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

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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.

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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.

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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

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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

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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 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 Wales and in London respectively.

2. Materials and methods

2.1. Scope of analysis

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 air pollutant (WHO, 2014).

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

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[1]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).

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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

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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 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 morbidity endpoint.

2.3. Model structure

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", 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.

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",

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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 assumed 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 initiative 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 characteristics, 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 classification 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 recurrence, 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 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: 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 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 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 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.

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 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 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 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 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. 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 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.

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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.
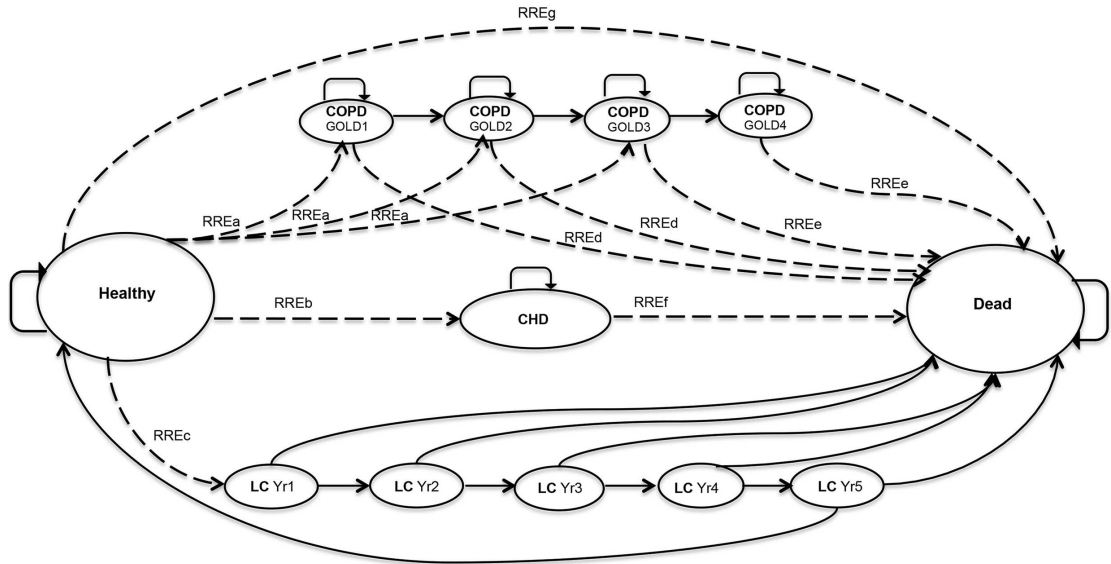

Figure 1: Diagram of the intervention arm of developed Markov model.

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

| Parameter Name | Transition Probability $P_{X,Y}$[a] | Pop. age | Risk Reduction Estimates (RRE) | | Mean (95%CI) |
| | | | Risk Estimates | | |
			Definition	Source	$\triangle_{PM2.5} = -1\mu g/m^3$
RREa	$P_{H,COPDi}$ i=GOLD1,..., 3	All	$OR_{Dev.COPD}$	Schikowski et al. (2014)[b]	0.988 (0.918-1.065)
RREb	$P_{H,CHD}$	All	$HR_{Dev.CHD}$	Cesaroni et al. (2014) [b]	0.976 (0.949-1.004)
RREc	$P_{H,LC}$	All	$HR_{Dev.LC}$	Hamra et al. (2014)[b]	0.985 (0.980-0.991)
RREd	$P_{COPDi,D}$ i=GOLD1,...,2	All	$HR_{DeathAC}$	Hoek et al. (2013)[b]	0.993 (0.991-0.995)
RREe	$P_{COPDi,D}$ i=GOLD3,...,4	< 65	$HR_{DeathAC}$	Hoek et al. (2013)[b]	0.993 (0.991-0.995)
		≥ 65	$HR_{DeathAC|COPD}$	Zanobetti et al. (2008)[c]	0.980 (0.976-0.984)
RREf	$P_{CHD,D}$	< 75	$HR_{DeathAC}$	Hoek et al. (2013)[b]	0.993 (0.991-0.995)
		≥ 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.

[a] 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.

[b] Meta-analysis study.

[c] Results based on PM_{10} data.

2.4. Parameterising the model for UK case study

2.4.1. Case study definition

The intervention is an hypothetical sustained and immediate $1\mu g/m^3$ 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[2] (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).

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[2]Reduction of $PM_{2.5}$ concentrations at all locations, including a 15% reduction at all urban locations, by 2020.

2.4.2. Population modelling

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.

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 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 UK Clinical Practice Research Datalink were obtained from the open-access model DYNAMO-HIA[3].

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 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

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[3]http://www.dynamo-hia.eu

of COPD patients in England by smoking status from Shahab et al. (2006).
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 mortality in COPD patients estimated by Mannino et al. (2006). The incidence of the disease by severity stage was estimated by combining disease progression and GOLD-stratified death risks with estimates of the disease "true" underlying 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 Office for National Statistics (ONS, 2013) and reflect the assumption of competitive 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 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.

2.4.4. HRQoL weights

The EuroQol five dimensional instrument (EQ-5D), which is the most commonly 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.

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 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 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).

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 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 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 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.

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HRQoL scores (EQ-5D)			Mean annual cost
Age	Severity	Value (SE)	/ patient (2013 prices)
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)[a]
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.

[a] Converted in GBP using the average EUR/GBP exchange rate for 2013.

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 (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 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 [a]

- 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 [c]

- Correct estimation of the total life expectancy gain from air pollution reduction requires valid baseline: (i) incidence of the three life-shortening conditions modelled [b] and (ii) death risks stratified by health status

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

[a] Air pollution deleterious effects on children lung development are nevertheless expected to be partially encompassed in the excess risk of developing COPD in adulthood.
[b] 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)
[c] 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

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 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 with a chronic cardio-respiratory condition[4], 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 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, 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

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[4]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).

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 England and Wales.

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

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

around 65 years old. Indeed, as the risk of experiencing adverse health events increases with age, young individuals are expected to benefit from the intervention 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 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 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 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 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.
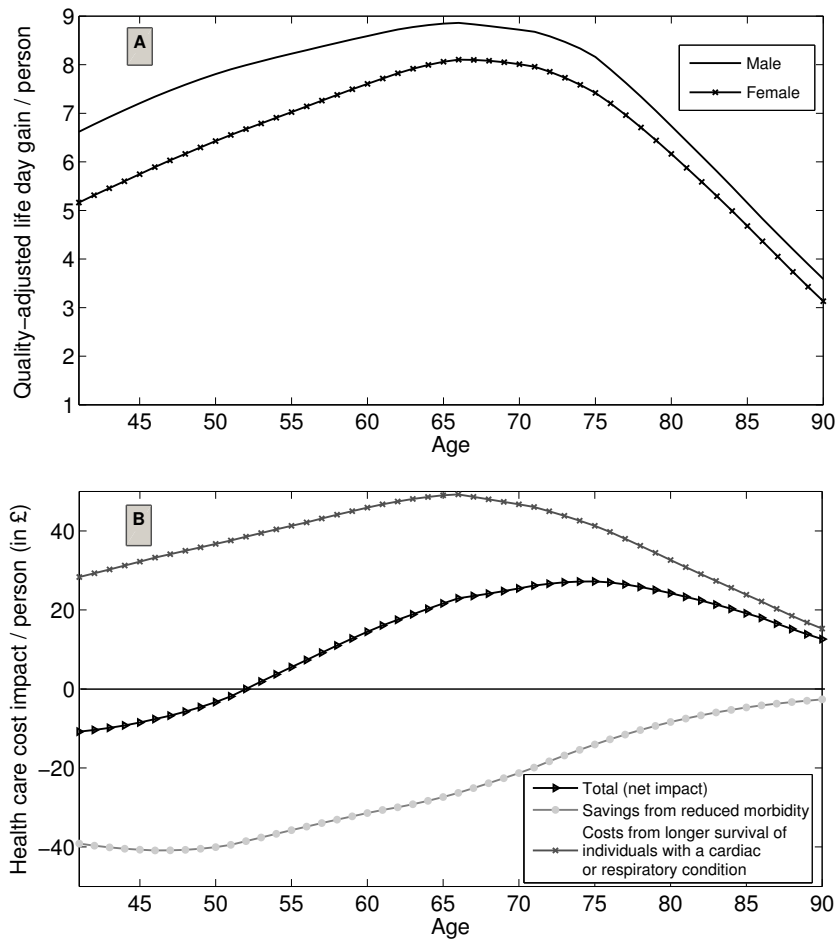
22

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

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 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 $\triangle_{PM2.5} = -1\mu g/m^3$. [5]

3.4. Results sensitivity to discount rate and cessation lag

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 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 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 level (increase by about 3%).

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[5] 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 of air pollution control on both quality and length of life dimensions that encompasses 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 exposure 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 trajectories over time from the health states "healthy" to "dead", across three diseases that represent the body of epidemiological evidence on the cardio-respiratory effects 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 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 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 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

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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[6] in Europe and MESA Air[7] 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 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

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[6]European Study of Cohorts for Air Pollution Effects.
[7]Multi-Ethnic Study of Atherosclerosis and Air Pollution.

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

Acknowledgments

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