



Deposited via The University of Leeds.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/id/eprint/100198/>

Version: Accepted Version

---

**Article:**

Schmitt, LHM (2016) QALY gain and health care resource impacts of air pollution control: A Markov modelling approach. *Environmental Science & Policy*, 63. pp. 35-43. ISSN: 1462-9011

<https://doi.org/10.1016/j.envsci.2016.05.015>

---

© 2016, Elsevier. Licensed under the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International <http://creativecommons.org/licenses/by-nc-nd/4.0/>

**Reuse**

Items deposited in White Rose Research Online are protected by copyright, with all rights reserved unless indicated otherwise. They may be downloaded and/or printed for private study, or other acts as permitted by national copyright laws. The publisher or other rights holders may allow further reproduction and re-use of the full text version. This is indicated by the licence information on the White Rose Research Online record for the item.

**Takedown**

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing [eprints@whiterose.ac.uk](mailto:eprints@whiterose.ac.uk) including the URL of the record and the reason for the withdrawal request.

# QALY gain and health care resource impacts of air pollution control: a Markov modelling approach

Laetitia Helene Marie Schmitt\*

*Academic Unit of Health Economics, University of Leeds, Leeds, LS2 9LB, UK*

---

## Abstract

This paper proposes a novel complementary approach to evaluate the public health benefits of air pollution control, where the joint impact on individuals' quality and length of life is fully quantified using Markov modelling. A Markov model which captures, for the first time: (i) air pollution's influence on population individuals' quality of life and life expectancy at baseline and (ii) dynamics in individuals' susceptibility to air pollution exposure, is developed. In order to represent the body of epidemiological evidence on the cardio-respiratory effects of long-term exposure to fine particulate air pollution, the model is structured around three diseases: chronic obstructive pulmonary disease, coronary heart disease and lung cancer. Application of the model provides the first estimates of age and gender-specific quality-adjusted life years (QALY) gains from air quality improvement in the UK. Reducing mean  $PM_{2.5}$  concentrations by  $1\mu g/m^3$  in London and in England and Wales is expected to yield more than 63,000 and 540,000 QALYs respectively, to adults aged 40 and above over their remaining lifetime, discounting at 3.5% p.a. At a WTP value for a QALY of £65,000, which is in line with recommendations for the UK, the expected discounted monetary benefit of the intervention amounts to £4 billion in London and £34 billion in England and Wales.

---

\*Corresponding author.

*Email address:* l.h.m.schmitt@leeds.ac.uk +44(0)113 3430840 (Laetitia Helene Marie Schmitt\*)

*Keywords:* Air pollution, QALY, Health care cost, Economic evaluation, Markov modelling

---

## 1. Introduction

In recent years, as the body of evidence on the adverse health effects of air pollution has kept on growing, policy-makers have been increasingly under pressure to take action but also, to ensure that further air quality efforts are worthwhile (HEI, 2003). This has spurred several *ex ante* economic evaluations of large-scale regulatory interventions of air pollution control (e.g. Revisions to the National Ambient Air Quality Standards for Particulate Matter in the US (US EPA, 2012), Clear Air for Europe (Holland et al., 2005), revisions of the E.U. Gothenburg Protocol (Holland et al., 2011)) and of a large number of hypothetical scenarios of air pollution reduction on a local, national or global scale (Bell et al., 2011).

The mortality effects of reducing air pollution are traditionally quantified in premature deaths avoided or life expectancy gains using life-tables, whereas morbidity impacts are measured in counts of avoided morbid cases obtained by health impact functions (Medina et al., 2013). In addition to being quantified with a static quantification tool, the morbidity effects considered are primarily acute (e.g. hospitalizations, respiratory exacerbations) following short-term variations in air pollution exposure (WHO, 2013). Consequently, the long-term quality of life impacts associated with a reduction in chronic morbidity following a sustained decrement in ambient levels of air pollution, have largely been ignored.

This paper therefore proposes a novel complementary approach to evaluate the public health benefits from air pollution control, where the joint impact on individuals' quality and length of life, measured in quality-adjusted life years (QALYs), is fully quantified using Markov modelling.

The QALY combines morbidity and mortality effects into a single index and is obtained by multiplying the period of time spent in a given health state by health-related quality of life (HRQoL) weights associated with that state (Gold et al., 2002). The benefits of using this metric in environmental health policy include the ability to compare health outcomes from different policies, to consider another dimension than quantity of life and to encompass individuals' preferences between alternative health states (Ponce et al., 2001). In addition, since the QALY routinely supports health care resources allocation (Drummond et al., 2005), its use in the assessment of air pollution control interventions can support the comparison with health care interventions, for which cost-effectiveness decision rules are typically in place.

Whilst there have been a number of attempts to estimate the QALY gain from air pollution reduction, they all suffer from two main limitations. To put them into context, it should be noted that air pollution can affect individuals' health via three main pathways to effect: (A) development of chronic conditions that reduce life expectancy and quality of life but are unrelated to the timing of death; (B) death advancement, following acute exposure, in frail individuals whose frailty is unrelated to air pollution exposure; and (C) development of chronic conditions leading to frailty combined with death advancement following acute exposure (Künzli et al., 2001). Correct quantification of the QALY impacts of air pollution exposure requires to jointly consider these three pathways to effect, in particular to avoid under-estimating the life expectancy and quality of life loss associated with the premature deaths of individuals in pathway C (Hubbell, 2006). This challenging issue, however, has not yet been adequately addressed. Using the life-table method, Coyle et al. (2003) simply applied HRQoL weights for the general population to the life year gains from a lower risk of premature mortality and completely ignored the quality of life gains associated with reduced morbidity. Cohen et al. (2003) used a similar method but assumed that all the individuals who die prematurely from air pollution suffered from a preexisting coronary or respiratory condition, without accounting for air pollution's role in driving a subset of them to such health state. Such an

approach further contributed to underestimating the QALY gain of air pollution control. Whilst Hubbell (2006) partly accounted for air pollution's impact on quality of life via the development of chronic bronchitis, he did not use the resulting level of quality of life as a baseline to adjust the life years gains from a reduced mortality risk. This use of a double baseline of HRQoL weights to assess respectively morbidity and mortality effects - an approach also used by the US EPA (US EPA, 2006) to estimate MILYs - no longer allows a linear substitution between quality and quantity of life and thus, clearly departs from the QALY.

Second, none of the above-mentioned studies accounted for the fact that individuals suffering from a compromised health condition are expected to be more susceptible to air pollution exposure than healthier individuals (Peled, 2011; Sacks et al., 2011; US EPA, 2009). Health-related heterogeneity in susceptibility to air pollution drives the distribution of impacts among population subgroups stratified by health condition. It is therefore key to accurately adjust life expectancy effects with HRQoL weights.

In contrast, by simulating individuals' health trajectories over time to and from a set of mutually exclusive and exhaustive health states, the proposed Markov modelling-based approach provides two core advantages to estimate the QALY gain from air pollution abatement. First, individuals' quality of life and life expectancies are no longer treated as exogenous parameters. Instead, they are endogenously determined as a function of individuals' current health conditions, where the influence of air pollution in driving them to their respective states of health is fully accounted for. Second, individuals' change in susceptibility to air pollution exposure over time, as a consequence of a degraded health condition that may or may not be associated with air pollution exposure, is encompassed. Thanks to these two features, the lifetime impact of chronic air pollution exposure on individuals' quality and length of life is fully captured.

In addition, the proposed approach can quantify both the health care savings from a reduced occurrence of morbidity events, as well as the health care costs from extending the lives of individuals with chronic medical conditions. As a

90 consequence, the total health care budget impact of reducing air pollution can  
be evaluated.

The objective of this paper is threefold. It aims to: (i) translate the rich  
body of epidemiological evidence on the adverse health effects of fine particulate  
pollution into chronic conditions associated with well-documented effects on  
95 life expectancy, quality of life and health care costs; (ii) construct a Markov  
model that captures the main characteristics of these chronic conditions and  
encompasses the most relevant epidemiological evidence; (iii) apply the model  
to quantify, for the first time, age and gender-specific QALY gains and total  
health care resource impacts of reducing  $PM_{2.5}$  concentrations in England and  
100 Wales and in London respectively.

## 2. Materials and methods

### 2.1. Scope of analysis

105

The present analysis aims to quantify the lifetime impacts on life expectancy,  
quality of life and health care resources of reducing population exposure to  
 $PM_{2.5}$ , i.e. particulate matter smaller than  $2.5\mu m$  in aerodynamic diameter,  
which is considered to adversely affect population health more than any other  
110 air pollutant (WHO, 2014).

Given the chosen timescale, only chronic health effects from long-term expo-  
sure are modelled. Consequently, short-term quality of life effects from morbid  
events triggered by acute exposure, such as respiratory exacerbations for in-  
stance, are not presently taken into account<sup>1</sup>. The latter are, however, not  
115 expected to drive levels of quality of life over a lifetime.

---

<sup>1</sup>It should be noted that the life-shortening effect of acute exposure is captured in the  
overall change in death risk associated with chronic exposure (Künzli et al., 2001).

Although children are expected to be particularly susceptible to air pollution (Peled, 2011), documented adverse effects primarily pertain to respiratory exacerbations following acute exposure, which are outside the present scope of analysis, or to subclinical respiratory conditions (e.g. reduced lung growth) which are not well characterised with incidence and prevalence statistics. On these grounds, the present analysis focuses on chronic health impacts experienced in adulthood. Importantly, since chronic respiratory impacts in adults partly derive from the worsening over time of subclinical conditions developed since childhood (Eisner et al., 2010; Peled, 2011), the long-term damaging impact of chronic  $PM_{2.5}$  exposure on children's lung development should to some extent, be encompassed in the analysis.

## 2.2. *Main chronic health impacts in adults*

As explained in section 1, the life shortening impact of particulate air pollution exposure is expected to be greatly mediated via the increase in the risks of developing chronic conditions. Epidemiological studies suggest a positive association between long-term exposure to fine particulate air pollution and coronary atherosclerosis (Adar et al., 2013), myocardial infarction (Lipsett et al., 2011), coronary re-vascularization (Miller et al., 2007) and acute and sub-acute forms of coronary heart disease (Cesaroni et al., 2014). Whilst particulate matter (PM) exposure has also been associated with stroke (Miller et al., 2007), to date the overall evidence of association with regards to long-term exposure remains weak (Brook et al., 2010). Based on this body of evidence and constraints in terms of required population statistics, the impacts of chronic air pollution exposure on the cardiovascular system were modelled using coronary heart disease (CHD) - ICD-10 I20-I25 - as health endpoint.

A number of studies have also shown positive associations between PM exposure and respiratory symptoms (Schindler et al., 2009; Abbey et al., 1995) as

well as lung function decrements (Downs et al., 2007), all of which are associated with chronic obstructive pulmonary disease (COPD). Although the body of evidence linking PM exposure and COPD development remains incomplete (Schikowski et al., 2013), such association is likely as reduced pulmonary growth  
150 in childhood and adolescence - for which the link with PM exposure is now established - increases the incidence of COPD later in life (Eisner et al., 2010). The COPD disease pathway (ICD-10 J40-J44) was therefore chosen to model the chronic respiratory impacts of PM exposure.

Lung cancer (ICD-C33-34), which has repeatedly been found to be associated with chronic PM exposure (Hamra et al., 2014), was considered as a third  
155 morbidity endpoint.

### *2.3. Model structure*

#### *160 2.3.1. Markov models: key features*

Discrete time Markov models are extensively described in Sonnerberg and Beck (1993). They have two key structural components: (i) mutually exclusive and exhaustive health states and (ii) transition probabilities (TP) which represent the probability of transiting between health states during a cycle “c”,  
165 conditional on being in a given health state in cycle “c-1”. TP can, however, be conditional on past health history using tunnel states in which individuals can only spend one cycle. TP are typically stratified by age and gender and are time-dependent.

170

#### *2.3.2. Disease pathways*

The model was built around three disease pathways - one for each chronic morbid condition defined in section 2.2 - alongside the states “dead” and “healthy”,

175 where the latter represents a health state exempt of any of the three conditions.  
As the analysis timescale was the individual’s lifetime, the cycle period was set  
to one year. Due to data gaps pertaining to co-morbidity risks, the model as-  
sumed competitive risk between the three diseases, i.e. one individual cannot  
suffer from two or more conditions at the same time. In addition, each disease  
180 pathway was underpinned by the following structural assumptions:

*COPD.* As health care cost, quality of life decrements and mortality risk greatly  
depend on the level of airflow obstruction, the COPD pathway was structured  
around the four severity stages: GOLD 1 to GOLD 4, defined by the Global ini-  
tiative for chronic Obstructive Lung Disease (GOLD, 2014). Although COPD is  
185 treatable, it is not reversible and typically slowly worsens over time. In addition,  
it is often diagnosed in late stages (GOLD, 2014). To reflect these characteris-  
tics, the COPD pathway was designed as unidirectional - i.e. transitions back  
to “healthy” or to a less severe state were not permitted - and upon entry into  
the disease pathway, no jump of severity stage was allowed. By contrast, to  
190 reflect the reality of late diagnosis, transitions from the state “healthy” to the  
first three severity levels of the disease were allowed (see Figure 1).

*CHD.* Although CHD also has different levels of severity that will influence  
quality of life and life expectancy, in the absence of a widely accepted classifica-  
tion of the disease by severity stages, the CHD pathway was composed of only  
195 one state. The CHD pathway was also designed as unidirectional, since CHD is  
a chronic condition that requires long-lasting disease management.

*Lung cancer.* Whilst 5-year lung cancer survivors remain at risk of cancer re-  
currence, most recurrences (around 80%) occur about 2 years after surgical  
resection (Maeda et al., 2010). Consequently, it was assumed that after 5 years  
200 alive with the condition, individuals would transit back to the state “healthy”,  
from where they would face the same risks of adverse health events and enjoy  
the same quality of life as “healthy” individuals of same age and gender. The  
disease pathway was structured around five tunnel states, in order to differenti-

ate lung cancer patients and their survival probabilities according to the period  
205 of time during which they had been suffering from the disease.

### *2.3.3. Intervention arm and risk reduction estimates*

To evaluate an intervention of air pollution reduction, the model requires:  
210 a “baseline” arm populated with baseline TP and (ii) an “intervention” arm  
in which baseline TP are combined with risk reduction estimates (RRE). The  
latter are epidemiological risk estimates scaled to the decrement in exposure  
associated with the intervention under evaluation.

In addition to morbidity RRE that represent the decrease in the risks of  
215 developing lung cancer, CHD and COPD, mortality RRE were applied in the  
“intervention” arm so that the total life expectancy gain from air pollution  
reduction, mediated by the three pathways to effect described in section 1,  
would be captured.

In line with WHO (2013)’s recommendations, mortality RRE pertaining to  
220 all causes of death were used. The specificity of the present model, however,  
is that it relies on mortality RRE stratified by health status, i.e. conditional  
on having CHD or COPD or LC or on being “healthy”. Such an approach is  
key to: (i) capture health-related differential susceptibility to air pollution, by  
allowing for a different magnitude of death risk reduction according to whether  
225 individuals are frail or not; and (ii) avoid double-counting the life expectancy  
gains from the reduced risk of developing a chronic cardio-respiratory condition,  
which are already encompassed via the application of morbidity RRE in the  
model. It follows that the change in death risk that was applied to “healthy”  
individuals pertains to all the other causes of death than the three modelled.

230 The change in death risk in individuals who had developed COPD and CHD,  
be it due to air pollution exposure or for any other reasons, was informed by  
Zanobetti et al. (2008) and Tonne and Wilkinson (2013)’s respective estimates  
of excess risk of all-cause mortality associated with chronic PM exposure in

these two populations subgroups. Zanobetti et al. (2008) results, however, were  
235 based on COPD patients who were aged above 65 years old and had been  
identified using hospital discharge data. As the risk of hospital admission for  
COPD greatly increases with disease severity, in order to limit study results  
extrapolation, the study's risk estimate was applied only to individuals aged 65  
and above if they were in GOLD 3 or 4 states. Individuals with COPD in GOLD  
240 stages 1 and 2 or, in GOLD stages 3 and 4 but aged below 65, were instead  
assumed to face the same reduction in mortality risk as the general population.

Similarly, Tonne and Wilkinson (2013)'s study was based on patients above  
25 years of age admitted to hospital following acute coronary syndrome (ACS).  
ACS reflects a more severe health condition than CHD as a whole. Since the risk  
245 of ACS strongly increases with age (Simms et al., 2012), Tonne and Wilkinson  
(2013)'s risk estimate was applied to individuals suffering from CHD only if they  
were aged 75 or above. Individuals with CHD aged below 75 were assumed to  
face the same reduction in mortality risk as the general population.

Finally, since lung cancer is associated with a high risk of death, the impact  
250 of  $PM_{2.5}$  exposure was restricted to disease development ( $RRE_c$ ). In other  
words, reducing air pollution was assumed to have no impact on the mortality  
risk of individuals with lung cancer.

RRE and the TP they apply to are presented in Table 1. Risk estimates  
were preferably taken from meta-analyses to decrease parameter uncertainty.  
255 They were obtained from studies undertaken in developed countries that are  
characterised by  $PM_{2.5}$  concentrations ranging from about 7 to 35  $\mu g/m^3$ , for  
which linearity in health impacts and absence of threshold to effects has typically  
been found (Lepeule et al., 2012; Crouse et al., 2012; Krewski et al., 2009).  
This implies that within the above concentrations range: (i) estimates of health  
260 effects for a different level of pollution reduction may be obtained to a very good  
approximation by proportional scaling of the results obtained for a 1  $\mu g/m^3$   
reduction; (ii) RRE can be derived from risk estimates - typically expressed  
per 10 $\mu g/m^3$  increment - using logarithmic multiplicative scaling. RRE values  
provided in Table 1 are expressed for a 1  $\mu g/m^3$  decrement.

Figure 1 represents the structure of the intervention arm of the model, where ovals represent health states and arrows represent the allowed transitions between them. Dotted arrows represent RRE-adjusted transitions, i.e. transitions for which the underlying risk of event is reduced under pollution reduction, whereas full arrows represent transitions for which the underlying risk of event is assumed to be unchanged under intervention.

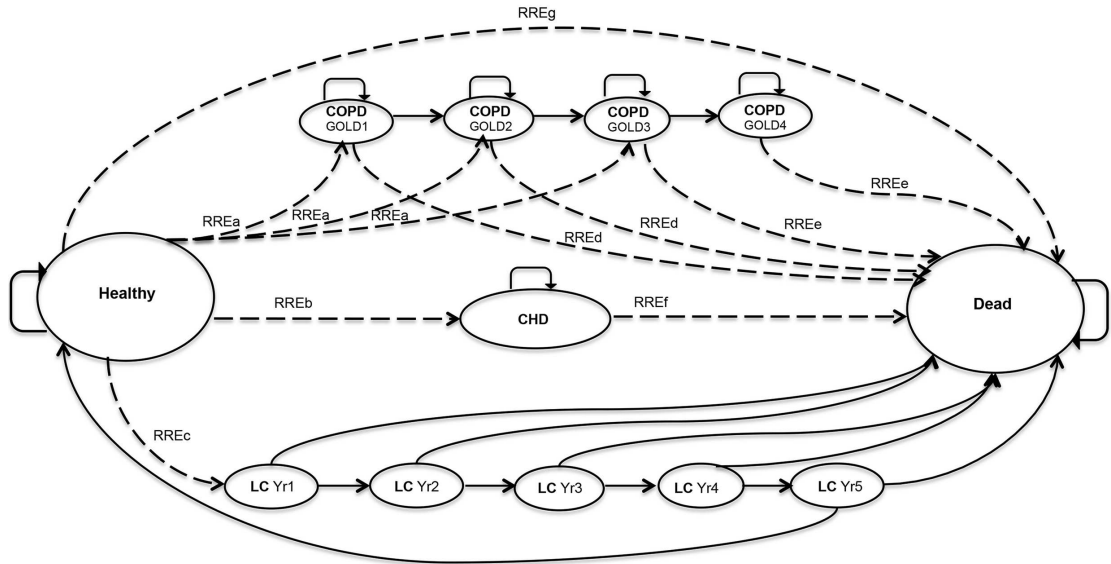


Figure 1: Diagram of the intervention arm of developed Markov model.

*Abbreviations:* COPD: chronic obstructive pulmonary disease; CHD: coronary heart disease; LC: lung cancer; Yr: year. Risk reduction estimates  $RRE_a, \dots, g$  are defined in Table 1.

Parameter Name	Transition Probability $P_{X,Y}^{(a)}$	Pop. age	Risk Reduction Estimates (RRE)		
			Risk Estimates		Mean (95%CI) $\Delta_{PM2.5} = -1\mu g/m^3$
			Definition	Source	
RREa	$P_{H,COPDi}$ $i=GOLD1,\dots,3$	All	$OR_{Dev.COPD}$	Schikowski et al. (2014) <sup>(b)</sup>	0.988 (0.918-1.065)
RREb	$P_{H,CHD}$	All	$HR_{Dev.CHD}$	Cesaroni et al. (2014) <sup>(b)</sup>	0.976 (0.949-1.004)
RREc	$P_{H,LC}$	All	$HR_{Dev.LC}$	Hamra et al. (2014) <sup>(b)</sup>	0.985 (0.980-0.991)
RREd	$P_{COPDi,D}$ $i=GOLD1,\dots,2$	All	$HR_{DeathAC}$	Hoek et al. (2013) <sup>(b)</sup>	0.993 (0.991-0.995)
RREe	$P_{COPDi,D}$ $i=GOLD3,\dots,4$	$< 65$	$HR_{DeathAC}$	Hoek et al. (2013) <sup>(b)</sup>	0.993 (0.991-0.995)
		$\geq 65$	$HR_{DeathAC COPD}$	Zanobetti et al. (2008) <sup>(c)</sup>	0.980 (0.976-0.984)
RREf	$P_{CHD,D}$	$< 75$	$HR_{DeathAC}$	Hoek et al. (2013) <sup>(b)</sup>	0.993 (0.991-0.995)
		$\geq 75$	$HR_{DeathAC CHD}$	Tonne and Wilkinson (2013)	0.982 (0.968-0.996)
RREg	$P_{H,D}$	All	$HR_{DeathAOC H}$	Pope III et al. (2002)	0.999 (0.994-1.005)

Table 1: Risk reduction estimates used to parametrise the intervention arm.

*Abbreviations:*  $P_{X,Y}$  : age and gender-specific annual probability of developing disease/ experiencing event “Y”, conditional on being in health state “X”; Dev. = developing; COPD = chronic obstructive pulmonary disease; CHD = coronary heart disease; LC = lung cancer; H = healthy; D = dead; HR = hazard ratio;  $HR_{Y|X}$ : hazard ratio of event “Y” in population with health condition “X”; OR = odd ratio; AC = all causes; AOC = all other causes than COPD, CHD and LC.

<sup>(a)</sup> As TP are non-linear function of time, their multiplication with RRE is carried out on the transition rate scale. The obtained product is then converted back to probability to parameterise the intervention arm.

<sup>(b)</sup> Meta-analysis study.

<sup>(c)</sup> Results based on  $PM_{10}$  data.

*2.4.1. Case study definition*

The intervention is an hypothetical sustained and immediate  $1\mu\text{g}/\text{m}^3$  reduction in mean ambient concentrations of  $PM_{2.5}$  in England and Wales or in London only. This would represent a 9% and 7% reduction of respective current concentration levels (COMEAP, 2010), which is in line with the UK Air Quality Strategy’s reduction target<sup>2</sup> (DEFRA, 2007).

The target population was defined as the current adult population aged 40 to 90, living in England and Wales (or in London only for London results) and followed until death, with a cut-off at 100 years old. The analysis time horizon is therefore 60 years. Whilst WHO (2013) recently recommended to apply mortality risk estimates to adults aged 30 and over, the restriction to individuals aged 40 and above was driven by the availability of routine disease incidence and prevalence statistics. Since the risk of mortality below 40 remains low, this restriction is not expected to lead to a substantial underestimation of the health benefits of air pollution control.

The lag between exposure decrement and health risks reduction was assumed to follow the 20-year distributed lag developed and currently used by the US EPA: 30% risk reduction in year 1, an additional 12.5% every year between year 2 to year 5 and the final 20% being phased in gradually over year 6 to year 20 (US EPA, 2010). However, since the US EPA’s lag was developed to evaluate the change in the risk of all-cause mortality, sensitivity analysis using different lags for morbid endpoints will be performed. For comparability with health care interventions, a discount rate of 3.5% was applied to health care costs and QALY gains, in line with guidelines for England and Wales (NICE, 2013).

---

<sup>2</sup>Reduction of  $PM_{2.5}$  concentrations at all locations, including a 15% reduction at all urban locations, by 2020.

### 2.4.2. Population modelling

305 Modelling of currently alive adults aged 40 to 90 years old, was based on a total of 102 age and gender-specific cohorts of 1,000 individuals each. Results were then re-scaled to the populations of England and Wales and London, in line with their respective age and gender-distributions (2011 census). The model was built and evaluated in MATLAB.

310

### 2.4.3. Baseline Transition Probabilities (TP)

Data for England and Wales, or alternatively for the UK were used (i.e. no London-specific data was used). Disease prevalence data was used to distribute 315 each of the 102 cohorts into the model’s states at cycle 0, whereas annual disease incidence statistics informed cohorts’ transitions from the state “healthy” to each disease state during each yearly cycle. Individuals were assumed to move between states at mid-cycle.

For CHD and lung cancer, incidence and prevalence data provided by the 320 UK Clinical Practice Research Datalink were obtained from the open-access model DYNAMO-HIA<sup>3</sup>.

Parametrisation of the COPD pathway was slightly more complex, owing to the need to account for disease progression at patient-level as well as severe under-diagnosis of the disease, whereby less than a third of individuals 325 with probable airflow limitation reported a doctor-diagnosis of COPD in 2010 Health Survey for England (Aresu et al., 2011). COPD progression probabilities were derived by combining annual progression probabilities stratified by smoking status provided by Atsou et al. (2011) with data on the distribution

---

<sup>3</sup><http://www.dynamo-hia.eu>

of COPD patients in England by smoking status from Shahab et al. (2006).  
330 This approach was justified by the lack of strong evidence to date that suggests  
that smoking could impact upon individuals' biological response to air pollution  
exposure (Laurent et al., 2007). Death probabilities associated to the COPD  
pathway were calculated using GOLD-stratified hazard ratios of excess mortal-  
ity in COPD patients estimated by Mannino et al. (2006). The incidence of  
335 the disease by severity stage was estimated by combining disease progression  
and GOLD-stratified death risks with estimates of the disease "true" under-  
lying prevalence provided by the UK Department of Health (2010). Incidence  
estimation results are provided in Appendix A.

Mortality statistics for the general population were obtained from the UK  
340 Office for National Statistics (ONS, 2013) and reflect the assumption of compet-  
itive risk that underpins the model (see section 2.3.2). The probability of death  
conditional on having CHD was derived from life-table computations, assuming  
suffering from the condition did not affect the risk of death from all other causes  
than CHD. The probabilities of death in lung cancer patients were based on age  
345 and gender-specific ratios of relative survival at 1 and 5 years since diagnosis  
(ONS, 2011). Estimation of relative survival ratios at the other time points (i.e.  
at 2, 3 and 4 years) was carried out by fitting a Weibull survival function to the  
data.

#### 350 2.4.4. HRQoL weights

The EuroQol five dimensional instrument (EQ-5D), which is the most com-  
monly used HRQoL metric for cost-effectiveness analysis (De Smedt et al., 2014)  
was chosen to express the quality of life associated with each health state.

355 Age and gender-specific HRQoL scores experienced by "healthy" individuals  
were obtained from Kind et al. (1999). HRQoL scores associated with each  
condition are presented in Table 2 (left-hand side). HRQoL weights applied to  
each condition were upper-bounded by the age and gender-matched scores of

“healthy” individuals. Scores for COPD (by GOLD stages) and lung cancer  
360 were taken from meta-analyses (Pickard et al., 2008; Sturza, 2010) and CHD  
scores were based on a very large patient population size (n=7,242) as part of  
the EUROASPIRE III study (De Smedt et al., 2014).

The HRQoL score for lung cancer was based on results for non-small cell  
cancer, which accounts for about 90% of all cases of cancer in England (Riaz  
365 et al., 2012). The final HRQoL score was obtained by weighting HRQoL results  
for metastatic and non-metastatic non-small cell cancer by respectively 75% and  
25%, based on the fact that 75% of non-small cell cancers are detected at an  
advanced stage (NHSC, 2010).

#### 370 2.4.5. Health care costs

“Healthy” individuals were assumed not to generate any health care cost.  
The average annual health care cost per patient in each condition is provided  
in Table 2 (right-hand side). Costs were inflated to 2013 prices, based on the  
375 hospital and community services’ inflation index for the UK NHS (PSSRU,  
2013).

In the absence of UK specific data, COPD costs stratified by GOLD stage  
were based on a Swedish study (Jansson et al., 2013). The average annual cost  
of a CHD patient was obtained by scaling the total annual cost of CHD in the  
380 UK (£1.8 billion as of 2009, Nichols et al., 2012), to the number of CHD patients  
registered in the UK the same year (n= 2,330,277, British Heart Foundation,  
2010). While the obtained annual cost per patient is low (£836), it was applied  
from condition onset until death.

The annual cost of a lung cancer patient was provided by the National Cancer  
385 Research Institute (NCRI, 2012), based on patients who have been diagnosed  
with cancer and are still alive. This includes newly diagnosed individuals and  
individuals with stable disease or considered to be cured who are being followed-  
up.

	HRQoL scores (EQ-5D)			Mean annual cost / patient (2013 prices)
	Age	Severity	Value (SE)	
COPD	All	GOLD 1	0.74 (0.064)	£249
		GOLD 2	0.74 (0.043)	£951
		GOLD 3	0.69 (0.046)	£2,033
		GOLD 4	0.61 (0.084)	£4,943
	source: Pickard et al. (2008)			source: Jansson et al. (2013) <sup>(a)</sup>
CHD	≤ 40	All	0.85 (0.069)	£836
	50-69		0.80 (0.079)	
	≥ 70		0.73 (0.059)	
	source: De Smedt et al. (2014)			source: Nichols et al. (2012) and British Heart Foundation (2010)
Lung cancer	All	Non-metastatic	0.85 (0.074)	£9,283
		Metastatic	0.57 (0.067)	
	source: Sturza (2010)			source: NCRI (2012)

Table 2: Condition-specific HRQoL and health care costs.

<sup>(a)</sup> Converted in GBP using the average EUR/GBP exchange rate for 2013.

390 *2.5. Sensitivity analyses*

Joint-uncertainty in a subset of parameters was handled probabilistically by fitting lognormal distributions to risk estimates and beta distributions to HRQoL scores (Briggs et al., 2006) and by performing Monte Carlo simulations 395 (10,000 draws). In addition, the sensitivity of results to discount rate and to lags in risk reduction was evaluated.

## *2.6. Summary of assumptions*

In order to point out potential biases associated with the model and its  
400 application to the UK case study, a list of the main assumptions/limitations is  
provided in Table 3.

---

---

### Limitations expected to led to a moderate under-estimation of impacts

---

---

*Case study:*

- The target population is a static adult population aged 40 and above
- 

*Nature of effects captured in the model:*

- Adverse effects in children are not encompassed <sup>(a)</sup>
  - Quality of life effects from acute exposure are not captured
- 

*Model structure:*

- Competitive risks between each three diseases is assumed
- 

---

---

### Limitations for which the direction of the potential bias is unclear

---

---

*Model parameterisation:*

- All-cause mortality RRE applied to individuals with CHD or COPD are based on single study results, as opposed to meta-analyses
  - For individuals with CHD or COPD, the use of all-cause mortality RRE does not exactly match with the baseline probability of death of these individuals, because of the competitive risk assumption <sup>(c)</sup>
  - Correct estimation of the total life expectancy gain from air pollution reduction requires valid baseline: (i) incidence of the three life-shortening conditions modelled <sup>(b)</sup> and (ii) death risks stratified by health status
- 

Table 3: Model limitations and expected direction of potential biases.

<sup>(a)</sup> Air pollution deleterious effects on children lung development are nevertheless expected to be partially encompassed in the excess risk of developing COPD in adulthood.

<sup>(b)</sup> This prompted the estimation of the “true” underlying incidence of COPD, in order to address the fact that this disease is severely under-diagnosed (see section 2.4.3)

<sup>(c)</sup> This is not an issue for “healthy” individuals or for those with lung cancer since the change in death risk that was applied to “healthy” individuals pertains to all the other causes of death than the three modelled and for those with lung cancer, no PM-related excess death risk was applied.

### 3. Results

405 *3.1. Total QALY gain, health care resource impact and monetary benefit of intervention*

Detailed summary results are provided in Table 4. Reducing mean  $PM_{2.5}$  concentrations by  $1\mu g/m^3$  is expected to generate more than 63,000 QALYs in London and 540,000 QALYs in England and Wales, among adults currently  
410 aged 40 and above over their remaining lifetime, discounting at 3.5% p.a.

The total net health care resource impact of the intervention, which corresponds to the health care savings from a reduction in cases of CHD, COPD and lung cancer, net of the health care costs from extending the lives of individuals  
415 with a chronic cardio-respiratory condition<sup>4</sup>, is slightly cost increasing. It accounts for respectively £24 million in London and £263 million in England and Wales.

In England, health care costs to the National Health Service can be expressed as QALY losses using an estimate of the NHS expenditure required to deliver  
420 one QALY. The latter was recently estimated at £13,000/QALY (Claxton et al., 2013). Based on this estimate, the QALY loss equivalent from net health care costs accounts for 2.8% and 3.7% of the health benefits expected to be generated by the intervention in London and in England and Wales respectively.

If the intervention is expected to be funded by raising new tax revenue,  
425 it will displace private consumption and consequently, the population health benefits it generates should be monetized based on the consumption value of a QALY. The UK Department of Health recommends to use a willingness to pay (WTP) value of a QALY of £60,000 in 2009 prices (Glover and Henderson, 2010). In addition, Ryen and Svensson (2014)'s recent review of WTP values for

---

<sup>4</sup>It should be reminded that the intervention is not expected to impact upon the life expectancy of individuals with lung cancer (see section 2.3.3).

430 a QALY found a trimmed mean estimate of €74,159 (2010 prices), with most  
estimates coming from European and US studies. At a value of £65,000/QALY,  
which approximately corresponds to the two above cited values in GBP and  
2013 prices, the intervention’s discounted monetized benefit over the 60-year  
time horizon amounts to respectively £4 billion in London and £34 billion in  
435 England and Wales.

	<b>London</b>	<b>England &amp; Wales</b>
Target population size <sup>(a)</sup>	3,215,975	27,273,400
QALY gain <sup>(b)</sup>	63,293	541,217
Net health care costs <sup>(c)</sup>	£24 million	£263 million
QALY loss equivalent <sup>(d)</sup>	1,825	20,219
Net QALY gain	£61,467	£520,998
Total monetary benefit <sup>(e)</sup>	£3,995 million	£33,865 million

Table 4: Total health gain, health care resource impact and monetary benefit of reducing ambient  $PM_{2.5}$  concentrations in the UK by  $1\mu g/m^3$ .

- (a) Currently alive adults aged 40 to 90 years old.
- (b) 60-year time horizon, applying a discount rate of 3.5 % p.a.
- (c) Savings from a reduction in cases of CHD, COPD and lung cancer, net of costs from extending the lives of individuals with a chronic cardio-respiratory condition.
- (d) Using a value of £13,000/QALY as the shadow price of the NHS budget constraint.
- (e) Using £65,000/QALY as the consumption value of a QALY.

### 3.2. QALDays and health care costs distributions by age and gender

440 Figure 2A depicts the expected quality-adjusted life day (QALD) gain per  
person associated with the intervention over his/her remaining lifetime. Al-  
though health gain cumulates over time, due to discounting, the main ben-  
eficiaries of the intervention are not the youngest individuals but those aged

around 65 years old. Indeed, as the risk of experiencing adverse health events  
445 increases with age, young individuals are expected to benefit from the interven-  
tion much later in the future than older individuals. Sensitivity analysis of the  
age-distribution of health gain to the discount rate is provided in Appendix D.

Figure 2A shows the presence of a substantial gender-gap in health gain,  
especially among young age groups, with the average QALD gain enjoyed by  
450 40-year old men being nearly a third (28%) higher than the gain accruing to  
their female counterparts. This gap reflects gender-differences in baseline risks  
of adverse health events, whereby men aged between 40 to 70 in the UK are  
on average twice more likely to develop CHD and 60% more likely to die from  
all causes than women. Whilst gender-differences in baseline health risks do  
455 persist at older ages, there are substantially smaller. In addition, since women  
face a lower death risk, they are expected to enjoy the intervention’s benefit for  
a slightly longer time period than men. As a consequence, the gender-gap in  
health gain is a decreasing function of individuals age.

Figure 2B represents the expected health care cost impact of the intervention  
460 per person (gender average). For individuals aged 53 and above, the health  
care savings from reducing their lifetime risk of developing COPD, CHD and  
lung cancer are on average, more than compensated by the health care costs  
associated with extending the lives of those with a chronic cardiac or respiratory  
condition. It should be underlined that the latter are expected to be more  
465 susceptible to air pollution exposure than “healthy” individuals and thus, to  
greatly benefit from pollution decrement.

The distributions of the expected QALY gain and total health care resource  
impact of the intervention scaled to each target population are provided in  
Appendix B.

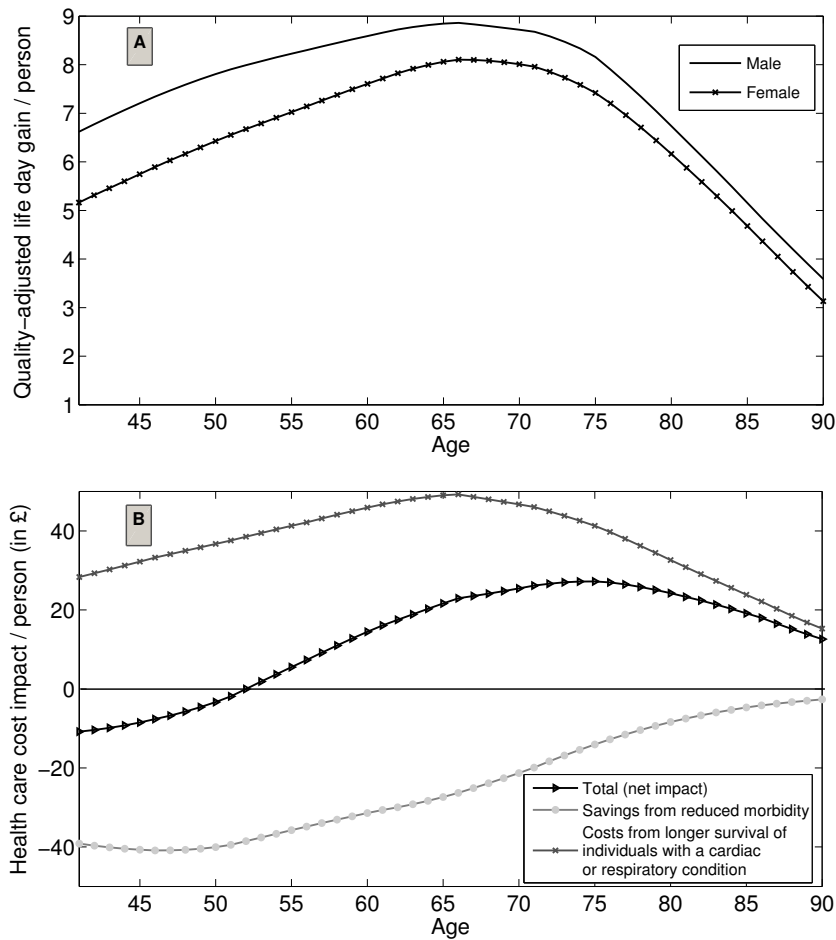


Figure 2: Intervention's average quality-adjusted life day gain (A) and health care cost impact (B) per person.

470

### 3.3. Avoided cases of adverse endpoints/cohort and life expectancy gain/person

The cumulative numbers of cases of CHD, COPD and lung cancer avoided over the remaining lifetime of individuals in each age and gender-specific cohorts (see section 2.4.2) is provided in Appendix C, alongside the expected gain in life expectancy per person. A 40 year-old person living in England and Wales

is expected to gain about 23 days of life expectancy for a  $1\mu g/m^3$  decrement in  $PM_{2.5}$  concentrations. This is in line with Pascal et al. (2013)'s results for London. The authors reported a 2.5 months gain/person aged 30 for a decrement  
480 in  $PM_{2.5}$  concentrations by  $3.1\mu g/m^3$ , which is roughly equivalent (see section 2.3.3) to a gain of 24.2 life day/person for  $\Delta_{PM_{2.5}} = -1\mu g/m^3$ .<sup>5</sup>

### 3.4. Results sensitivity to discount rate and cessation lag

485

Two scenarios of staged-discounting, based on recommendations from the UK treasury for long-term investments (Lowe, 2008) were evaluated against the base scenario, which applies a 3.5% discount rate p.a. Results are provided in Appendix D. Decreasing the discount rate to 3% p.a. after the first 30 years  
490 would lead to an increase in total net QALY gain at population level by about 7%, whereas applying a 3% rate p.a. in the first 30 years and a 2.57% rate p.a. afterwards would boost net QALY gain by about 20%.

The sensitivity of results to cessation lag were evaluated by applying a combination of different lags to the change in health risks, namely: (i) the US EPA  
495 20-year distributed lag (described in section 2.4.1) for the excess risk of death; (ii) a 5-year progressive lag for the change in the excess risks of developing CHD and COPD and (iii) a 20-year progressive lag for the change in the excess risk of developing lung cancer. Results are provided in Appendix E. This “mixed lag” was found to have a minor effect on the total net QALY gain at population  
500 level (increase by about 3%).

---

<sup>5</sup>Whilst Pascal et al. (2013) did not apply a cessation lag, the present application of the US EPA cessation lag to RRE is expected to have a relatively small effect on the health gain accruing to young individuals since 80% of the risk reduction is assumed to happen after only 5 years since decrement.

## 4. Conclusions

This study provides a novel approach to evaluating the public health benefits  
505 of air pollution control on both quality and length of life dimensions that en-  
compasses for the first time: (i) air pollution’s influence on individuals’ quality  
of life and life expectancy at baseline and (ii) dynamics in individuals’ levels of  
susceptibility to air pollution exposure, as a consequence of a degraded health  
condition that may or may not, be related to cumulative air pollution expo-  
510 sure. In addition, the proposed approach supports the evaluation of the health  
care resource impact associated with a joint reduction in chronic morbidity and  
premature mortality.

A Markov model was developed to follow adult individuals’ health trajecto-  
ries over time from the health states “healthy” to “dead”, across three diseases  
515 that represent the body of epidemiological evidence on the cardio-respiratory ef-  
fects of long-term exposure to fine particulate air pollution: chronic obstructive  
pulmonary disease, coronary heart disease and lung cancer.

Application of the model provides the first age and gender-specific estimates  
of QALY gain from air quality improvement in the UK, alongside an assessment  
520 of health care budget impact. Reducing mean  $PM_{2.5}$  concentrations by  $1\mu g/m^3$   
in London and in England and Wales (i.e. by 7% and 9% respectively) is  
expected to yield more than 63,000 and 540,000 QALYs respectively, to adults  
aged 40 and above over their remaining lifetime when discounting at 3.5% p.a.

Against expectations, such an intervention is expected to slightly increase  
525 health care costs. Indeed, after the age of 53, the health care savings from  
reducing the probability that individuals develop COPD, CHD or lung cancer  
are on average, more than compensated by the costs associated with extending  
the lives of those with a chronic cardiac or respiratory condition. Net health  
care costs, however, represent less than 4% of total health benefits, assuming  
530 the NHS delivers 1 QALY for every £13,000 it receives. At a WTP value for  
a QALY of £65,000, which is in line with recommendations for the UK, the

expected discounted monetary benefit of the intervention amounts to £4 billion in London and £34 billion in England and Wales.

In a context of increasing interest for the chronic morbidity impacts of long-term air pollution exposure, as exemplified by large-scale epidemiological projects such as ESCAPE<sup>6</sup> in Europe and MESA Air<sup>7</sup> in the US, the proposed Markov-based approach to fully capture the lifetime impact of chronic air pollution exposure on individuals' quality and length of life is expected to be of particular relevance to support air quality targets. The structure of the model and its thorough use of epidemiological evidence could be easily replicated - and extended if evidence linking PM exposure to other chronic health effects strengthens in the future - to evaluate the QALY gain and health care resource impacts of air pollution control elsewhere.

The model developed has, nevertheless, a number of limitations, which were outlined in Table 3. In particular, its parameterisation is relatively complex, which may introduce a number of biases. It is therefore worth noting that life-expectancy results appear in line with previous findings in the health impact assessment literature (see section 3.3). Although air pollution's association with subclinical respiratory symptoms in children is partly captured in the increased risk of developing COPD later in adulthood, wider benefits to children, especially to those suffering from asthma (Peled, 2011), are not taken into account. Furthermore, quality of life impacts from acute exposure are ignored. The model also assumes competitive risk between disease pathways, which is a simplification of the clinical reality given that COPD is a multi-component systemic disease that is associated with a greater risk of cardiovascular events and lung cancer (GOLD, 2014). Whilst the model accounts for COPD and lung cancer characteristics in terms of severity levels and survival pattern over time, the CHD condition was modelled via a single state, which prevented a refined analysis of impacts. Finally, the model only considered particulate air pollution

---

<sup>6</sup>European Study of Cohorts for Air Pollution Effects.

<sup>7</sup>Multi-Ethnic Study of Atherosclerosis and Air Pollution.

<sup>560</sup> whilst the benefits from abating other air pollutants, such as nitrogen dioxide,  
may also need to be considered.

### **Acknowledgments**

The author wishes to thank Professors Richard Cookson, Karl Claxton and  
<sup>565</sup> Piran White for commenting on an earlier draft and Miss Bryony Dawkins for  
proofreading the manuscript.

## References

- Abbey DE, Ostro BE, Petersen F, Burchette RJ. Chronic respiratory symptoms  
570 associated with estimated long-term ambient concentrations of fine particu-  
lates less than 2.5 microns in aerodynamic diameter (PM<sub>2.5</sub>) and other air  
pollutants. *Journal of Exposure Analysis and Environmental Epidemiology*  
1995;5(2):137–59.
- Adar SD, Sheppard L, Vedal S, Polak JF, Sampson PD, et al. Fine particu-  
575 late air pollution and the progression of carotid intima-medial thickness: A  
prospective cohort study from the multi-ethnic study of atherosclerosis and  
air pollution. *PLOS medicine* 2013;10(4):1–9.
- Aresu M, Boodhna G, Bryson A, et al. Health Survey for England 2010. Vol-  
ume 1: Respiratory health; . Health and Social Care Information Centre.;  
580 Canterbury, UK; 2011.
- Atsou K, Chouaid C, Hejblum G. Simulation-based estimates of effectiveness  
and cost-effectiveness of smoking cessation in patients with chronic obstruc-  
tive pulmonary disease. *PLOS One* 2011;6(9):1–9.
- Bell ML, Morgenstern RD, Harrington W. Quantifying the human health ben-  
585 efits of air pollution policies: Review of recent studies and new directions in  
accountability research. *Environmental Science and Policy* 2011;14:357–68.
- Briggs A, Claxton K, Sculpher M. Decision modelling for health economic  
evaluation. Oxford, UK: Oxford University Press, 2006.
- British Heart Foundation . Coronary Heart Statistics. Techni-  
590 cal Report; . [https://www.bhf.org.uk/publications/statistics/  
coronary-heart-disease-statistics-2010](https://www.bhf.org.uk/publications/statistics/coronary-heart-disease-statistics-2010) (Accessed 5th April 2014);  
2010.
- Brook RD, Rajagopalan S, Pope III CA, Brook JR, Bhatnagar A, et al. Par-  
ticulate air pollution and cardiovascular disease: an update to the scientific

- 595 statement from the American Heart Association. *Circulation* 2010;121:2331–78.
- Cesaroni G, Forastiere F, Stafoggia M, Andersen ZJ, Badaloni C, et al. Long-term exposure to ambient air pollution and incidence of acute coronary events: prospective cohort study and meta-analysis in 11 European cohorts from the ESCAPE project. *British Medical Journal* 2014;248:f7412.  
600
- Claxton K, Martin S, Soares M, Rice N, Spackman E, et al. *Methods for the Estimation of the NICE Cost Effectiveness Threshold*. CHE Research Paper 81.; Centre for Health Economics.; University of York, UK; 2013.
- Cohen JT, Hammit JK, Levy JI. Fuels for urban transit buses: A cost-effectiveness analysis. *Environmental Science and Technology* 2003;37:1477–84.  
605
- COMEAP . *The Mortality Effects of Long-Term Exposure to Particulate Air Pollution in the United Kingdom*. Technical Report (ISBN: 978-0-85951-685-3); . Committee on the Medical Effects of Air Pollutants.; London, UK; 2010.
- 610 Coyle D, Stieb D, Burnett R, DeCivita P, Krewski D, Chen Y, Thun M. Impact of particulate air pollution on quality-adjusted life expectancy in Canada. *Journal of Toxicology and Environmental Health* 2003;66:1847–63.
- Crouse DL, Peters PA, van Donkelaar A, Goldberg MS, Villeneuve PJ, Brion O, et al. Risk of nonaccidental and cardiovascular mortality in relation to long-term exposure to low concentrations of fine particulate matter: a Canadian national-level cohort study. *Environmental Health Perspectives* 2012;120:708–14.  
615
- De Smedt D, Clays E, Annemans L, De Bacquer D. EQ-5D versus SF-12 in coronary patients: Are they interchangeable? *Value in Health* 2014;17:85–9.
- 620 DEFRA . *An Economic Analysis to inform the Air Quality Strategy*. Updated Third Report of the Interdepartmental Group on Costs and Benefits (PB

12637); . UK Department for Environment Food and Rural Affairs.; London, UK; 2007.

Downs SH, Schindler C, Saly Liu LJ, Keidel D, Bayer-Oglesby L, et al. Reduced  
625 exposure to PM10 and attenuated age-related decline in lung function. *The New England Journal of Medicine* 2007;357(23):2338–47.

Drummond MF, Sculpher MJ, Torrance GW, O’Brien BJ, Stoddart GL. *Methods for the Economic Evaluation of Health Care Programmes*. 3rd ed. Oxford, UK: Oxford University Press, 2005.

630 Eisner MD, Anthonisen N, Coultas D, Kuenzli N, Perez-Padilla R, et al. An official American Thoracic Society public policy statement: Novel risk factors and the global burden of chronic obstructive pulmonary disease. *American Journal of Respiratory and Critical Care Medicine* 2010;182:693–718.

Glover D, Henderson J. *Quantifying health impacts of government policies. A how-to guide to quantifying the health impacts of government policies*; . UK  
635 Department of Health.; London, UK; 2010.

GOLD . *Global Strategy for the Diagnosis, Management and Prevention of COPD - Updated 2014. Consensus report*; . Global Initiative for Chronic Obstructive Lung Disease; . [http://www.goldcopd.org/uploads/users/files/GOLD\\_Report2014\\_Feb07.pdf](http://www.goldcopd.org/uploads/users/files/GOLD_Report2014_Feb07.pdf) (Accessed 20th February 2015); 2014.  
640

Gold MR, Stevenson D, Fryback DG. HALYs and QALYs and DALYs, Oh My: similarities and differences in summary measures of population health. *Annual Review of Public Health* 2002;23:115–34.

Hamra GB, Guha N, Cohen A, Laden F, Raaschou-Nielsen O, et al. Outdoor  
645 particulate matter exposure and lung cancer: A systematic review and meta-analysis. *Environmental Health Perspectives* 2014;122(9):906–11.

HEI . *Assessing Health Impact of Air Quality Regulations: Concepts and Methods for Accountability Research. Communication 11*; . Health Effects Institute.; Boston, USA; 2003.

- 650 Hoek G, Krishnan RM, Beelen R, Peters A, Ostro B, Brunekreef B, Kaufman  
JD. Long-term air pollution exposure and cardio-respiratory mortality: a  
review. *Environmental Health* 2013;12(43):1–16.
- Holland M, Hurley F, Hunt A, Watkiss P. Methodology for the Cost-Benefit  
Analysis for CAFE: Volume 3: Uncertainty in the CAFE CBA: Methods and  
655 First Analysis. Report to the European Commission (AEAT/ED51014); 2005.
- Holland M, Wagner A, Hurley F, Miller B, Hunt A. Cost Benefit Analysis for  
the Revision of the National Emission Ceilings Directive: Policy Options for  
revisions to the Gothenburg Protocol to the UNECE Convention on Long-  
Range Transboundary Air Pollution. Report to the European Commission;  
660 2011.
- Hubbell . Implementing QALYs in the analysis of air pollution regulations.  
*Environmental and Resource Economics* 2006;34:365–84.
- Jansson SA, Backman H, Stenling A, Lindberg A, Rönmark E, Lundbäck B.  
Health economic costs of COPD in Sweden by disease severity - has it changed  
665 during a ten years period? *Respiratory Medicine* 2013;107(12):1931–8.
- Kind P, Hardman G, Macran S. UK population norms for EQ-5D. Discussion  
paper 172; . Centre for Health Economics.; University of York, UK; 1999.
- Krewski D, Jerrett M, Burnett RT, Ma R, Hughes E, et al. Extended follow-up  
and spatial analysis of the American Cancer Society study linking particulate  
670 air pollution and mortality. Research Report 140; . Health Effect Institute.;  
Boston, MA; 2009.
- Künzli N, Medina S, Kaiser R, Quénel P, Horak Jr F, Studnicka M. Assessment  
of deaths attributable of air pollution: Should we use risk estimates based  
on time series or on cohort studies? *American Journal of Epidemiology*  
675 2001;153(11):1050–5.

- Laurent O, Bard D, Filleul L, Segala C. Effect of socioeconomic status on the relationship between atmospheric pollution and mortality. *Journal of Epidemiology and Community Health* 2007;61:665–75.
- Lepeule J, Laden F, Dockery DW, Schwartz J. Chronic exposure to fine particles  
680 and mortality: An extended follow-up of the Harvard Six Cities study from 1974 to 2009. *Environmental Health Perspectives* 2012;120:965–70.
- Lipsett MJ, Ostro BD, Reynolds P, Goldberg D, Hertz A, et al. Long-term exposure to air pollution and cardiorespiratory disease in the California Teachers study cohort. *American Journal of Respiratory and Critical Care Medicine*  
685 2011;184:828–35.
- Lowe J. Intergenerational wealth transfers and social discounting. Supplementary Green Book guidance; . HM Treasury.; London, UK; 2008.
- Maeda R, Yoshida J, Hishida T, Aokage K, Nishimura M, Nishiwaki Y, Nagai K. Late recurrence of non-small cell lung cancer more than 5 years after  
690 complete resection. *CHEST* 2010;138(1):145–50.
- Mannino DM, Doherty DE, Buist AS. Global initiative on obstructive lung disease (GOLD) classification of lung disease and mortality: findings from the atherosclerosis risk in communities (ARIC) study. *Respiratory Medicine* 2006;100:115–22.
- 695 Medina S, Ballester F, Chanel O, Declercq C, Pascal M. Quantifying the health impacts of outdoor air pollution: useful estimations for public health action. *Journal of Epidemiology and Community Health* 2013;67(6):480–3.
- Miller KA, Siscovick DS, Sheppard L, Shepherd K, Sullivan JH, Anderson GL, Kaufman JD. Long-term exposure to air pollution and incidence of  
700 cardiovascular events in women. *The New England Journal of medicine* 2007;356(5):447–58.
- NCRI . Lung cancer cost. Press release; . National Cancer Research Institute. London, UK; . <http://conference.ncri.org.uk/archive/2012/>

press-releases/LUNG\_CANCER\_UK\_PRICE\_TAG\_ECLIPSES\_THE\_COST\_OF\_

705 ANY\_OTHER\_CANCER.pdf (Accessed 20th February 2015); 2012.

NHSC . Pemetrexed (Alimta) for locally advanced and/or metastatic non-small cell lung cancer (NSCLC) - first line, induction and maintenance. Technical Report; . National Horizon Scanning Centre.; Birmingham, UK; 2010.

NICE . Guide to the methods of technology appraisal. NICE article PMG9; .

710 National Institute for Health and Care Excellence.; London, UK; 2013.

Nichols M, Townsend N, Scarborough P, Rayner M. European Cardiovascular Disease Statistics 2012. Brussels, Belgium: European Heart Network and European Society of Cardiology, 2012.

ONS . Cancer survival in England. Patients diagnosed 2004-2008, followed up

715 to 2009; . Office for National Statistics. London, UK; . <http://www.ons.gov.uk/ons/datasets-and-tables/index.html> (Accessed 20th February 2015); 2011.

ONS . Interim Life Tables. England and Wales, 1980-82 to 2010-12; . Office for National Statistics. London, UK; . <http://www.ons.gov.uk/ons/datasets-and-tables/index.html> (Accessed 20th February 2015);

720 2013.

Pascal M, Corso M, Chanel O, Declercq C, Badaloni C, et al. Assessing the public health impacts of urban air pollution in 25 European cities: Results of the Aphekom project. *Science of the Total Environment* 2013;449:390–400.

Peled R. Air pollution exposure: Who is at high risk? *Athmospheric Environment*

725 2011;45:1781–5.

Pickard AS, Wilke C, Jung E, Patel S, Stavem K, Lee TA. Use of a preference-based measure of health (EQ-5D) in COPD and asthma. *Respiratory Medicine* 2008;102:519–36.

Ponce RA, Wong EY, Faustman EM. Quality adjusted life years (QALYs) and

730 dose-response models in environmental health policy analysis - methodological considerations. *The Science of the Total Environment* 2001;264:79–91.

- Pope III CA, Burnett RT, Thun MJ, Calle EE, Krewski D, Ito K, Thurston GD. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. *Journal of American Association* 2002;287:1132–41.
- 735 PSSRU . Unit Costs of Health and Social Care 2013. Technical Report; .  
Personal Social Services Research Unit.; Canterbury, UK; 2013.
- Riaz SP, Luchtenborg M, Coupland VH, Spicer J, Peake MD, Moller H. Trends in incidence of small cell lung cancer and all lung cancer. *Lung Cancer* 2012;75:280–4.
- 740 Ryen L, Svensson M. The willingness to pay for a quality adjusted life year: a review of the empirical literature. *Health Economics* 2014;DOI: 10.1002/hec.3085.
- Sacks JD, Stanek LW, Luben TJ, Johns DO, Buckley BJ, Brown JS, Ross M. Particulate matter–induced health effects: Who is susceptible? *Environmental Health Perspectives* 2011;119:446–54.
- 745 Schikowski T, Adam M, Marcon A, Cai Y, Vierkötter A, et al. Association of ambient air pollution with the prevalence and incidence of COPD. *European Respiratory Journal* 2014;44(3):614–26.
- Schikowski T, Mills IC, Anderson HR, Cohen A, Hansell A, et al. Ambient air pollution: a cause of COPD? *European Respiratory Journal* 2013;43:250–63.
- 750 Schindler C, Keidel D, Gerbase MW, Zemp E, Bettschart R, et al. Improvements in PM10 exposure and reduced rates of respiratory symptoms in a cohort of Swiss adults (SAPALDIA). *American Journal of Respiratory and Critical Care Medicine* 2009;179:579–87.
- 755 Shahab L, Jarvis MJ, Britton J, West R. Prevalence, diagnosis and relation to tobacco dependence of chronic obstructive pulmonary disease in a nationally representative population sample. *Thorax* 2006;61:1043–7.

- Simms AD, Batina PD, Kurian J, Durham N, Dale CP. Acute coronary syndromes: an old age problem. *Journal of Geriatric Cardiology* 2012;9:192–6.
- 760 Sonnerberg FA, Beck JR. Markov models in medical decision making: a practical guide. *Medical Decision Making* 1993;13:322–8.
- Sturza J. A review and meta-analysis of utility values for lung cancer. *Medical Decision Making* 2010;30(6):685–93.
- Tonne C, Wilkinson P. Long-term exposure to air pollution is associated  
765 with survival following acute coronary syndrome. *European Heart Journal* 2013;34:1306–11.
- UK Department of Health . Consultation on a Strategy for Services for Chronic Obstructive Pulmonary Disease (COPD) in England. Technical Report (PB 11943); . Medical Directorate, Respiratory Team.; London, UK; 2010.
- 770 US EPA . Health-based cost-effectiveness of reductions in ambient PM<sub>2.5</sub> associated with illustrative PM NAAQS attainment strategies. In: *National Ambient Air Quality Standards for Particle Pollution: Regulatory Impact Analysis*,. Research Triangle Park, NC, USA: U.S. Environmental Protection Agency; 2006. p. G1–.
- 775 US EPA . Integrated Science Assessment for Particulate Matter. Technical Report; . U.S. Environmental Protection Agency.; Research Triangle Park, NC, USA; 2009.
- US EPA . Review of EPA’s DRAFT Health Benefits of the Second Section 812 Prospective Study of the Clean Air Act. Letter from Chairs of the  
780 Health Effects Sub-Committee and Advisory Council; . U.S. Environmental Protection Agency. Research Triangle Park, NC, USA; . <http://yosemite.epa.gov/sab/SABPRODUCT.NSF/0/72D4EFA39E48CDB28525774500738776/File/EPA-COUNCIL-10-001-unsigned.pdf> (Accessed 20th February 2015); 2010.

785 US EPA . Regulatory Impact Analysis for the Proposed Revisions to the National Ambient Air Quality Standards for Particulate Matter. Technical Report; . U.S. Environmental Protection Agency.; Research Triangle Park, NC, USA; 2012.

WHO . Health risks of air pollution in Europe (HRAPIE project). Recommendations for concentration-response functions for cost-benefit analysis of  
790 particulate matter, ozone and nitrogen dioxide; . World Health Organisation, Regional Office for Europe.; Copenhagen, Denmark; 2013.

WHO . Health and the environment: addressing the health impact of air pollution. Report by the secretariat (EB136/15); . World Health Organisation.;  
795 Geneva, Switzerland; 2014.

Zanobetti A, Bind MAC, Schwartz J. Particulate air pollution and survival in a COPD cohort. *Environmental Health* 2008;48(7):1–9.