Health impacts of indoor air contaminants determined using the DALY metric

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1. ABSTRACT

Common metrics used for assessing air quality are based on guidelines and/or standards for regulating concentrations that should not be exceeded over a period. Exceeding those values would represent problematic situations. A lack of agreement on appropriate norms or standards deem this approach sub-optimal. Moreover, this approach does not relate a proportion of exceedance to specific health outcomes. A need to develop health-centered IAQ metrics that can quantify burden of disease in terms of epidemiological evidence of population morbidity and mortality supported by the best knowledge of health effects, is pressing. This work proposes an approach that harnesses the advantages of using Disability Adjusted Life Years (DALYs) as a valuable metric to quantify and rank the burden of household air pollution, as a global perspective. Two methods were used to compute DALYs, one mainly based on incidence data and another mainly based on effect factors (i.e. DALYs per unit-intake of contaminant of interest). The methods are based on the following parameters: risk estimates, baseline incidence rates, damage factors, indoor air contaminant concentrations, human toxicological & epidemiological effect factors, dose-response factors, cancer-related variables and breathing rates. Systematic searches and reviews of peer-reviewed literature (including systematic reviews and meta analyses) were performed to find information on said input parameters. Meta-analysis was used to pooled and synthesize data from different studies. A Monte Carlo approach was used to model results in disability-adjusted life-years (DALYs) lost. Over 1000 articles were revised and overall ~200 unique sources were used as sources of data.

Ten contaminants were accounted for with specific risk estimates and damage factors data, for which human epidemiological effect factors were derived. Representative concentrations of 45 contaminants were calculated. 39 contaminants were accounted for human toxicological effect factors. Total pooled DALYs were estimated per 100,000 exposed population with corresponding uncertainty intervals. Estimated population-averaged annual cost, in DALYs lost, of chronic air contaminant inhalation in dwellings indicate that the contaminants with highest median DALY loss estimates are PM_{10} and $PM_{2.5}$ (magnitudes of 10^3); PM_{coarse}, formaldehyde, and NO_2 could be found with magnitudes of 10^2; contaminants with magnitudes of 10^1 include radon and ozone, finally SO_2 and acrolein would have magnitudes of 10^0; mould-related bioaerosols could be of interest as well. The updated strategies allowed for the quantification of contaminants and health outcomes that were not accounted for in previous works. Computed DALYs have lower uncertainty intervals than those previously proposed. The updated methodology presented in this study may be used to assess cumulative health impacts of indoor air contaminants.

2. KEYWORDS

DALYs; IAQ; health; dwellings

1 INTRODUCTION

Air pollution is one of the most serious health risks (WHO, 2021), and there now is enough scientific evidence to justify establishing and/or upgrading approaches for quantifying the health burden of (indoor)-air contaminants using current epidemiological and toxicological research. Common metrics used for assessing air quality are based on guidelines and/or standards for regulating concentrations that should not be exceeded over a period. Exceeding them would be problematic but the magnitude of doing so is unclear (Jones, 2017). This is because the approach does not relate a proportion of exceedance to specific health outcomes. Therefore, there is a pressing need to develop health-centered IAQ metrics that can quantify burden of disease in terms of epidemiological evidence of population morbidity and mortality supported by the best knowledge of health effects. Consequently, the Disability Adjusted Life Year (DALY) has been adopted worldwide in air pollution global burden of disease studies (Cohen et al., 2017). It was developed in the 1990s and is the sum of the years of life lost, and the time lived with a disability, attributable to some cause (Homedes, 1996).

A methodology to estimate the population-average health effects attributable to the inhalation of selected air contaminants in U.S. residences was proposed in Logue *et al.* (2012) using disease incidence data and health-related effect factors, and accounting for output uncertainty. It uses the DALY metric by defining an Intake-Incidence DALY (IND) method and an Intake-DALY (ID) method. Although the method proposed by Logue *et al.* (2012) is pioneering because it quantified DALY losses based on two distinct methods, the approach has limitations. Here we provide a way of strengthening the method, harnessing the advantages of using Disability Adjusted Life Years (DALYs) as a valuable metric to quantify and rank the burden of household air pollution, using a global perspective.

2 METHODS

Two methods were used to compute DALYs, one based on incidence data [IND-method], and another based on effect factors that use a DALY value per unit-of-mass-intake of the contaminant of interest [ID-method] (Logue *et al.*, 2012).

2.1. THE IND METHOD

The IND method (Equation 1) uses an epidemiologically-based concentration-response function to quantify disease incidence, which, when combined with a damage factor (DF), yields an expected DALY loss.

$$DALY\ losses = \frac{\partial DALYs}{\partial(incidence)case} \times \partial(incidence)case \quad (1)$$

In the IND model, a damage factor is used to represent the life-years adversely impacted by each disease event, in DALY.(incidence)case^{-1}. The DF$_{IND}$ is expressed for a specific contaminant h and disease k as

$$\frac{\partial DALYs}{\partial(incidence)case} = DF_{IND\ k,h} = Damage\ factor \quad (2)$$

The second term on the right of Eq 1, the disease incidence, refers to the relationship between contaminant concentration (IAP), risk of disease (β), and baseline incidence (γ_0); see Eq (3). This relationship is modeled using a log-linear concentration response function given by Eq. (3). As mortality is expected to have a greater impact on the global disease burden than morbidity, it is recommended that mortality data be used to represent disease incidence for most air pollution-related diseases (Cohen *et al.*, 2017).

$$\partial(incidence)case = \gamma_{0k,h} \times (1 - e^{-(\beta_{k,h} \times IAP_h)}) \times population \quad (3)$$

where, $\gamma_{0k,h}$ is the baseline incidence of disease k of contaminant h, and IAP_h is a statistic describing the concentration of contaminant h. Beta $\beta_{k,h}$ is an empirical parameter representing the estimated change in risk for a given change in contaminant concentration, ΔC, for disease k and contaminant h. This is expressed as

$$\beta_{k,h} = \frac{Ln(Risk\ Estimate)}{\Delta C} \quad (4)$$

A breathing rate (BR, in $m^3.yr^{-1}$) combined with the IAP_h parameter (in unit-intake.m^{-3})[1] is used to obtain an estimate of the human epidemiological effect factor (EF_{IND}, in DALYs per unit-intake of contaminant) via the IND method, as shown in Eq. (5)

$$Effect\ factor\ (EF_{IND\ k,h}) = \frac{DALY\ losses}{intake} = \frac{DALY\ losses}{BR \times IAP_h} \quad (5)$$

2.2. THE ID METHOD

The ID method (Eq. 6) quantifies DALYs as the product of effect factors (EF_{ID}), intakes, a cancer-related parameter (ADAF), and breathing rates (BR), involving Eq. (6) to (9). In this method, the EF_{ID} is the product of a dose–response factor (DRF, in case.kg_{intake}^{-1}) and a damage factor (DF_{ID}, in DALY.(cancer or non-cancer)case^{-1}).

$$DALY\ losses = \frac{\partial DALYs}{\partial intake} \times \partial intake \quad (6)$$

$$\partial intake = IAP_h \times Breating\ Rate \quad (7)$$

$$\frac{\partial DALYs}{\partial intake} = Effect\ factor\ (EF_{ID\ j,h}) = DRF_{j,h} \times DF_{ID(cancer\ or\ non-cancer)j} \quad (8)$$

$$With\ DRF_{j,h} = \left(\frac{0.5}{ED_{50j,h}}\right) \quad (8a)$$

$$And\ \frac{\partial DALYs}{\partial intake} = EF_{ID\ combined\ j} = (\frac{\partial DALYs_{cancer}}{\partial intake} \times ADAF) + (\frac{\partial DALYs_{non-cancer}}{\partial intake}) \quad (8b)$$

or

$$\frac{\partial DALYs}{\partial intake} = Effect\ factor\ (EF_{IND\ k,h}) = DRF_{k,h} \times DF_{IND\ k,h} \quad (9)$$

$$With\ DRF_{k,h} = (\frac{CRF_{k,h}}{Breating\ Rate}) \quad (9a)$$

2.3. THE INPUT DATA

Parameters described in Section 2, can have more than one available value or set of data; see Datasets in Table 1. Thus, pooling independent data points is the recommended strategy for data synthesis (Schmid et al., 2020).

For the IND method, values of the parameters beta (β), baseline incidence (γ_0), representative contaminant concentration (IAP_h), and damage factor (DF_{IND}) are obtained by combining systematic reviews with supplementary references. Baseline disease incidences are derived from epidemiological studies.

For the ID method, damage factors, representing overall cancer or non-cancer effects should be based on the latest available data from the World Health Organization (WHO) and/or the Global Burden of Disease studies. The DRF takes as a point of departure either the ED_{50} (median effective dose) benchmark measure (see Eq. 8a) or concentration-response factors (CRF) (see Eq. 9a). The ED_{50} is the human-equivalent lifetime daily dose per person, related to inhalation (intake) of a substance that produces a specific effect (e.g carcinogenic or non-carcinogenic

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[1] A *unit-intake* could be kg, Bq, or Colony Forming Units (CFU).

effects) in 50% of the population that takes that dose (Fantke *et al.,* 2021) and CRFs are contaminant-associated mortality or morbidity rates per unit concentration of contaminant inhaled (Gronlund et al., 2015). ED_{50} based- DRF (ED_{50}-DRF) for the contaminants of interest are extracted from Life Cycle Impact Assessment (LCIA) databases. CRF based- DRF (CRF-DRF) are compute using the same epidemiological inputs as the IND method and can be derived following Fantke *et al.* (2019). When EFs are based on the ED_{50}, they are referred to as human toxicological effect factors (Eq. 8) while those based on CRFs are called human epidemiological effect factors (Eq. 9). The ADAF parameter used for the estimation of cancer risks and the breathing rates representing the volume of air breathed indoors each year, are determined from relevant sources following a focused literature review.

2.4. THE MODELLING

Since each method will derive an estimate of DALY and EF (one estimate via IND method and two estimates via ID method, for a total of three theoretically possible independent DALY and EF estimations), we pooled the results from each independent method via meta-analysis to obtain *pooled DALYs* and *pooled Effect Factors*. To account for the uncertainty of the parameters, the Monte Carlo (MC) method is applied. First, a bootstrapping technique is applied to populate a synthetic database for each parameter and described using a probability distribution function (PDF). The PDF is then combined with the bootstrapped results to generate random samples of the inputs, which in turn are used to compute the three outputs: i) disease incidence, ii) effect factors and iii) DALYs. We repeated this process until the means of the results were normally distributed. All outputs are reported by their median and 95% confidence interval of its distribution, representing the range that contains 95% of the population values.

Preliminary analysis of the input data showed that they can be well described by a lognormal distribution around its median. This type of distribution is widely used and accepted to adequately adjust for right-skewed data (Crow and Shimizu 1987). A MATLAB code was used to run the Monte Carlo simulations. All pooled estimates (meta-analysis) were computed with STATA 16.0's "metan" commands, using the DerSimonian and Laird (random effects) estimators (Harris *et al.*, 2008).

3   RESULTS

Systematic searches and reviews of peer-reviewed literature (including systematic reviews and meta-analyses) were performed to extract information on the input parameters. Over 1000 articles were identified and ~200 unique sources were used as sources of data. Tables 1 and 2 provide descriptive statistics and recommended values for each input parameter for IND and ID model, respectively. Ten contaminants were accounted for with specific risk estimates and damage factors data: Acrolein, Benzene, Mould-related bioaerosols, Formaldehyde, NO_2, O_3, PM_{10}, $PM_{2.5}$, Radon and SO_2 (see Table 1). The methodology allowed for the identification, using the literature, of a single representative health outcome for each of the ten contaminants (see Table 1). The health outcome chosen to represent each contaminant is the most reported health impact associated with it, either for mortality or morbidity endpoints.
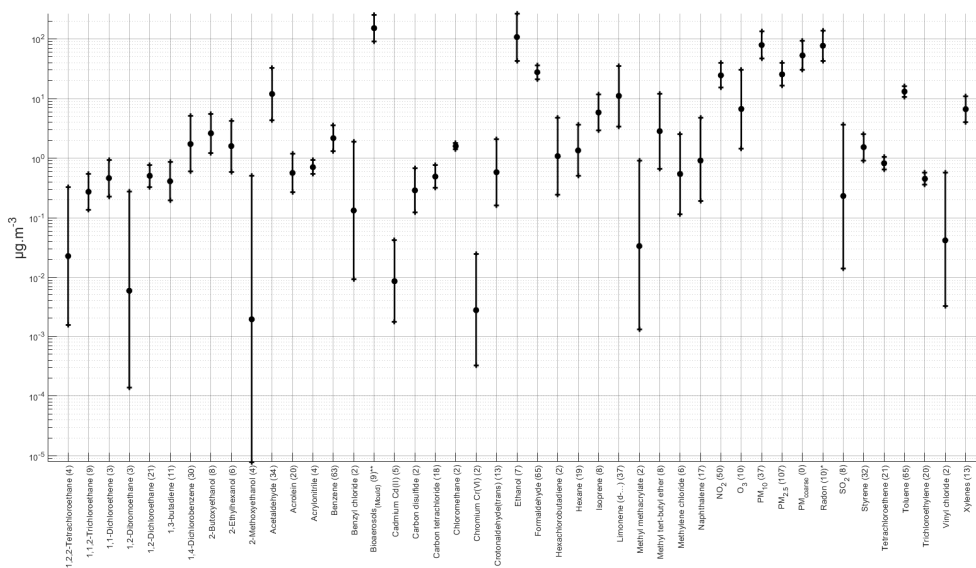
Representative concentrations of 45 contaminants were calculated. They are all included because they have previously been identified as contaminants of interest in dwellings (Logue *et al*., 2011). Fig. 1 shows the representative mid-range concentrations, including a 95% CI and the magnitude of individual values (data sets) used to obtain them. Mid-range indoor concentrations for the contaminants are, in general, within the values reported by others

(Vardoulakis et al., 2020, Logue et al., 2011). With over 50 data sets, PM$_{2.5}$, formaldehyde, Toluene, Benzene, and NO$_2$ would be the contaminants with the most reported values.

Table 1: Summary descriptive of the IND model inputs and disease incidence output for selected contaminants[+].

Contaminant	Health outcome	Beta parameter (β)	Baseline incidence rate (γ$_0$)	Damage factor (DF$_{IND}$)	Annual disease incidences, per 10^5 pop.
		Parameter values [Datasets] {Main reference}			
Acrolein	Asthma	0.141 (95%C.I.-0.082-0.200) [2] {Annesi et al. (2012)}	0.001 {Annesi et al. (2012)}	0.588 (95%C.I.0.059-5.875) [1] {GBD (2019)}	8.287 (95%C.I. 3.577-18.729)
HCHO	Added effects*	--*		9.789 (95%C.I.4.249-54.005)	46.478 (95%C.I. 9.607-1015.678)
O$_3$	ACM	0.001 (95%C.I.0.000-0.002) [7] {WHO (2021)}	0.008 (95%C.I.0.004-0.016) {Crouse et al. (2015)}	15.346 (95%C.I.6.856-34.348) [3] {OS/RD)}	1.305 (95%C.I. 0.031-55.739)
PM$_{10}$	ACM	0.004 (95%C.I.0.003-0.006) [17] {WHO (2021)}	0.013 (95%C.I.0.007-0.026) {Fischer et al. (2015)}	9.554 (95%C.I.2.528-36.101) [3] {OS/RD)}	349.077 (95%C.I. 190.536-603.739)
PM$_{2.5}$	ACM	0.008 (95%C.I.0.000-0.002) [25] {WHO (2021)}	0.007 (95%C.I.0.003-0.018) {Crouse et al. (2015)}	15.303 (95%C.I.11.798-19.850) [40] {OS/RD)}	102.893 (95%C.I. 24.256-433.625)

ACM: All-Cause Mortality. LCM: Lung Cancer Mortality. HCHO: Formaldehyde. OD/SR: Own data/ systematic review. *added effects of epidemiological data from LCM, leukaemia and asthma. [+]Other contaminants not shown due to spacing issues and are available upon request.

[*]Radon in Bq.m^{-3}. [**]Bioaerosols in CFU.m^{-3}

Figure 1: Recommended representative concentrations for the 45 contaminants included in the analysis. In alphabetical order. Central estimate and 95% C.I. of distribution in black. Datasets in parenthesis

The annual incidence of disease for the ten indoor contaminants and selected typical health outcomes was calculated using Eq. (3) and data inputs are presented in Table 1. The highest disease incidences are found in PM_{10}, $PM_{2.5}$, and mould, with estimates exceeding magnitudes of 10^2. Because particle contaminants are based on all-cause mortality risk estimations, this is to be expected. Mould-bioaerosols have a high value because asthma morbidity in children accounts for a large portion of the illness burden.

Table 1 presents the damage factors for the contaminants in the IND model and their corresponding number of datasets found. Our method for calculating this parameter yielded novel damage factors for a broader range of contaminants not presented before in related works (Fazli et al., 2018). Results are based on contaminant and health outcome-specific effects, which allows the information gaps on contaminant-related damage factors to be reduced.

To account for updated information and variability of data for standard breathing rates (Phillips and Moya, 2013), we pool recommended values for long-term inhalation rates for adults aged 16-81+ yrs (USEPA, 2011). For the ADAF parameter, the review of pertinent references indicates that the USEPA (2005) recommendations are still in use; see CalEPA (2009). The recommended estimate for the standard breathing rate is 14.80 $m^3.(pop.d)^{-1}$ (95%C.I.13.50-16.20) and for the ADAF parameter is 1.6 (95%C.I.1-10). The USEtox database was used to extract ED_{50}-DRFs (Fantke *et al.,* 2017). The USEtox model is chosen because it is a widely used global scientific consensus model for characterising human toxicological consequences in LCIA. CRF-DRFs were calculated following Fantke *et al.* (2019). Regarding the DF_{ID} parameter, we use the latest results from the 2019 GBD study. Table 2 shows descriptive for ID model.

Table 2: Summary descriptive of the ID model inputs, for selected contaminants[+]

Contaminant	ED_{50}-DRFc	ED_{50}-DRFnonc	CRF-DRF	DF_{IDc}	DF_{IDnonc}
	From USEtox Database		Own computation	From GBD (2019)	
Acrolein	NA	59.74 (95%C.I. 1.82-1963.49) {non-carcinogenic effects}	25.15 (95%C.I. 7.34-83.37) {Asthma}	NA	0.59 (95%C.I. 0.44-0.77) {Asthma}
HCHO	1.06 (95%C.I. 0.27-4.25) {carcinogenic effects}	0.01 (95%C.I. 0.00-0.15) {non-carcinogenic effects}	2.92 (95%C.I. 0.52-63.65) {Added effects}	41.77 (95%C.I. 38.60-45.15) {added Leukaemia and lung cancer}	0.59 (95%C.I. 0.44-0.77) {Asthma}
O_3	1.09 (95%C.I. 0.16-7.60) {carcinogenic effects}	NA	0.29 (95%C.I. 0.00-18.70) {ACM}	21.18 (95%C.I. 20.06-22.36) {Lung Cancer}	NA
PM_{10}	NA		7.98 (95%C.I. 3.21-18.91) {ACM}	NA	
$PM_{2.5}$			7.33 (95%C.I. 1.58-33.75) {ACM}		

Note. Curly brackets represent {health outcome}. ACM: All-Cause Mortality. ED_{50}-DRFc = carcinogenic Dose-Response Factor; ED_{50}-DRFnonc = non-carcinogenic Dose-Response Factor; CRF-DRF = concentration-response based Dose-Response Factor; DF_{ID}c = ID model carcinogenic Damage Factor; DF_{ID}nonc = ID model non-carcinogenic Damage Factor. HCHO = Formaldehyde. Added effects from LCM, leukaemia and asthma. OD/SR: Own data/ systematic review. NA= not applicable. GBD (2019):https://ghdx.healthdata.org/gbd-results-tool
[+]Other contaminants not shown due to spacing issues and are available upon request.

Combined carcinogenic and non-carcinogenic (toxicological)-effect factors were computed for 39 contaminants using Eq. (8b) whilst (epidemiological)-effect factors were computed for ten contaminants using Eq. (5) and Eq. (9). The results are pooled, giving 45 contaminants with effect factors. Results are shown in Fig. 2. $PM_{2.5}$ has the highest pooled effect factor [1.1×10^2 (95%C.I. 3.6×10^1-3.3×10^2)] (an order of magnitude higher than the other contaminants) indicating that this would be the contaminant with the highest chronic health impacts per kg inhaled in the exposed population, in dwellings. Other PMs are among the contaminants with the highest EFs, with chromium, NO_2 and formaldehyde having all $>10^1$ effect factors. These results represent an update to the preeminent work on human-toxicological&epidemiological effect and damage factors of carcinogenic and noncarcinogenic chemicals for life cycle impact assessment presented by Fantke *et al.* (2019) and Huijbregts *et al.* (2005). The results given in Fig. 2 have narrower confidence intervals when compared with those of Huijbregts *et al.* (2005).

Total pooled DALYs were estimated per 100,000 population with corresponding uncertainty intervals; see Fig. 3. Estimated population-averaged annual cost, in units of DALYs lost, of chronic air contaminant inhalation in dwellings, indicate that the contaminants with the highest median pooled DALY loss estimates are PM_{10} [1.9×10^3 (95%C.I. 4.4×10^2-8.7×10^3)] and $PM_{2.5}$ [1.5×10^3 (95%C.I. 5.3×10^2-4.4×10^3)]. PM_{coarse}, formaldehyde, NO_2, radon and ozone have medians among 10^2-10^1. Acrolein and SO_2 are within 10^0. Mould-related bioaerosols could still be of interest having >0.5 DALYs per 100.000 exposed population. The confidence intervals of the results indicate a lower uncertainty range than those presented by Logue *et al.* (2012).

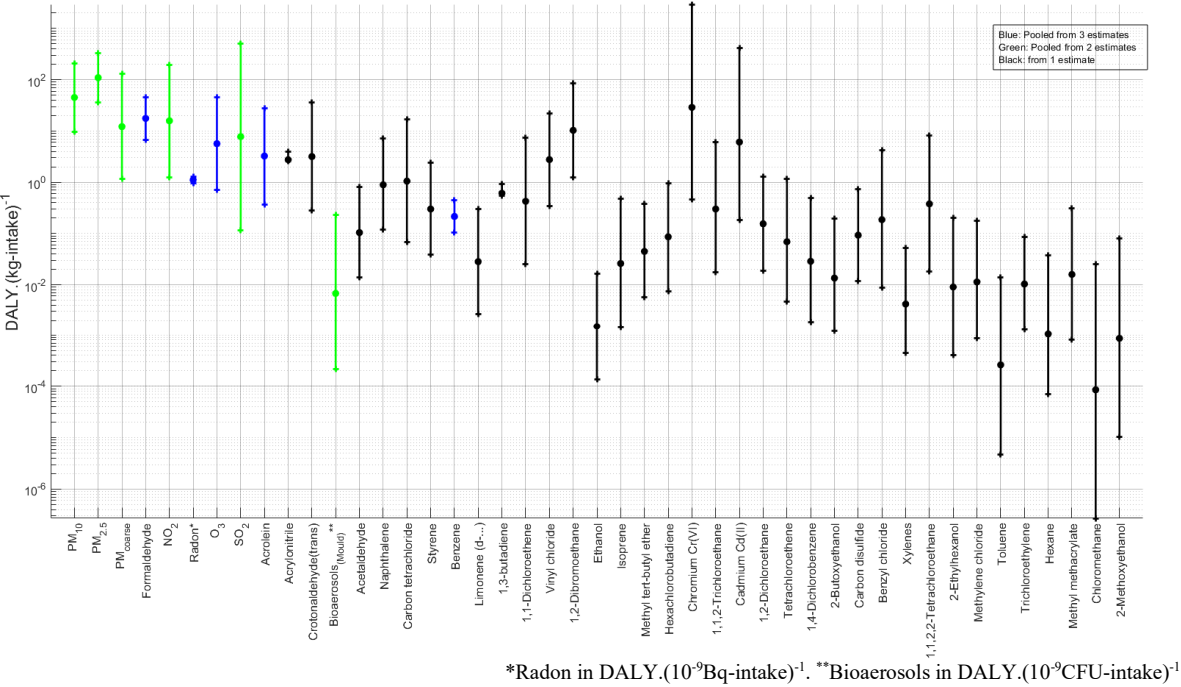*Radon in DALY.(10^{-9}Bq-intake)$^{-1}$. **Bioaerosols in DALY.(10^{-9}CFU-intake)$^{-1}$

Figure 2: Pooled effect factors. Highest to lowest DALY median. Central estimate and 95% C.I. of distribution in black.

Contaminant with highest median DALYs include the so called criteria pollutants, which are defined as the indoor contaminants with the highest health impacts based on the DALY metric. There is sufficient epidemiological evidence that indicates PM_{10}, $PM_{2.5}$, NO_2, O_3 and SO_2 have the potential to be associated with harm in humans, using other health based-metrics such as relative risks (WHO, 2021). Other airborne contaminants where health based-evidence exists to indicate that they are contaminants of interest in the indoor environment, having also elevated DALY values, include Formaldehyde (Golden, 2011), Radon (Pawel and Puskin, 2004), Acrolein (Ghilarducci and Tjeerdema, 1995) and mould (Heseltine and Rosen, 2009).
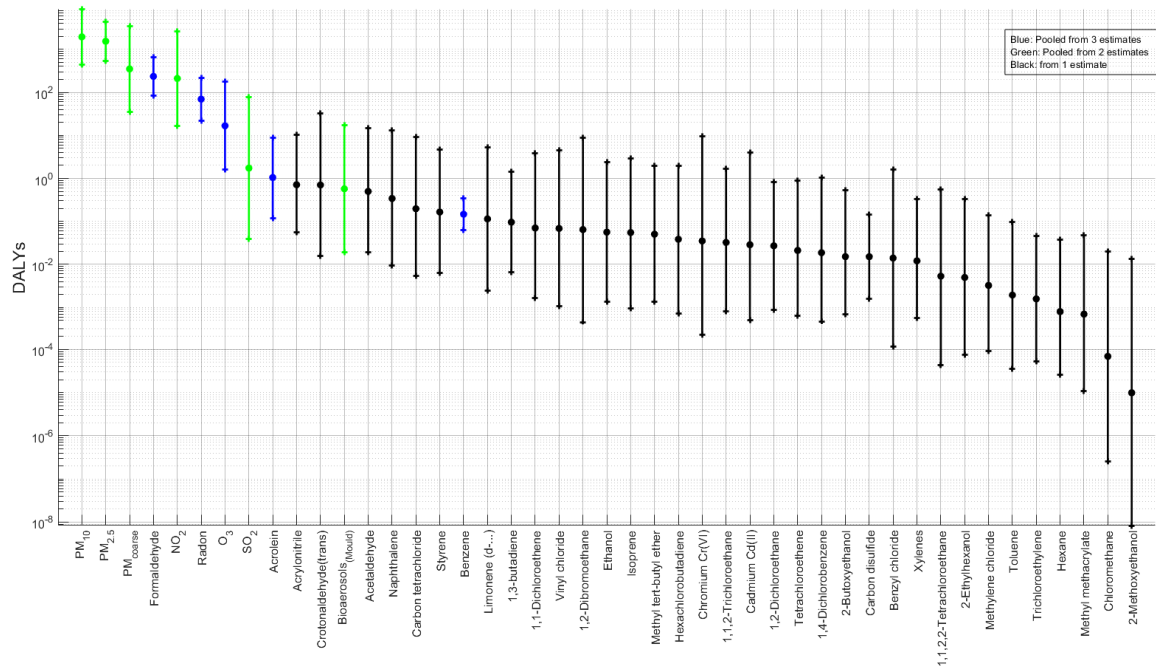
Figure 3: Pooled DALYs. Highest to lowest median. Central estimate and 95% C.I. of distribution in black.

4 CONCLUSIONS

$PM_{2.5}$ have the highest median DALYs per unit intake (1.1×10^2 (95%C.I. 3.6×10^1-3.3×10^2)), being one order of magnitude above the rest of contaminants included in the analysis, indicating that higher harm is associated with fine PM. The highest absolute DALY medians were found for PM_{10} with 1.8×10^3 (95%C.I. 4×10^2 -9×10^3) and $PM_{2.5}$ with 1.9×10^3 (95%C.I. 4.4×10^2-8.7×10^3). PM_{10} is higher because it includes the burden associated with the $PM_{2.5}$ fraction. Reporting representative indoor concentrations or disease incidence as the sole metrics to assign harm from exposure to contaminants, is rendered suboptimal. Computed DALYs have lower uncertainty intervals than those previously proposed. The updated methodology presented in this study may be used to assess cumulative health impacts of indoor air contaminants and contribute to the development of standards.

5 ACKNOWLEDGEMENTS

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