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A framework for estimating the United States depression burden attributable to indoor fine particulate matter exposure

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HIGHLIGHTS

- Major depressive disorder impacted 17.7 million Americans in 2018.
- $PM_{2.5}$ indoors may impact depression, potentially 0.07%–6.1% (2.7%) of cases.
- Increasing HVAC filter efficiency has minor reductions in depressive disorders.
- The model could estimate $PM_{2.5}$ exposure influence on other mental illnesses.
- The model could be modified for other pollutants or building factors.

GRAPHICAL ABSTRACT

Modeling Major Depressive Disorder and Indoor Particulate Matter Exposure
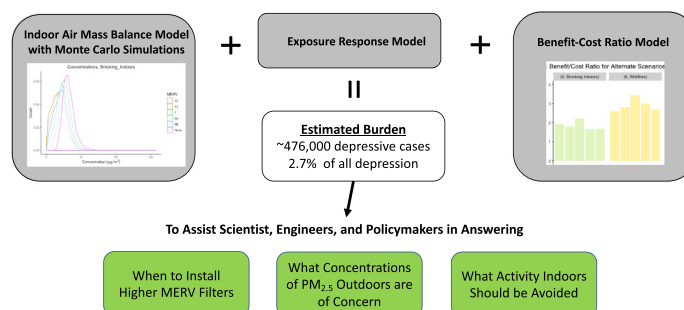
ARTICLE INFO

ABSTRACT

Recently published exploratory studies based on exposure to outdoor fine particulates, defined as particles with a nominal mean diameter less than or equal to 2.5 μm ($PM_{2.5}$) indicate that the pollutant may play a role in mental health conditions, such as major depressive disorder. This paper details a model that can estimate the United States (US) major depressive disorder burden attributable to indoor $PM_{2.5}$ exposure, locally modifiable through input parameter calibrations. By utilizing concentration values in an exposure-response function, along with relative risk values derived from epidemiological studies, the model estimated the prevalence of expected cases of major depressive disorder in multiple scenarios. Model results show that exposure to indoor $PM_{2.5}$ might contribute to 476,000 cases of major depressive disorder in the US (95% confidence interval 11,000–1,100,000), approximately 2.7% of the total number of cases reported annually. Increasing heating, ventilation, and air conditioning (HVAC) filter efficiency in a residential dwelling results in minor reductions in depressive disorders in rural or urban locations in the US. Nevertheless, a minimum efficiency reporting value (MERV) 13 filter does have a benefit/cost ratio at or near one when smoking occurs indoors; during wildfires; or in locations with elevated outdoor $PM_{2.5}$ concentrations. The approach undertaken herein could provide a transparent strategy for investment into the built environment to improve the mental health of the occupants.

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1. Introduction

The field of mental health research is expanding (ScienceDirect, n. d.), with good reason, as one in five Americans adults have a diagnosis of mental illness (Merikangas et al., 2010). One mental illness, major depressive disorder, impacted 17.7 million Americans in 2018 (*2018 NSDUH Annual National Report | CBHSQ Data*, n.d.) and globally was the third leading cause of disability in 2017 (*Global Burden of Disease Study 2017* (*GBD 2017*) *Burden by Risk 1990–2017 | GHDx*, n.d.). Previous research has identified risk factors for mental health disorders to include genetics (Silventoinen et al., 2010), environment factors (Kendler and Baker, 2007), and social determinants (Allen et al., 2014). Another potential contributor to negative mental health outcomes might be found in the built environment (Hoisington et al., 2019). Risk of a negative health outcome is often a function of exposure time, and in the case of the built environment, Americans spend 93% of their time indoors (Leech et al., 2002) and 70% of the time in their residence (Klepeis et al., 2001).

Major depressive disorder, also colloquially known as clinical depression, is characterized by a wide variety of symptoms that cause significant distress and impairment that affects individuals for a sustained period of time (American Psychiatric Association, 2013). Symptoms may consist of a persistent sad mood, loss of pleasure derived from or interest in hobbies or routinely pleasurable activities, a poor evaluation of the past, present, and future and of oneself, decreased energy, sleep, appetite or weight changes, and reduced functioning (American Psychiatric Association, 2013). Depression can co-occur with other mental health conditions/symptoms, including anxiety and posttraumatic stress disorder (Hirschfield, 2001; Spinhoven et al., 2014). Depressed individuals have higher odds of dying by suicide as compared to non-depressed individuals (Hawton et al., 2013).

Exposure to fine particulates, defined as particles with a nominal mean diameter less than or equal to 2.5 μm (PM$_{2.5}$), is a general health concern, providing the largest contributions to global mortality and morbidity due to air pollution (Hoek et al., 2013; Chen et al., 2008). PM$_{2.5}$ is theorized to influence depression and other mental health outcomes through two biological mechanisms, chronic inflammation and oxidative stress (Power et al., 2015). Chronic inflammation is an established contributor to mental health disorders (Anisman and Hayley, 2012; Raison et al., 2006; Bakunina et al., 2015; Rohleder, 2014; Miller and Raison, 2016), and PM$_{2.5}$ is associated with aggravation of chronic inflammation (Block and Calderón-Garcidueñas, 2009; Calderón-Garcidueñas et al., 2009). Inflammatory cytokines and other biological indicators of depression are more prevalent in individuals living in proximity to higher outdoor PM$_{2.5}$ concentrations (Block and Calderón-Garcidueñas, 2009; Calderón-Garcidueñas et al., 2009). Air pollutants such as PM$_{2.5}$ also can increase oxidative stress (Pham-Huy et al., 2008; Fournier et al., 2017). Specifically, free radicals associated with oxidative stress are highly reactive, producing harmful byproducts and tissue damage (Conner and Grisham, 1996). Oxidative stress has previously been connected to mental health outcomes, including depression (Black et al., 2015). Exploratory studies between outdoor PM$_{2.5}$ concentrations and mental health outcomes, including depression, have been noted (Power et al., 2015; Pun et al., 2017; Szyszkowicz et al., 2009; Kim et al., 2010; Yue et al., 2020; Lee et al., 2019). Specifically, long-term exposure to elevated PM$_{2.5}$ concentrations outdoors may increase the risk of depression by approximately 10% (95% confidence intervals = 2.3%–18.9%) (Braithwaite et al., 2019) and contribute to an acute depressive response in select individuals (Szyszkowicz et al., 2009).

Outdoor particles enter into the built environment and become indoor PM$_{2.5}$ (MacNeill et al., 2014; Qing et al., 2005; Weisel et al., 2005; Ji and Zhao, 2015) this concept has been applied in previous prospective studies that have correlated depression with outdoor concentrations of PM$_{2.5}$ measured at central outdoor monitoring stations (Braithwaite et al., 2019) that do not have spatial resolution (Chambliss et al.,

2020). Central filtration systems can abate indoor PM$_{2.5}$ concentrations (Brown et al., 2014; Bräuner et al., 2008; Montgomery et al., 2015; Fisk, 2013; Stephens and Siegel, 2013; Azimi et al., 2014), resulting in disease-related treatment cost avoidance (Fisk and Chan, 2017a; Zhao et al., 2015; Azimi and Stephens, 2013). The purpose of this paper was to develop an epidemiological model, using a mass-balance approach for PM$_{2.5}$ concentrations, that estimates the potential magnitude of the burden of indoor PM$_{2.5}$ and depression. A secondary focus of this paper was to determine the influence that different levels of filtration had upon the estimated cases of major depressive disorder. This is the first known use of an exposure-response model to estimate cases of depression resulting from indoor PM$_{2.5}$ exposure.

2. Methodology

This paper combines an epidemiological exposure-response function and indoor mass balance models to estimate the potential major depressive disorder impacts of indoor PM$_{2.5}$ exposure within a residential setting. To account for spatial variability of model input parameters in the US, Monte Carlo simulation was used to sample from known distributions of residential housing characteristics. Calculated indoor concentrations inform an exposure-response model to estimate the number of cases of major depressive disorder. Furthermore, an economic analysis was performed to identify the tradeoffs between the cost of various minimum efficiency reporting value (MERV) filter technologies, and major depressive disorder treatment cost avoidance. A summary schematic of the process used in the present paper is shown in Fig. 1. The modeling process includes eight different scenarios, representative of a range of outdoor PM$_{2.5}$ concentrations and indoor emissions: (1) US average; (2) New York City; (3) Cincinnati; (4) Sacramento; (5) homes with indoor smokers; (6) homes near wildfires; (7) extreme case 1; and (8) extreme case 2. No parameters were changed between model runs, other than the outdoor PM$_{2.5}$ concentrations and the indoor emissions in the smoking scenario. That is, all other model parameters are characteristic of nationally averaged US housing parameters. Therefore, these different scenarios represent the estimated depressive outcomes to occur if those conditions were present in the US.

2.1. Indoor air modeling

A mass balance approach was utilized to calculate the concentration of PM$_{2.5}$ within a typical US residence (Fisk and Chan, 2017a), as shown in Eqs. (1) and (2). Air within the homes was assumed to be well-mixed, and PM$_{2.5}$ concentrations were assumed to be steady state. All homes were assumed to utilize a forced-air heating, ventilation, and air conditioning (HVAC) system, as this is currently the most widely used system in the US (*Residential Energy Consumption Survey* (*RECS*) - *Analysis and Projections*, n.d.).

$$C = C_o \frac{P \lambda_V}{\lambda_V + \lambda_D + \lambda_F} + \frac{E}{(\lambda_V + \lambda_D + \lambda_F)V} \qquad (1)$$

where:

C = resulting concentration of PM$_{2.5}$ (μg/m^3)
C_o = the ambient air concentration of PM$_{2.5}$ (μg/m^3)
P = penetration factor (unitless)
λ_V = infiltration ventilation rate (h^{-1})
λ_D = rate of particle removal by deposition (h^{-1})
λ_F = rate of particle removal by filtration (h^{-1})
E = total emissions of PM$_{2.5}$ from indoor sources (μg/h)
V = building volume (m^3).

Discrete values for the factors in Eqs. (1) and (2) are summarized in Table 1. Ambient air concentrations were fit to lognormal distributions, calculated from mean and percentile values from 2018
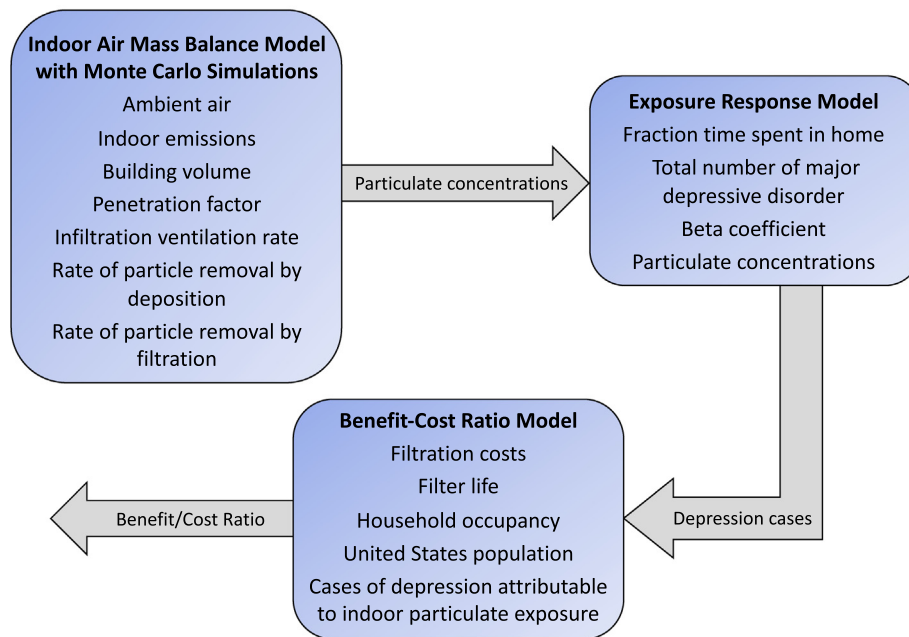
Fig. 1. Description of modeling process with input and output parameters. Blue boxes are for each major calculation, gray arrows are primary outputs.

(US EPA O, n.d.-a). The US scenarios all utilize data collected by the Environmental Protection Agency; this information as well as that about the other scenarios is referenced in the supplemental information. Cooking and smoking were the only sources of indoor emissions considered in the analysis. Cooking emissions were averaged over the course of a day in a normal distribution (Ozkaynak et al., 1996). Smoking was only considered in one of the eight case studies. Home volume was assumed to be normally distributed (Fisk and Chan, 2017a). Infiltration ventilation rate was fit to a lognormal distribution (Murray and Burmaster, 1995). Penetration factor and rate of particle removal by deposition were determined from residential studies (Ozkaynak et al., 1996; Williams et al., 2003). Penetration factor was determined using a cropped normal distribution, with an upper bound of one. The rate of particle removal by deposition was assumed to be normally distributed.

The rate of particle removal by filtration (λ_F) in the HVAC system was calculated using Eq. (2) (Fisk and Chan, 2017a). Duty cycle was a cropped normal distribution, with a minimum bound of zero (Fazli and Stephens, 2018). The flow rate through the residential HVAC

system was represented by a lognormal distribution, with distribution parameters obtained from two studies of residential housing characteristics (Jump et al., 2011; Stephens et al., 2011). Filter particle removal efficiency was assumed constant for each MERV rating (Brown et al., 2014), ignoring efficiency changes with increased dust buildup over time (Stephens and Siegel, 2011).

$$\lambda_F = DH\varepsilon_L \qquad (2)$$

where:

D = duty cycle (unitless)
H = airflow rate through HVAC system, divided by indoor volume (h^{-1})
ε_L = particle removal efficiency of filter in use (unitless).

Monte Carlo simulation methods were utilized to calculate concentration values and account for variability in the parameters used in Eqs. (1) and (2). First, distributions were created from the mean and

Table 1
Input parameter values and reference sources for Eqs. (1), (2), and (3).

Parameter (variable, units)	Values (mean, SD)	Source
Outdoor air (C_o, µg/m³)	Varies by scenario	(US EPA O, n.d.-b; Henderson et al., 2012; Sharma and Mandal, 2017; Zíková et al., 2016)
Emissions (E, µg/m³)	2.62, 1.11	(Ozkaynak et al., 1996)
Building volume (V, m³)	482, 28.68	(Fisk and Chan, 2017a)
Penetration Factor (P, unitless)	0.97, 0.06[b]	(Ozkaynak et al., 1996; Williams et al., 2003)
Infiltration ventilation rate (λ_V, h⁻¹)	0.53, 2.3[a]	(Murray and Burmaster, 1995)
Rate of particle removal by deposition (λ_D, h⁻¹)	0.39, 0.08	(Ozkaynak et al., 1996; Williams et al., 2003)
Rate of particle removal by filtration (λ_F, h⁻¹)	Variable	(Fisk and Chan, 2017a)
Duty cycle (D, unitless)	0.153, 0.051[c]	(Fazli and Stephens, 2018)
Airflow through residential HVAC system (Q, m³/s)	4.36, 1.44[a]	(Jump et al., 2011; Stephens et al., 2011)
Particle removal efficiency of filter in use (ε_L, unitless)	Variable	(Brown et al., 2014)
Percent of day spent within residence (F, unitless)	0.70	(Klepeis et al., 2001)
Annual number of major depressive disorder cases (m_0)	17,700,000	(2018 NSDUH Annual National Report | CBHSQ Data, n.d.)
Coefficient of exposure-response function (β, unitless)	0.009691	(Gu et al., 2019)
Median PM₂.₅ concentration of residence (Δx, µg/m³)	Varied by scenario	Eq. (1)

Abbreviations: HVAC, heating, ventilation, and air conditioning; PM₂.₅, particulate matter₂.₅, defined as particles with a nominal mean diameter less than or equal to 2.5 µm.
[a] Geometric mean and standard deviation.
[b] Maximum of 1.
[c] Minimum of 0.

standard deviation values for each parameter. Next, 100,000 concentrations were calculated using Eqs. (1) and (2), with random values selected from the distributions of each variable. Finally, the calculated concentrations were used to estimate major depressive disorder outcomes in the exposure-response function, detailed below. This process was replicated for each filtration system and each scenario, to understand the influence that filtration has on the estimated prevalence of major depressive disorder.

2.2. Exposure-response model

To quantify the number of major depressive disorder cases that can be attributed to indoor $PM_{2.5}$ exposure, an exposure-response function was utilized, Eq. (3) (Boulanger et al., 2017).

$$\Delta y = F m_o \left(1 - e^{(-\beta * C)}\right) \tag{3}$$

where:

Δy = number of adults diagnosed with a major depressive disorder as a result of indoor $PM_{2.5}$ exposure (incidences year^{-1})
F = average percent of day that the population spends in a residence (unitless)
m_0 = the number of adults diagnosed with major depressive disorder (incidences year^{-1})
β = coefficient of exposure-response function, selected from different epidemiology study results. $\beta = log(RR_{10})/10$, with RR_{10} describing the relative risk for an increase of 10 $\mu g/m^3$ in $PM_{2.5}$ concentration (unitless)
C = the median $PM_{2.5}$ concentration of the residence, calculated using the results of Eqs. (1) and (2) ($\mu g/m^3$).

It was assumed that US adults spend 70% of their day within their residence (Klepeis et al., 2001). The number of episodes of depression in the US was based on reports for adults (over 18 years old) in 2018 (*Results From the 2017 National Survey on Drug Use and Health: Detailed Tables*, n.d.). Beta values were converted from odds ratio values developed from epidemiological studies, summarized in a meta-analysis (Braithwaite et al., 2019), which included long-term odds ratio of 1.102 for depression cases associated with $PM_{2.5}$, with a 95% confidence interval of 1.023–1.189. Many applications of an exposure-response function utilize a relative risk instead of an odds ratio. Herein the relative risk and odds ratio can be considered equivalent since the baseline prevalence for depression is low (Braithwaite et al., 2019). The median $PM_{2.5}$ concentrations were calculated based on Eqs. (1) and (2). Some exposure-response studies utilize a baseline exposure value for concentrations, assuming that no adverse health effects occur below a select concentration (Boulanger et al., 2017; Cohen et al., 2017). However, the present analysis assumes a baseline exposure value of zero, practically meaning that any concentration could have an adverse health effect (Crouse et al., 2012; Pinault et al., 2016; Roman et al., 2008).

2.3. Economic analysis

To determine the value of indoor air filtration as a method to remove $PM_{2.5}$ for a health benefit, major depressive disorder treatment cost avoidance was estimated. Downscaling the estimated direct and indirect cost of depressive disorders in the US to individual cases resulted in an average annual cost of $14,926 (2017 dollars) per incidence of major depressive disorder (Greenberg et al., 2015). Multiplying the per-case cost by the estimated number of cases for each scenario yielded a total scenario cost. To determine the value of filtration, particulate matter filtration costs for filters with different efficiencies were compared to the potential cost avoidance of the reduced numbers of major depressive disorder cases, using Eq. (4). Hereafter, cost avoidance is

referred to as benefits, to conform with benefit-to-cost ratio (BCR) methodology, and to avoid confusion between costs of filtration and cost avoidance.

$$FC = \frac{F_i}{S} \tag{4}$$

where:

FC = annual cost of filter implementation (US dollars/capita)
F_i = annual operating cost of filter (US dollars)
S = average household occupancy (1.98 people over 18 years old/ household) (Bureau UC, n.d.)

The total cost of filtration assumes every house in the US has the same filter. Filter operating costs were taken from (Brown et al., 2014). The treatment cost avoidance was calculated with Eq. (5).

$$B = \frac{(\$MDD - \$MDD_i)}{N} \tag{5}$$

where:

B = benefit of filtration implementation, per person
$\$MDD$ = baseline cost of major depressive disorder attributable to indoor $PM_{2.5}$ exposure
$\$MDD_i$ = cost of major depressive disorder attributable to indoor $PM_{2.5}$ exposure with different filtration implementations
N = US population over 18 years old (255,190,602)

Calculating both costs and benefits of filtration allows a BCR to be calculated. The baseline cost of major depressive disorder attributable to indoor $PM_{2.5}$ exposure ($\$MDD$) assumes that the home has no filter on the HVAC system, allowing any $PM_{2.5}$ to recirculate within the home without reduction. The baseline cost value is calculated using Eqs. (1) and (2), with the particle removal efficiency (ε_L) set to zero. The resulting concentration is entered into Eq. (3) to estimate the number of major depressive disorder cases, and then multiplied by the cost of each case of depression ($14,926), ultimately representing the baseline cost of major depressive disorder attributable to indoor $PM_{2.5}$ exposure ($\$MDD$). Repeating this process for each individual MERV rating resulted in the cost of major depressive disorder attributable to indoor $PM_{2.5}$ exposure with different filtration implementations ($\$MDD_i$). The difference between each value and the baseline value, divided by the adult US population (N), results in a benefit value per person. All analysis was conducted in R (version 3.6.0) (R Development Core Team, 2011) and visualization was completed with the ggplot2 package (Wickham, 2011). R code used for the models and figures is provided in the supplemental information to enable further work by others in this field.

3. Results

The modeled residential $PM_{2.5}$ concentrations were calculated using Eqs. (1) and (2), in scenarios of different MERV filter use across the US and in specific US cities (Fig. 2A). Resulting concentrations (see Supplemental Figs. 1–8) and the median levels in the present model were lower than estimated values in other studies modeling indoor $PM_{2.5}$ (Fisk and Chan, 2017a; Azimi and Stephens, 2018), and measured concentrations in US residential environments (Qing et al., 2005; Walker et al., 2019).

The modeled concentrations for alternate scenarios (indoor smoking, wildfires, and extreme scenarios) of different MERV filters are shown in Fig. 2B. The wildfire scenario shows the highest indoor concentrations of any scenario. Measurements of $PM_{2.5}$ emissions from wildfires vary (Henderson et al., 2012; Rittmaster et al., 2006; Van Donkelaar et al., 2011), and, notably, the selected concentrations are high. Wildfires aside from the incident modeled in this analysis may not have the same concentration levels and impact on indoor
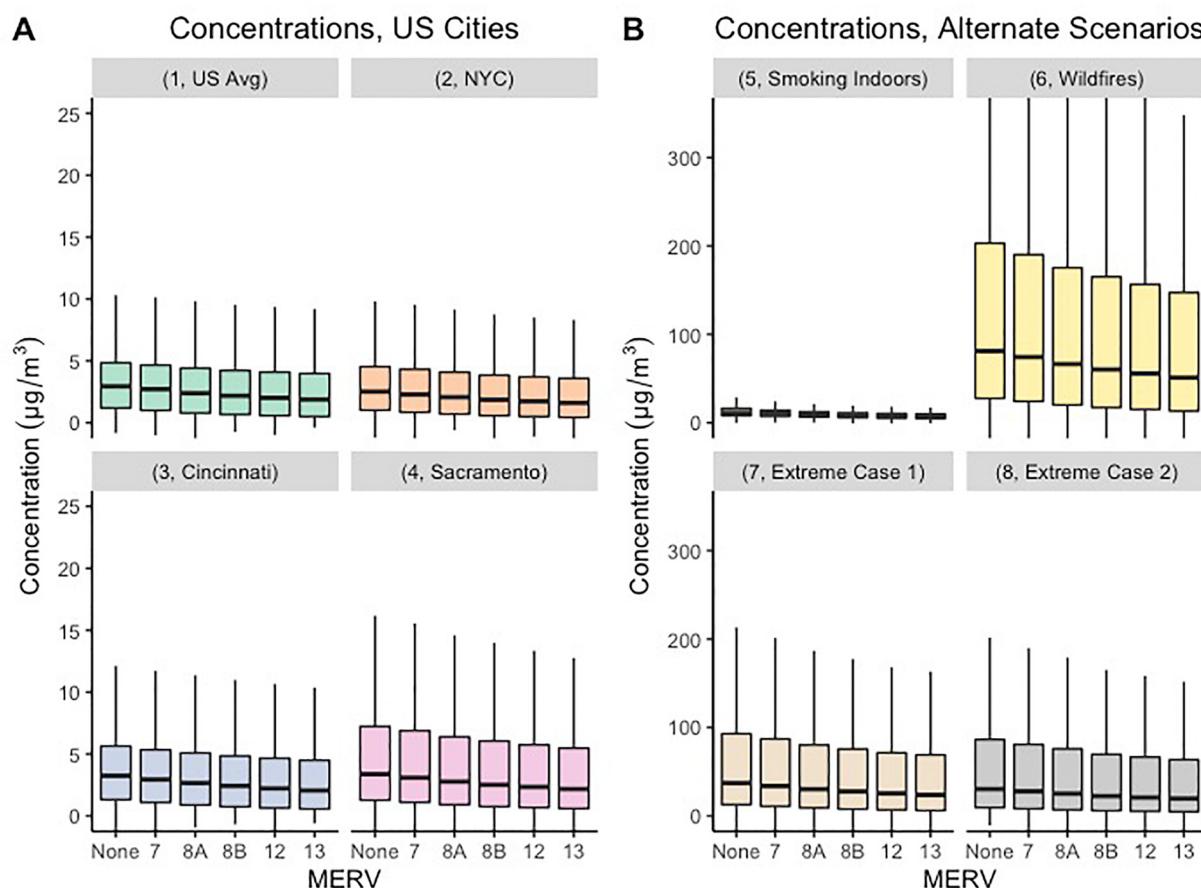
Fig. 2. Modeled indoor PM$_{2.5}$ concentrations across filters for A) United States cities and B) indoor smoking, wildfires, and extreme cases. Abbreviations: Avg, average; MERV, minimum reporting efficiency reporting values; NYC, New York City; US, United States.

PM$_{2.5}$ and, subsequently, health effects. The extreme case scenarios, as expected, show modeled indoor concentrations substantially higher than any of the other scenarios aside from the wildfire scenario. The extreme case scenarios use ambient PM$_{2.5}$ concentrations from large international cities, and as such are unlikely to be representative of conditions in the US. Certain locations close to high industrial activity or vehicular traffic may experience these levels of ambient PM$_{2.5}$.

The use of HVAC filters reduced the indoor concentrations of PM$_{2.5}$ in the US city scenarios from a no-filter condition by an average of approximately 8%, 18%, 24%, 31%, and 34%, for MERV 7, MERV 8A, MERV 8B, MERV 12, and MERV 13, respectively (Fig. 2A). Similar results were observed in the alternate scenarios; namely, filters reduced the modeled concentrations of PM$_{2.5}$ in alternate scenarios by an average of approximately 9%, 18%, 22%, 26%, and 32%, for MERV 7, MERV 8A, MERV 8B, MERV 12, and MERV 13, respectively (Fig. 2B). Studies of filtration efficiency vary in estimates of PM$_{2.5}$ removed when passing through the filter of the HVAC system (Azimi et al., 2014; Azimi et al., 2016), but they are consistent in the determination that increasing MERV ratings lowers indoor concentrations of PM$_{2.5}$.

Fig. 3A and B display the estimated incidences of major depressive disorder per million people, attributable to residential PM$_{2.5}$ exposure. The estimated cases of major depressive disorder in the model of the US average scenario are approximately 2.7% of the total number of major depressive disorder cases in the US, annually. Fig. 4 highlights the results of BCR calculations for implementation of different filtration systems in each scenario. BCR was generally higher in scenarios with higher indoor PM$_{2.5}$ values. Moreover, the filter with MERV rating 8B had the highest BCR among all scenarios, due to the balance of low price and relatively high removal efficiency.

For a direct comparison of the use of filters to impact the incidence of major depressive disorder, the same model parameters were used for each scenario. A comparison was made on the percent reduction in estimated incidence of major depressive disorder between no filter relative to MERV 7 in the US (Fig. 5A), and alternate scenarios (Fig. 5C), and then again from MERV 7 relative to MERV 13 in US (Fig. 5B), and alternate scenarios (Fig. 5D). The percent reduction in estimated incidence of major depressive disorder in the US cities scenario from zero filtration relative to a MERV 7 was independent of the outdoor concentration of PM$_{2.5}$ in the model and the 90th percentile was at 25.7% reduction in cases of major depressive disorder. In contrast, reduction from MERV 7 to MERV 13 in US scenarios has a less skewed distribution in the percent reduction, with the 90th percentile at 68.0% reduction in cases of major depressive disorder. The alternate scenario with elevated outdoor PM$_{2.5}$ concentrations (i.e. wildfires) did have some differences due to outdoor concentration levels.

4. Discussion

Indoor PM$_{2.5}$ concentrations were estimated using a mass balance approach, varying building parameters with Monte Carlo simulations. The resultant concentrations then provided an estimate of expected cases of major depressive disorder in an epidemiological exposure-response function. The BCR was based on a comparison of expected treatment costs avoided and the cost of residential filters, in order to determine which filter provided the best return on investment. Finally, the percent reduction in major depressive disorder was estimated based on increased filter efficiency. The analysis provides a framework for researchers to include major depressive disorder and other mental
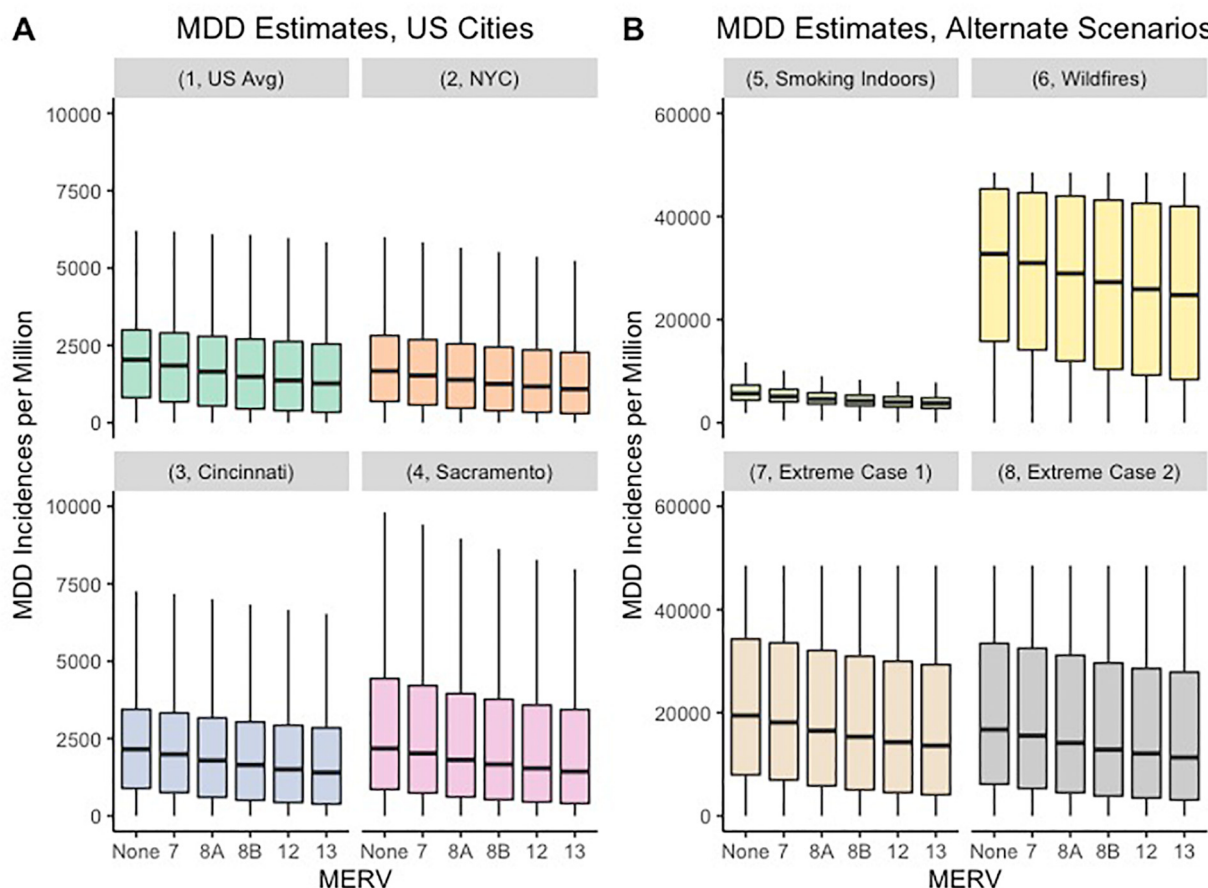
Fig. 3. Incidences per million people of major depressive disorder attributable to indoor PM$_{2.5}$ exposure across filter systems for A) United States cities and B) alternate scenarios. Abbreviations: Avg, average; MDD, major depressive disorder; MERV, minimum reporting efficiency reporting values; NYC, New York City; US, United States.

illnesses in burden of disease studies for indoor air pollutants such as PM$_{2.5}$ or other indoor air pollutants with established odds ratios.

The model estimates for concentrations of indoor PM$_{2.5}$ might be lower than previously reported, providing a conservative estimate for the incidence of major depressive disorder due to indoor pollutants in the present study. For example, the model estimates for the US average indoor PM$_{2.5}$ scenario with a MERV 7 filter calculated an indoor to outdoor (I/O) ratio of 0.37. This was lower than values reported in a meta-analysis of IO ratios (Chen and Zhao, 2011) (mean 0.92). The smoking scenario with a MERV 7 filter installed resulted in a median indoor PM$_{2.5}$ concentration of 10.33 μg/m^3. Two studies measuring indoor PM$_{2.5}$ concentrations in smoking households found median concentrations of 31 μg/m^3 (Semple et al., 2015) and 27.7 μg/m^3 (Wallace et al., 2003). However, the estimated outdoor concentrations of PM$_{2.5}$ in the US have been declining since 2000, which might have some influence on the comparisons (US EPA O, n.d.-b).

The impact of filter efficiency on the incidence of major depressive disorder was dependent on indoor emissions. It was observed that increases in filter efficiency had a higher impact on PM$_{2.5}$ concentrations in the smoking scenario compared to other scenarios, due to the emission of indoor PM$_{2.5}$ as opposed to contamination of indoor air by outdoor air, which is reduced by the build envelope. The American Society of Heating, Refrigeration, and Air Conditioning Engineers (ASHRAE) recommends at least a MERV 7 filter in residential buildings (American Society of Heating Refrigerating and Air Conditioning Engineers, 2019). However, in 2015 ASHRAE published new recommendations for residential units to install MERV 13 filters or higher in guideline 24-2015. The model estimates presented here reinforce that guidance, suggesting a change from a MERV 7 to a MERV 13 filter

could create a meaningful difference in reducing the incidence of major depressive disorder due to elevated PM$_{2.5}$ levels in indoor air.

While it does not appear there are any other studies estimating the impact that indoor PM$_{2.5}$ has upon depressive outcomes, comparisons to morbidity and mortality studies show similar trends to what was observed in this study. Specifically, a positive relationship exists between PM$_{2.5}$ concentrations and health outcomes (Cohen et al., 2017). A recently published meta-analysis of PM$_{2.5}$ exposure and mental illness (Braithwaite et al., 2019) included a population attributable fraction (PAF) model. The model estimated that the United Kingdom's rate of depression could be reduced by 2.5%, if the ambient PM$_{2.5}$ concentration dropped from 12.8 μg/m^3 to the World Health Organization's recommended limit of 10 μg/m^3 (Krzyzanowski and Cohen, 2008). However, the PAF model does not account for the lower levels of PM$_{2.5}$ concentrations experienced in indoor environments, as shown in this analysis, suggesting that the 2.5% reduction could be an overestimate. The caveat to that statement is when indoor emissions of PM$_{2.5}$ are present at meaningful levels (e.g., smoking).

Although the BCRs are below 1.0 for all of the US city scenarios, this analysis does not include the benefit of filtration for the purposes of avoiding any physical diseases associated with PM$_{2.5}$, such as asthma (Brown et al., 2014), lung cancer (Zhao et al., 2015), or chronic obstructive pulmonary disease (MacIntosh et al., 2010), suggesting that these are again conservative estimates. Since these BCRs are calculated based on median concentration values, variation in actual scenarios exist, with higher BCRs in some homes, and lower BCRs in others. For sensitive individuals, alternative means of filtration, used in addition to HVAC filters, may be an effective solution. Alternative means of filtration include portable air cleaners (Fisk, 2013; Spilak et al., 2014; Cox
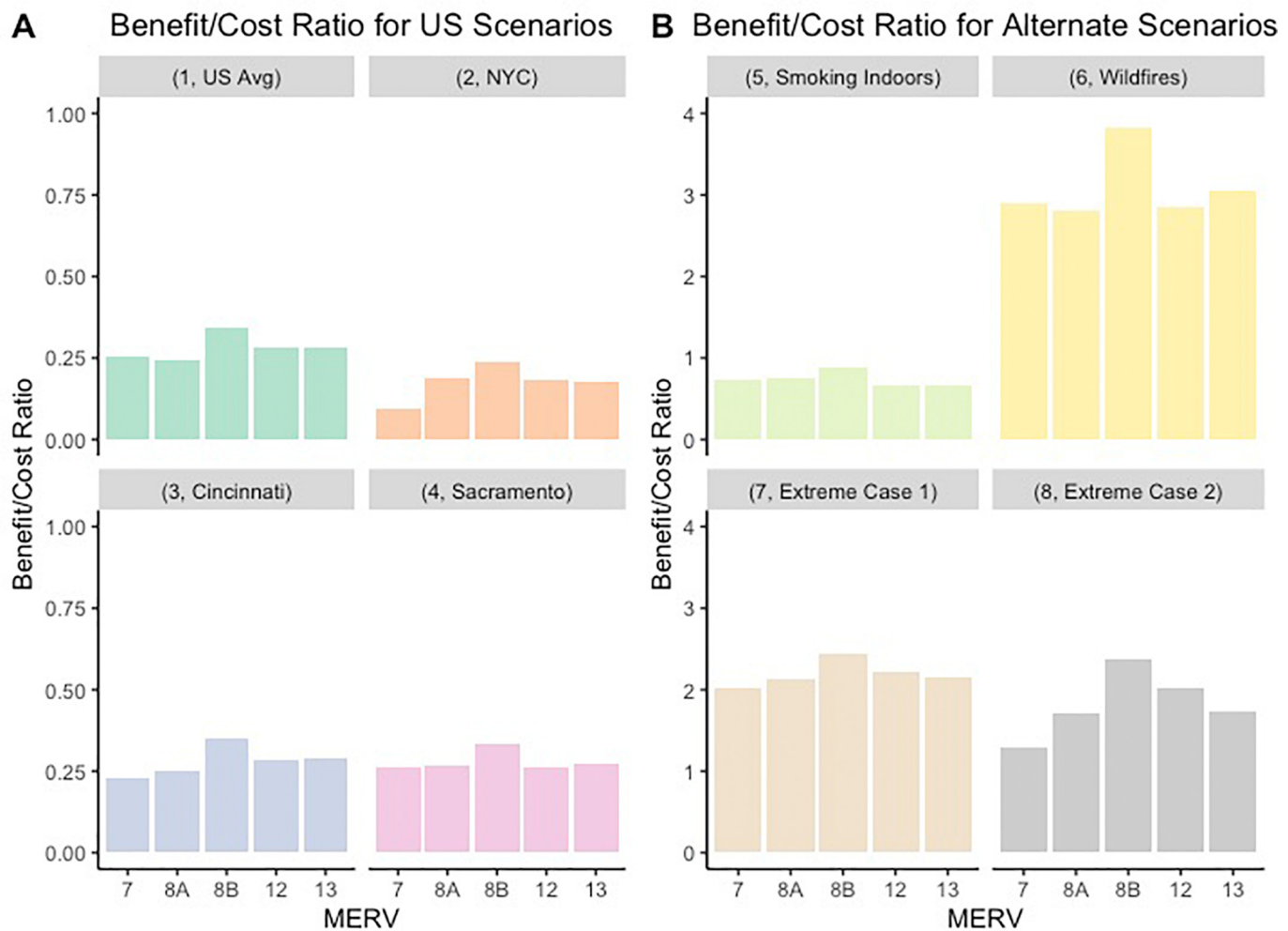
Fig. 4. Benefit/cost ratios (BCRs) for filter implementation in A) US Scenarios and B) Alternate Scenarios. Abbreviations: Avg, average; MDD, major depressive disorder; MERV = minimum reporting efficiency reporting values; NYC, New York City; US, United States.

et al., 2018), activated carbon filters (Kabrein et al., 2017; Yang et al., 2017), or even green walls (Perini et al., 2017; Pettit et al., 2017). An economic analysis of filtration methods for reducing $PM_{2.5}$ found that portable air filters had a mean BCR between 7.7 and 13, and provided more of a reduction in expected mortality rates than just HVAC filters alone (Fisk and Chan, 2017b).

Chronic inflammation and oxidative stress are both thought to contribute to depression and other mental health outcomes, and air pollutants other than $PM_{2.5}$, such as volatile organic compounds and mold, are associated with both of these mechanisms (Hope, 2013; Ratnaseelan et al., 2018; Kim et al., 2011; Grešner et al., 2016). $PM_{2.5}$ is also shown to influence gut microbiome profiles (Fitch et al., 2020), which some literature proposes are connected to mental health outcomes (Lowry et al., 2016; Hoisington et al., 2015). This introduces the possibility that poor indoor air quality could be contributing to more cases of depression than were estimated with this model. Although $PM_{2.5}$ comprises the bulk of disease research due to poor air quality (Chen et al., 2008), it cannot be ruled out that other pollutants may increase the burden of disease. Future models estimating depressive risk due to indoor pollutants should seek to include other pollutants in addition to $PM_{2.5}$.

Sensitivity analysis was performed on the odds ratio, the variable parameter in the model that was not considered in the Monte Carlo simulations. Maintaining the other parameters in the exposure-response function constant, the odds ratio has a strong influence on the predicted incidence of major depressive disorder in the model. The confidence interval bounds from the odds ratio (1.023, 1.189) in average US

concentrations with a MERV 7 filter produced an estimated number of major depressive disorder cases of 122,791 and 904,718, respectively. A difference of that magnitude in the model estimates highlights the urgent need to refine the relationship between $PM_{2.5}$ and depression in large population studies.

The model described in this paper was created to be adaptable to estimate major depressive disorder outcomes within other populations. To be as accurate as possible, mass balance input parameter distributions would need to be created for the population set to be analyzed. That is, estimates would need to be considered on parameters in Table 1 that are specific to the population of interest. Additionally, the total number of major depressive disorder cases within the region would replace the value used in this paper (17,700,000), and the population of the region would replace the value used in this paper (255,190,602). Finally, costs of residential air filters could be sourced for the area in order to create accurate BCR results.

4.1. Limitations

As this is the first known epidemiological model connecting indoor $PM_{2.5}$ concentrations and depression, we acknowledge there are several limitations in the present study. First, the relationship between $PM_{2.5}$ exposure and depressive outcomes is not clearly defined yet. A limited number of meta analyses of the relationship between $PM_{2.5}$ and depression are currently published, yet have similar results in their pooling of odds ratios from the available epidemiological studies, with values of
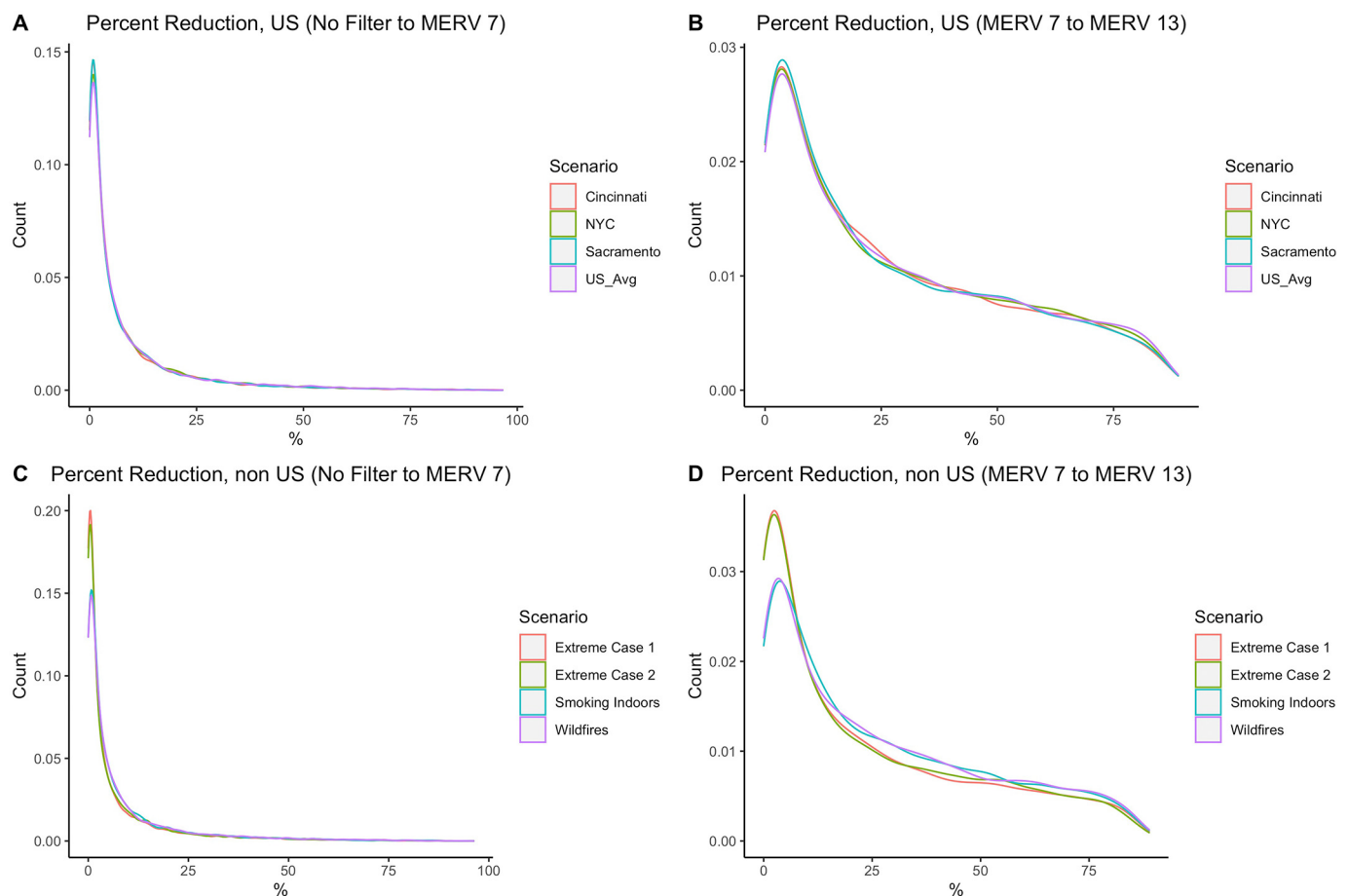
Fig. 5. Percent reduction in estimated incidence of major depressive disorder due to PM$_{2.5}$ in A) US cities, based on PM$_{2.5}$ concentrations in households with no filter relative to households using a MERV 7 filter, B) US cities, based on PM$_{2.5}$ concentrations in households with a MERV 7 filter relative to households with a MERV 13 filter, C) alternate scenarios based on PM$_{2.5}$ concentrations levels from households with no filter relative to households with a MERV 7 filter, D) alternate scenarios based on PM$_{2.5}$ concentrations in households with a MERV 7 filter relative to a MERV 13 filter. The y-axis "Count" indicates how many values of the results fall into each corresponding bin. Abbreviations: Avg, average; MDD, major depressive disorder; MERV, minimum reporting efficiency reporting values; NYC, New York City; US, United States.

1.10 (Braithwaite et al., 2019) and 1.12 (Fan et al., 2020). The mean number of studies analyzed in these meta analyses was 8.5. In comparison, a brief search of the more well-researched relationship between PM$_{2.5}$ and lung cancer mortality yielded four meta analyses, with values of 1.11 (RR) (Cui et al., 2015), 1.11 (RR) (Huang et al., 2017), 1.14 (OR) (Chen et al., 2015), and 1.09 (RR) (Hamra et al., 2014). The mean number of studies analyzed in those meta analyses was 12.25. Furthermore, differences in physiology between populations could influence the relationship between PM$_{2.5}$ and depression. At the time of this writing, no studies exist that attempted to quantify this relationship in the US population. As ORs become more established, the methods used in this paper (and code provide in the Supplementary Material) could be reanalyzed for PM$_{2.5}$ and depression, or other conditions as desired.

While the relationship between PM$_{2.5}$ and major depressive disorder may not be as robust as that between PM$_{2.5}$ and physical health, it is becoming increasingly clear there exists a relationship between the two variables. Establishing a causal relationship between PM$_{2.5}$ exposure and depressive outcomes via an exposure-response function can be accomplished through additional epidemiological studies. All PM$_{2.5}$ exposure was assumed to result in the same magnitude of depressive outcomes, regardless of source-specific PM$_{2.5}$ and evidence exists to suggest that this is a reasonable assumption (Cohen et al., 2017).

PM$_{2.5}$ levels were assumed as a snapshot in time, but it is acknowledged that while PM$_{2.5}$ concentrations have been decreasing across the US since 2000, they are increasing worldwide (Butt et al., 2017), and may remain elevated in the US due to scenarios such as proximity

to wildfires or environmental regulation changes. Approximately 90% of new homes in the US are constructed with central forced air systems, but the total number of homes with central forced air systems are lower across the entire nation (Agency UEI, 2018). The model for calculating indoor PM$_{2.5}$ concentrations will not be accurate for homes without central forced air systems, adding more uncertainty to the final estimate of the calculated depression cases. In addition, other models of indoor air quality calculate duty cycle based on site location and typical heating and cooling loads. This analysis forgoes this method and represents the variability in duty cycle values with the Monte Carlo sampling. Due to the analysis being applied to an annual period, the duty cycle was more accurately represented as a distribution. Cooking and smoking were the only sources of indoor PM$_{2.5}$ considered in this analysis, due to their well-documented emission values (Ozkaynak et al., 1996; Semple et al., 2015; Wallace et al., 2003; Hu et al., 2012). Other activities may also contribute to indoor PM$_{2.5}$ concentrations, such as cleaning or occupant movement (Ferro et al., 2004). However, these activities were considered too variable to include in this analysis. As a result, the calculated PM$_{2.5}$ concentrations and major depressive disorder estimates may be a conservative estimate, and not representative of all PM$_{2.5}$ sources potentially present in the indoor environment.

PM$_{2.5}$ composition may vary based on source apportionment (Titos et al., 2014; Mazzei et al., 2008; Pey et al., 2009), and estimates of morbidity and mortality assume that all PM$_{2.5}$ provides the same level of toxicity (Cohen et al., 2017). The model described in this paper assumes that the ambient PM$_{2.5}$ and the indoor generated PM$_{2.5}$ influence

human physiology in the same manner. Current literature suggests that there is no relationship between $PM_{2.5}$ composition and toxicity (Stanek et al., 2011), and that magnitude of exposure is the sole predictor for health effects. However, it is possible that composition of $PM_{2.5}$ may affect major depressive disorder outcomes in a manner different from physical mortality and morbidity, changing the estimation of the incidence of major depressive disorder described within this analysis. Microbial components and endotoxins are present in some sources of $PM_{2.5}$ (Jalava et al., 2016), and are potentially a source of influence on major depressive disorder outcomes (De La Garza, 2005) through inflammatory mechanisms (Tonelli et al., 2008; Tonelli and Postolache, 2010). $PM_{2.5}$ retained in the nasal passage can bypass the blood brain barrier (Tonelli and Postolache, 2010) and lead to worse depressive like behavior, brain expression of cytokines, and corticosteroid production compared to intraperitoneal transmission (Tonelli et al., 2008).

Finally, indoor $PM_{2.5}$ concentrations were assumed to occur in a well-mixed environment. In reality, residential homes can be poorly mixed, and some areas of the home will experience higher concentrations of $PM_{2.5}$, while others will have lower concentrations. This variability is accounted for in the Monte Carlo simulations, via random sampling of the distributed parameters. However, select indoor activities may cause a spike in $PM_{2.5}$ concentrations and exposure, such as cooking or resuspension of $PM_{2.5}$ due to cleaning. These spikes in $PM_{2.5}$ concentration may increase risk of acute depressive symptoms, but the epidemiological data do not exist to accurately model that impact. Specifically, the model described in this paper was not applied to analyze acute depressive symptoms due to indoor $PM_{2.5}$ exposure, but evidence exists to suggest that effect may occur (Semple et al., 2015; Hiscock et al., 2012).

5. Conclusions

The results of this analysis highlight the role that $PM_{2.5}$ has upon depressive outcome. The model described herein could be used to estimate the influence that $PM_{2.5}$ exposure has upon other mental illnesses, provided those illnesses have established relationships (ORs or RRs) with $PM_{2.5}$. These results raise the question of how impactful other indoor air pollutants are on mental health outcomes. While $PM_{2.5}$ has the highest contribution to mortality estimates of air quality (Hoek et al., 2013; Chen et al., 2008), other pollutants may have a higher degree of impact on mental health outcomes. Future research may want to include socioeconomic status, as it may represent a potential confounding factor in linking analysis of particulate matter with major depressive disorder. For example, people of lower socioeconomic status are more likely to live in areas of higher air pollution (Evans and Kantrowitz, 2002), have poor quality homes that potentially lead to higher rates of pollutant exposure (Adamkiewicz et al., 2011), and higher rates of depression (Everson et al., 2002). Moreover, smoking is a more popular activity among less affluent groups (Hiscock et al., 2012), and is associated with depression (Glassman et al., 1990; Brown et al., 1996; Fergusson et al., 2003). Additionally, socioeconomic status has an established relationship with physical morbidity (Luepker et al., 1993; Connolly et al., 2000; Ward et al., 2004), itself a risk factor for mental illness (Geerlings et al., 2000). Yet not all confounders are negative. For instance, household size is larger in areas of lower socioeconomic status (Espenshade et al., 1983), which would result in shared benefit of a higher quality filter for additional people at reduced per capita cost.

CRediT authorship contribution statement

William L. Taylor: Conceptualization, Methodology, Software, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization. **Steven J. Schuldt:** Formal analysis, Writing – review & editing. **Justin D. Delorit:** Validation, Formal analysis, Writing – review & editing. **Christopher M. Chini:** Software, Formal analysis, Writing –

review & editing, Visualization. **Teodor T. Postolache:** Conceptualization, Writing – review & editing. **Christopher A. Lowry:** Conceptualization, Writing – review & editing. **Lisa A. Brenner:** Conceptualization, Writing – review & editing. **Andrew J. Hoisington:** Conceptualization, Methodology, Investigation, Resources, Writing – original draft, Writing – review & editing, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2020.143858.

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