP, Trupin L, Yelin EH, Blanc PD. Lifetime environmental tobacco smoke exposure and the risk of chronic obstructive pulmonary disease. *Environ Health* 2005;4(1):7.
131. Oono IP, Mackay DF, Pell JP. Meta-analysis of the association between secondhand smoke exposure and stroke. *J Public Health* 2011;33:496-502.
132. Whincup PH, Gilg JA, Emberson JR, et al. Passive smoking and risk of coronary heart disease and stroke: prospective study with cotinine measurement. *BMJ* 2004;329:200-5.
133. Iribarren C, Darbinian J, Klatsky AL, Friedman GD. Cohort study of exposure to environmental tobacco smoke and risk of first ischemic stroke and transient ischemic attack. *Neuroepidemiology* 2004;23:38-44.
134. Thefeld W, Stolzenberg H, Bellach BM. The federal health survey: response, composition of participants and non-responder analysis. Gesundheitswesen 1999; 61 Spec No:S57-S61.
135. Jaakkola MS, Piipari R, Jaakkola N, Jaakkola JJ. Environmental tobacco smoke and adult-onset asthma: a population-based incident case-control study. *Am J Public Health* 2003;93:2055-60.
136. ANRF. Summary of 100% smokefree state laws and population protected by 100% US smokefree laws. Berkeley, CA: American Nonsmokers' Right Foundation, 2012 (cited 20 January 2012). http://www.no-smoke.org/pdf/SummaryUSPopList.pdf (accessed 18 Jan 2012).
137. National Institute for Health and Welfare (THL). Tupakkatilasto 2012. Statistical Report 27/2013. http://www.julkari.fi/bitstream/handle/10024/110551/Tr27_13.pdf?sequence=4 (accessed on 15 July 2014).
138. Shrubsole MJ, Gao YT, Dai Q, et al. Passive smoking and breast cancer risk among non-smoking Chinese women. *Int J Cancer* 2004;110:605-9.
139. Etzel RA, Pattishall EN, Haley NJ, Fletcher RH, Henderson FW. Passive smoking and middle ear effusion among children in day care. *Pediatrics* 1992;90:228-32.
140. Jones L, Hashim A, McKeever T, Cook DG, Britton J, Leonardi-Bee J. Parental and household smoking and the increased risk of bronchitis, bronchiolitis and other lower respiratory infection in infancy: systematic review and meta-analysis. *Respir Res* 2011;12:5.
141. Smoking-Attributable Mortality, Morbidity, and Economic Costs (SAMMEC) [computer program]. http://apps.nccd.cdc.gov/sammec/index.asp. (Accessed March 9, 2011).
142. Martin JA, Hamilton BE, Sutton PD, et al. Births: final data for 2006. National Vital Statistics Reports 2009;57(7)
143. Anderson HR, Cook DG. Passive smoking and sudden infant death syndrome: review of the epidemiological evidence. *Thorax* 1997;52:1003-9.
144. Lewis S, Richards D, Bynner J, Butler N, Britton J. Prospective study of risk factors for early and persistent wheezing in childhood. *Eur Respir J* 1995;8:349-56.
145. Ronmark E, Perzanowski M, Platts-Mills T, Lundbäck B. Incidence rates and risk factors for asthma among school children: A 2-year follow-up report from the obstructive lung disease in Northern Sweden (OLIN) studies. *Respir Med* 2002;96:1006-13
146. Tinuoye O, Pell JP, Mackay DF. Meta-analysis of the association between secondhand smoke exposure and physician-diagnosed childhood asthma. *Nicotine Tob Res*. 2013;15:1475-83.
147. Hänninen O, Knol A, eds. European Perspectives on Environmental Burden of Disease: Estimates for Nine Stressors in Six Countries. 2011. http://www.thl.fi/thl-client/pdfs/b75f6999-e7c4-4550-a939-3bccb19e41c1 [accessed 7 March 2013]
148. Windham GC, Eaton A, Hopkins B. Evidence for an association between envi- ronmental tobacco smoke exposure and birthweight: a meta-analysis and new data. *Paediatr Perinat Epidemiol*.1999;13:35–57.
149. WHO. The current status of the tobacco epidemic in Poland. Copenhagen: WHO; 2009.

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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, the Netherlands)	LC, IHD, asthma	CRA	DALY
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, LBW, spontaneous abortion	simplified CRA‡	loss-of-life and healthcare costs§
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 Definition	RR Endpoint*	RR Source	RR^	SHS exposure Definition	SHS exposure Source	SHS exposure %	PAF (%)	Notes
Lung cancer									
World									
Öberg et al., 2011 [13] World	NA	Inc/Mort	[2]	H: 1·21 Wo: 1·22	At home or at work			1.8 (DALYs)	Only PAF for DALYs was provided.
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	1.7	
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	1.6	
North America									
Waters et al., 2009 [37] USA	NA	NA	[2]	NA	NA	National survey from Minnesota Department of Health	NA	4.9	Non-original. PAF from [98-99]
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: 51.9 Women: 44.2	Total: 9.5	PAF for Minnesota only are also available
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	NHANES	Scenario 1 18-50 y: 48 51-64 y: 46 65-84 y: 38	Scenario 1 18-50 y: 9 51-64 y: 9 65-84 y: 7	

					level ≥0.05 ng/mL. Scenario 2: serum cotinine level ≥0.015 ng/mL.		≥85 y: 38 Scenario 2 18-50 y: 81 51-64 y: 79 65-84 y: 75 ≥85 y: 75	≥85 y: 7 Scenario 2 18-50 y: 15 51-64 y: 14 65-84 y: 14 ≥85 y: 14	
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	1.4	
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: 32.8 Women: 22.9	Cases Total: 2.7 Men: 3.1 Women: 2.3 Deaths Total: 2.8 Men: 3.2 Women: 2.3	
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: 17 Women: 25	Total: 6.4 Men: 6.1 Women: 6.7	
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	1.1	PAFs estimated by us from RR and % SHS exposure.
Permitasari et al., 2018 [56] Indonesia	NA	NA	[105]	M: 2.28 W: 1.31	NA	NA	Men: 81 Women: 75	Men: 50.90 Women: 18.86	Prevalence of SHS estimated by us inversely by RR and PAF.
Europe									
López et al., 2007 [66] Spain	Spousal smoking	Inc/Mort	[106]	HM: 1.34 HW: 1.24 Wo: 1.39	SHS exposure in never smokers. At least one hour	Regional surveys in Spain [107-109]	At home only Men 35-64 y: 22.6	At home only Men 35-64 y: 7.1	Some PAFs estimated by us

				H&Wo: 1.39	per week at home and/or at work.		≥65 y: 28.6 Women 35-64 y: 33.0 ≥65 y: 30.8 At work only Men 35-64 y: 35.9 Women 35-64 y: 19.3 At home and work Men 35-64 y: 9.5 Women 35-64 y: 12.0	≥65 y: 8.9 Women 35-64 y: 7.3 ≥65 y: 6.9 At work only Men 35-64 y: 12.3 Women 35-64 y: 7.0 At home and work Men 35-64 y: 3.6 Women 35-64 y: 4.5	from RR and % SHS exposure.
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: 19 Work: 47 Home and/or work: 58	Home: 0.6 Work: 24 Home and/or work: 16	
Parkin, 2011 [72] UK	SHS exposure from spouse/at workplace	NA	[104]	M: 1.37 W: 1.24			Men: 17 Women: 23	Men: 5.9 Women: 5.2	PAFs estimated by us from RR and % SHS exposure.
Järvholm et al., 2013 [89] Sweden	NA	NA	NA	1.25	SHS exposure in non-smoking women.	[112]	Women: 5.0	Women: 1.2	
Schram-Bijkerk et al., 2013 [63] The Netherlands	NA	NA	[102]	1.21	SHS exposure in non-smokers. Daily exposure.	[113]	18-40 (mean: 29)	5.7	
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 close enough to smell the SHS.	Representative national survey	At home only Men 35-64 y: 9.4 ≥65 y: 10.0 Women 35-64 y: 9.0 ≥65 y: 9.8 At work only Men 35-64 y: 8.1 Women	At home only Men 35-64 y: 3.1 ≥65 y: 3.3 Women 35-64 y: 2.1 ≥65 y: 2.3 At work only Men 35-64 y: 3.1 Women	For PAF computation, we used RR estimates from [66]

							35-64 y: 4.9 At home and work Men 35-64 y: 1.7 Women 35-64 y: 0.4	35-64 y: 1.9 At home and work Men 35-64 y: 0.7 Women 35-64 y: 0.2	
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: 39.5 Women: 23.5	Men: 7.7 Women: 4.7	
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: 35.3 35-39 y: 37.5 40-44 y: 37.2 45-49 y: 39.7 50-54 y: 37.9 55-59 y: 32.9 60-64 y: 28.4 65-69 y: 18.0 70-74 y: 15.7 75-79 y: 11.1 80-84 y: 10.5 ≥85y: 10.5 Women 30-34 y: 41.7 35-39 y: 44.1 40-44 y: 45.2 45-49 y: 50.9 50-54 y: 50.3 55-59 y: 56.2 60-64 y: 57.6 65-69 y: 62.1 70-74y: 59.6 75-79 y: 62.4 80-84 y: 56.4 ≥85 y: 56.4	Men: 4.2 Women: 6.7	
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: 36.7 Workplace: 8.4	11.1	They report PAF for at home and workplace combined

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: 22.2 Women: 19.9	Men: 6.0 Women: 5.5
Park et al., 2014 [57] Korea	SHS exposure at home/at workplace	Inc/Mort	Meta-analysis conducted by the authors	INC 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	SHS exposure in non-smokers. At home or workplace.	KNHANES [117]	At home only Men: 14.8 Women: 60.1 At workplace only Men: 42.2 Women: 14.7	INCIDENCE At home only Men: - Women: 16.3 At workplace only Men: 5.9 Women: 5.2 At home or workplace Men: 5.9 Women: 20.7 MORTALITY At home only Men: 4.8 Women: 16.1 At workplace only Men: 5.9 Women: 5.2 At home or workplace Men: 10.5 Women: 20.5

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: 24.7 Men: 24.1 Woman: 25.2		Total: 6.7 Men: 6.5 Women: 6.8		PAFs estimated by us from RR and % SHS exposure.
Yao et al., 2015 [44] China	NA	NA	[119]	1.13	Participants living with a current smoker.	National Rural Household Survey (NRHS)	Men: 35.0 Women: 62.2		Men: 4 Women: 7		
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: 41.7 30-34 y: 59.0 35-39 y: 56.4 40-44 y: 66.0 45-49 y: 59.0 50-54 y: 53.3 55-59 y: 53.5 60-64 y: 37.4 65-69 y: 27.5 70-74 y: 16.3 75-79 y: 17.9 ≥80 y: 5.2 Women 25-29 y: 42.5 30-34 y: 23.3 35-39 y: 30.0 40-44 y: 30.0 45-49 y: 34.2 50-54 y: 34.3 55-59 y: 33.1 60-64 y: 23.2 65-69 y: 14.9 70-74 y: 16.2 75-79 y: 8.5 ≥80 y: 4.4		Men 25-29 y: 17 30-34 y: 23 35-39 y: 22 40-44 y: 25 45-49 y: 23 50-54 y: 21 55-59 y: 21 60-64 y: 16 65-69 y: 12 70-74 y: 8 75-79 y: 8 ≥80 y: 3 Women 25-29 y: 18 30-34 y: 11 35-39 y: 13 40-44 y: 13 45-49 y: 15 50-54 y: 15 55-59 y: 14 60-64 y: 11 65-69 y: 7 70-74 y: 8 75-79 y: 4 ≥80 y: 2	
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		Total: 8.9 Men: 3.0 Women: 21.3		

Zahra and Park, 2018 [96] Korea	NA	NA	[120]	1.51	SHS exposure in nonsmokers at work or home	KCHS[118]	6-35	9.40	PAFs estimated by us from RR and % SHS exposure (mean prevalence: 20.5%).
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: 25.35 Women: 46.0	Men: 5.9 Women: 11.5	
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 only Men 35-64 y: 20.0 ≥65 y: 15.1 Women 35-64 y: 38.4 ≥65 y: 25.0 At work only Men 35-64 y: 57.4 Women 35-64 y: 25.5 At home and work Men 35-64 y: 25.3 Women 35-64 y: 17.7	At home only Men 35-64 y: 6.4 ≥65 y: 4.9 Women 35-64 y: 8.4 ≥65 y: 5.6 At work only Men 35-64 y: 18.3 Women 35-64 y: 9.0 At home and work Men 35-64 y: 9.0 Women 35-64 y: 6.5	Some PAFs estimated by us from RR and % SHS exposure.
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.			4.5 (DALYs)	Only PAF for DALYs was provided.
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	4.3	

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	3.5	
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: 51.9 Women: 44.2	Total: 11.4	PAF for Minnesota only are also available
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 level ≥0.015 ng/mL.	NHANES	Scenario 1 51-64 y: 46 65-84 y: 38 ≥85 y: 38 Scenario 2 51-64 y: 79 65-84 y: 75 ≥85 y: 75	Scenario 1 51-64 y: 11 65-84 y: 9 ≥85 y: 9 Scenario 2 51-64 y: 18 65-84 y: 17 ≥85 y: 17	
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	2.4	
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	1.4	PAFs estimated by us from RR and % SHS exposure.
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 only Men 35-64 y: 22.6 ≥65 y: 28.6 Women 35-64 y: 33.0 ≥65 y: 30.8 At work only Men 35-64 y: 35.9 Women 35-64 y: 19.3 At home and work Men 35-64 y: 9.5 Women 35-64 y: 12.0	At home only Men 35-64 y: 6.3 ≥65 y: 7.9 Women 35-64 y: 9.0 ≥65 y: 8.5 At work only Men 35-64 y: 7.0 Women 35-64 y: 3.9 At home and work Men 35-64 y: 2.8 Women 35-64 y: 3.5	Some PAFs estimated by us from RR and % SHS exposure.
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 (mean: 29)	7.3	
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: 72.0 30-39 y: 49.0 40-49 y: 46.4 50-59 y: 42.5 60-69 y: 27.0 ≥70 y: 16.2 Women 18-29 y: 61.6 30-39 y: 27.0 40-49 y: 28.1 50-59 y: 24.8 60-69 y: 17.0 ≥70 y: 8.9	Men 18-29 y: 4.1 30-39 y: 2.9 40-49 y: 2.7 50-59 y: 2.5 60-69 y: 1.6 ≥70 y: 1.0 Women 18-29 y: 23.5 30-39 y: 11.9 40-49 y: 12.3 50-59 y: 11.0 60-69 y: 7.8 ≥70 y: 4.3	PAFs estimated by us from RR and % SHS exposure
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	Representative national survey	At home only Men 35-64 y: 9.4 ≥65 y: 10.0 Women 35-64 y: 9.0	At home only Men 35-64 y: 2.7 ≥65 y: 2.9 Women 35-64 y: 2.6	For PAF computation, we used RR estimates from [66].

					workpartner usually smoke close enough to smell the SHS.		≥65 y: 9.8 At work only Men 35-64 y: 8.1 Women 35-64 y: 4.9 At home and work Men 35-64 y: 1.7 Women 35-64 y: 0.4	≥65 y: 2.9 At work only Men 35-64 y: 1.7 Women 35-64 y: 1.0 At home and work Men 35-64 y: 0.5 Women 35-64 y: 0.1	
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: 19.0 Women: 11.3	Men: 3.48 Women: 2.43	
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: 22.2 20-29 y: 27.4 30-39 y: 36.9 40-49 y: 32.1 50-59 y: 25.5 60-69 y: 12.6 70+ y: 4.6 Women Total: 19.9 20-29 y: 22.5 30-39 y: 22.0 40-49 y: 28.2 50-59 y: 24.0 60-69 y: 13.9 70+ y: 8.3	Men Total: 4.7 20-29 y: 5.7 30-39 y: 7.5 40-49 y: 6.6 50-59 y: 5.3 60-69 y: 2.7 70+ y: 9.2 Women Total: 4.6 20-29 y: 5.1 30-39 y: 5.0 40-49 y: 6.3 50-59 y: 5.4 60-69 y: 3.2 70+ y: 2.0	PAFs estimated by us from RR and % SHS exposure.
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: 24.7 Men: 24.1 Woman: 25.2	Total: 5.4 Men: 5.3 Women: 5.5	PAFs estimated by us from RR and % SHS exposure.

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: 35.0 Women: 62.2	Men: 7 Women: 13	
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: 41.7 30-34 y: 59.0 35-39 y: 56.4 40-44 y: 66.0 45-49 y: 59.0 50-54 y: 53.3 55-59 y: 53.5 60-64 y: 37.4 65-69 y: 27.5 70-74 y: 16.3 75-79 y: 17.9 ≥80 y: 5.2 Women 25-29 y: 42.5 30-34 y: 23.3 35-39 y: 30.0 40-44 y: 30.0 45-49 y: 34.2 50-54 y: 34.3 55-59 y: 33.1 60-64 y: 23.2 65-69 y: 14.9 70-74 y: 16.2 75-79 y: 8.5 ≥80 y: 4.4	Men 25-29 y: 16 30-34 y: 20 35-39 y: 18 40-44 y: 20 45-49 y: 17 50-54 y: 14 55-59 y: 13 60-64 y: 8 65-69 y: 6 70-74 y: 3 75-79 y: 3 ≥80 y: 1 Women 25-29 y: 17 30-34 y: 9 35-39 y: 11 40-44 y: 10 45-49 y: 10 50-54 y: 9 55-59 y: 8 60-64 y: 5 65-69 y: 3 70-74 y: 3 75-79 y: 1 ≥80 y: 1	
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	25–29 y: 0.08.8 30–34 y: 0.08.2 35–39 y: 0.07.6 40–44 y: 0.07.0 45–49 y: 0.06.4 50–54 y: 0.05.9 55–59 y: 0.05.4 60–64 y: 0.04.8 65–69 y: 0.04.3 70–74 y: 0.03.8 75–79 y: 0.03.3 ≥80 y: 0.02.8	PAFs estimated by us from RR and % SHS exposure (mean prevalence: 20.5%).

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 only Men 35-64 y: 20.0 ≥65 y: 15.1 Women 35-64 y: 38.4 ≥65 y: 25.0 At work only Men 35-64 y: 57.4 Women 35-64 y: 25.5 At home and work Men 35-64 y: 25.3 Women 35-64 y: 17.7	At home only Men 35-64 y: 5.7 ≥65 y: 4.3 Women 35-64 y: 10.3 ≥65 y: 7.0 At work only Men 35-64 y: 10.8 Women 35-64 y: 5.1 At home and work Men 35-64 y: 7.1 Women 35-64 y: 5.0	Some PAFs estimated by us from RR and % SHS exposure
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	Deaths: 4.1 DALYs: 4.0	
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: 72.0 30-39 y: 49.0 40-49 y: 46.4 50-59 y: 42.5 60-69 y: 27.0 ≥70 y: 16.2 Women 18-29 y: 61.6 30-39 y: 27.0 40-49 y: 28.1 50-59 y: 24.8	Men 18-29 y: 26.5 30-39 y: 19.7 40-49 y: 18.8 50-59 y: 17.5 60-69 y: 11.9 ≥70 y: 7.5 Women 18-29 y: 41.9 30-39 y: 24.0 40-49 y: 24.7 50-59 y: 22.5	PAFs estimated by us from RR and % SHS exposure.

							60-69 y: 17.0 ≥70 y: 8.9	60-69 y: 16.6 ≥70 y: 9.4	
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: 22.2 Women: 19.9	Men: 10.9 Women: 9.9	
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: 24.7 Men: 24.1 Woman: 25.2	Total: 12.0 Men: 11.7 Women: 12.2	PAFs estimated by us from RR and % SHS exposure.
Stroke									
World									
Feigin et al., 2016 [88] World			Meta-analysis of published studies.					2.2 (DALYs)	Only PAF for DALYs was provided.
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	Ischemic stroke Deaths: 2.4 DALYs: 2.8 Hemorrhagic stroke Deaths: 3.1 DALYs: 3.5	

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	Ischemic stroke Deaths: 2.8 DALYs: 3.0 Hemorrhagic stroke Deaths: 3.2 DALYs: 3.5	
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	1.3	PAFs estimated by us from RR and % SHS exposure.
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: 10.0 Women: 13.6	Men: 1.8 Women: 2.4	PAFs estimated by us from RR and % SHS exposure. Authors reported PAF in the overall population, including current smokers (0.9% in men and 1.5% in 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: 72.0 30-39 y: 49.0 40-49 y: 46.4 50-59 y: 42.5 60-69 y: 27.0 ≥70 y: 16.2 Women 18-29 y: 61.6 30-39 y: 27.0 40-49 y: 28.1 50-59 y: 24.8 60-69 y: 17.0 ≥70 y: 8.9	Men 18-29 y: 22.4 30-39 y: 16.4 40-49 y: 15.7 50-59 y: 14.5 60-69 y: 9.7 ≥70 y: 6.1 Women 18-29 y: 20.9 30-39 y: 10.4 40-49 y: 10.8 50-59 y: 9.6 60-69 y: 6.8 ≥70 y: 3.7	PAFs estimated by us from RR and % SHS exposure.

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: 22.2 Women: 19.9	Men: 5.3 Women: 4.7	
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: 41.7 30-34 y: 59.0 35-39 y: 56.4 40-44 y: 66.0 45-49 y: 59.0 50-54 y: 53.3 55-59 y: 53.5 60-64 y: 37.4 65-69 y: 27.5 70-74 y: 16.3 75-79 y: 17.9 ≥80 y: 5.2 Women 25-29 y: 42.5 30-34 y: 23.3 35-39 y: 30.0 40-44 y: 30.0 45-49 y: 34.2 50-54 y: 34.3 55-59 y: 33.1 60-64 y: 23.2 65-69 y: 14.9	Men 25-29 y: 20 30-34 y: 24 35-39 y: 22 40-44 y: 23 45-49 y: 19 50-54 y: 16 55-59 y: 15 60-64 y: 10 65-69 y: 6 70-74 y: 3 75-79 y: 3 ≥80 y: 1 Women 25-29 y: 20 30-34 y: 11 35-39 y: 13 40-44 y: 12 45-49 y: 12 50-54 y: 11 55-59 y: 10 60-64 y: 6 65-69 y: 4	

							70-74 y: 16.2 75-79 y: 8.5 ≥80 y: 4.4	70-74 y: 3 75-79 y: 1 ≥80 y: 1	
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	25–29 y: 0.10.8 30–34 y: 0.10.0 35–39 y: 0.09.2 40–44 y: 0.08.4 45–49 y: 0.07.7 50–54 y: 0.06.9 55–59 y: 0.06.2 60–64 y: 0.05.5 65–69 y: 0.04.8 70–74 y: 0.04.1 75–79 y: 0.03.5 ≥80 y: 0.02.9	PAFs estimated by us from RR and % SHS exposure (mean prevalence: 20.5%).
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.			11.6 (DALYs)	Only PAF for DALYs was provided.
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]	Restaurants: 22.8 Bars: 29.6	Total: 24.0	PAF for Minnesota only are also available
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 1 18-50 y: 48 51-64 y: 46 65-84 y: 38 ≥85 y: 38 Scenario 2 18-50 y: 81 51-64 y: 79 65-84 y: 75 ≥85 y: 75	Scenario 1 18-50 y: 32 51-64 y: 31 65-84 y: 27 ≥85 y: 27 Scenario 2 18-50 y: 44 51-64 y: 43 65-84 y: 42 ≥85 y: 42	

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	4.6	
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 (mean: 29)	22.0	
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	8.8	PAFs estimated by us from RR and % SHS exposure.
Asia									
Heo et al., 2015 [60] Korea	SHS exposure at home and workplace in the previous 12 months	Inc	[135]	1.97	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: 22.2 Women: 19.9	Men: 17.7 Women: 16.2	
Sung et al., 2014 [76] Taiwan	SHS exposure at home and workplace in the	Inc	[135]	1.97	SHS exposure in non-smokers. Exposure at home or at	National survey (Adult Smoking	Total: 24.7 Men: 24.1 Woman: 25.2	Total: 19.3 Men: 18.9 Women: 19.6	PAFs estimated by us from RR and % SHS exposure.

	previous 12 months				workplace during the past week.	Behavior Survey)			
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: 35.0 Women: 62.2	Men: 25 Women: 38	
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	1.9	
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	2.1	
Europe									
Gram et al., 2016 [22] Norway	NA	Incidence	Original	1.18	SHS exposure in never smokers. NA	Original	64.8	10.4	PAF estimated by us from RR and % SHS exposure among never smokers.
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	27	
Diabetes									
World									
GBD, 2017 [26] World	NA	NA	From published	1.34	SHS exposure in non-smokers. Exposure by a	NA	NA	6.6	

			meta-analyses.		household member.				

* 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.

Study Country	RR				SHS exposure			PAF (%)	Notes
	Definition	Endpoint*	Source	RR	Definition	Source	%		
Otitis media									
World									
Öberg et al., 2011 [13] World	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)	Only PAF for DALYs was provided.
GBD, 2016 [25] World	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	
GBD, 2017 [26] World	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	
North America									
Waters et al., 2009 [37] USA				Not used			Not used	14.0	Non original PAF, from [98]

Study Country	RR				SHS exposure			PAF (%)	Notes
	Definition	Endpoint*	Source	RR	Definition	Source	%		
Mason et al., 2015 [53] USA	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	
Max et al., 2015 [49] USA	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	
Oceania									
Mason et al., 2016 [54] New Zealand	Children exposed to household smoking (middle ear infection)	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 car their child travelled in	New Zealand Health Surveys	8.7	2.7	PAFs estimated by us from RR and % SHS exposure
Europe									
Royal College of Physicians, 2010 [23] UK	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	
Schram-Bijkerk et al., 2013 [63] The Netherlands	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)	
Jarosińska et al., 2014 [97]	Children aged <3 years with	Inc	[101,139]	1.38	Children exposed to any tobacco smoke:	Scenario 1: national survey	Scenario 1: 48 Scenario 2: 60	Scenario 1: 15.4 Scenario 2: 18.6	

Study Country	RR				SHS exposure			PAF (%)	Notes
	Definition	Endpoint*	Source	RR	Definition	Source	%		
Poland	serum cotinine concentration greater than or equal to 2.5 ng/mL (otitis media with effusion)				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 2: GYTS			
SIDS									
North America									
Behm et al., 2012 [20] USA	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	
Max et al., 2012 [52] USA	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	PAFs estimated by us from RR and % SHS exposure
Mason et al., 2015 [53] USA	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	
Max et al., 2015 [49] USA	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	
Oceania									

Study Country	RR				SHS exposure			PAF (%)	Notes
	Definition	Endpoint*	Source	RR	Definition	Source	%		
Mason et al., 2016 [54] New Zealand	Children aged <1 year exposed to postnatal maternal smoking	Mort	[143]	1.94	Mothers with newborns smoking at two weeks after birth	Nationwide Well Child/Tamariki iOra health checks programme for infants	13	10.9	PAFs estimated by us from RR and % SHS exposure
Europe									
Jarosińska et al., 2014 [97] Poland	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	
Royal College of Physicians, 2010 [23] UK	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	
Schram-Bijkerk et al., 2013 [63] The Netherlands	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)	
LRI									
World									
Öberg et al., 2011 [13] world	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)	Only PAF for DALYs was provided.
GBD, 2016 [25] World	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	

Study Country	RR				SHS exposure			PAF (%)	Notes
	Definition	Endpoint*	Source	RR	Definition	Source	%		
GBD, 2017 [26] World	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	
North America									
Mason et al., 2015 [53] USA	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	
Max et al., 2015 [49] USA	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	
Oceania									
Mason et al., 2016 [54] New Zealand	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	PAFs estimated by us from RR and % SHS exposure
Europe									
Royal College of Physicians, 2010 [23] UK	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	
Schram-Bijkerk et al., 2013 [63] The Netherlands	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)	

Study Country	RR				SHS exposure			PAF (%)	Notes
	Definition	Endpoint*	Source	RR	Definition	Source	%		
Jarosińska et al., 2014 [97] Poland	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	
Asthma induction									
World									
Öberg et al., 2011 [13] world	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)	Only PAF for DALYs was provided.
North America									
Waters et al., 2009 [37] USA			[2]	1.23	NA	Minnesota Department of Health	not known	35	Non original PAF, from Zollinger et al., 2004
Simons et al., 2011 [79] Canada	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	PAFs estimated by us from RR and % SHS exposure. Age-specific PAF estimate reported is reported in the paper: 0-5 years: 2.9 6-11 years: 3.1
Mason et al., 2015 [53] USA	Children aged 1-17 years exposed to SHS by parental report	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)	NHANES	0.05 ng/mL: 61 0.015ng/mL: 85	0.05 ng/mL: 16.3 0.015ng/mL: 21.4	

Study Country	RR				SHS exposure			PAF (%)	Notes
	Definition	Endpoint*	Source	RR	Definition	Source	%		
	or by cotinine measurement				- Children 12-19 years: reporting no smoking in the previous 30 days, no use of any nicotine-containing product within the previous 5 days and a serum cotinine level > 0.05 /0.015 ng/mL.				
Max et al., 2015 [49] USA	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	
Oceania									
Mason et al., 2016 [54] New Zealand	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	PAFs estimated by us from RR and % SHS exposure
Europe									
Royal College of Physicians, 2010 [23] UK	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	
Schram-Bijkerk et al., 2013 [63] The Netherlands	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)	
Jarosińska et al., 2014 [97] Poland	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	Scenario 1: national survey Scenario 2: GYTS	Scenario 1: 48 Scenario 2: 60	Scenario 1: 13.3 Scenario 2: 16.1	

Study Country	RR				SHS exposure			PAF (%)	Notes
	Definition	Endpoint*	Source	RR	Definition	Source	%		
					in the presence of their children Scenario 2: children aged 13-15 years exposed in households and public place				
Rumrich et al., 2015 [62] Finland	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	PAFs estimated by us from RR and % SHS exposure
Asia									
Tabuchi et al., 2015 [21] Japan	Children aged 0-8 years exposed to parental indoor smoking	Inc	Estimated in nationally a representative 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	We consider only both parental indoor smoking (see corresponding appendix of [21])
LBW									
North America									
Max et al., 2012 [52] USA	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	PAFs estimated by us from RR and % SHS exposure
Mason et al., 2015 [53] USA	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	

Study Country	RR				SHS exposure			PAF (%)	Notes
	Definition	Endpoint*	Source	RR	Definition	Source	%		
Max et al., 2015 [49] USA	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	
Oceania									
Mason et al., 2016 [54] New Zealand	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	PAFs estimated by us from RR and % SHS exposure
Europe									
Jarosińska et al., 2014 [97] Poland	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.