# Appendices to document "Cost-effectiveness of Air PolluTiOn Reduction model (CAPTOR) – toolkit parameterisation and user guide"



CLAHRC Yorkshire and Humber

CHE Centre For Health Economics

UNIVERSITY OF LEEDS

**April 2016**

Laetitia Schmitt[1*], James Lomas[2], Gerry Richardson[2], Laura Bojke[2]

* Corresponding author: L.H.M. Schmitt@leeds.ac.uk
[1] University of Leeds – Academic Unit of Health Economics.
[2] University of York – Center for Health Economics.

This work was funded by CLAHRC Yorkshire and Humber.

## APPENDIX A: Comparison of endpoints considered in HIA of Leeds-Bradford LEZ with latest guidelines/ evidence assessment in the UK, EU and US.

| **HIA of Leeds-Bradford LEZ Cooper et al. (2014)** | | **Comparative analysis of HIA against latest guidelines / integrated science assessment (ISA) in the UK, EU and US** | | |
|---|---|---|---|---|
| Endpoint considered | Risk estimate | Q1) Strength of justification for inclusion | Q2) Need for evidence update/ adjustment? | Conclusions to A and B |
| PM2.5: All Cause Mortality in adults | Pope et al. (2002)<br><br>1.06 (1.02-1.11) for ΔPM2.5 = 10 µg/m$^3$ | Consensus within institutions to include this endpoint. | Hoek et al. (2013) meta-analysis (11 studies):<br>1.06 (1.04-1.08) for ΔPM2.5 = 10 µg/m$^3$ | A) Strong<br><br>B) Yes, if looking at uncertainty: Hoek et al. (2013)'s confidence interval for pooled estimate is narrower. |
| PM2.5: Coronary events | Cesaroni et al. (2014)<br><br>1.19 (1.01-1.42) for ΔPM2.5 = 5µg/m$^3$ | Coronary events from LT exposure are not considered as such in UK and EU guidelines, and are only suggested for sensitivity analysis by the US EPA impact assessments (using Miller at al 2007 results).<br><br>However:<br>1- Adverse effects on the cardiovascular system are typically assessed using deaths from cardiovascular causes.<br><br>2- The latest integrated science assessment (ISA) of the US EPA (US EPA 2009, 2012) concludes that existing evidence on the association between chronic PM exposure and adverse cardiovascular impacts indicates a causal relationship (= greatest strength of evidence on a 1 to 5 scale). | To date, Cesaroni et al. (2014) study represents the latest evidence on coronary impacts and comes from a meta-analysis of European cohorts (ESCAPE project). Note: The value reported in study abstract is 1.13 (0.98 to 1.30) as opposed to 1.19 (1.01 to 1.42) chosen for LEZ HIA, which applies to a smaller subset of participants.<br><br>An alternative source of evidence may be a UK study (Atkinson et al. 2013) but it focuses on heart failure: HR= 1.06 (1.01–1.11) for ΔPM10 = 3ug/m3 | A) Strong<br><br>B) No |

Table 1: Comparison of endpoints considered in HIA of Leeds-Bradford LEZ with latest guidelines/ evidence assessment in the UK, EU and US.

| **HIA of Leeds-Bradford LEZ Cooper et al. (2014)** | | **Comparative analysis of HIA against latest guidelines / integrated science assessment (ISA) in the UK, EU and US** | | |
|---|---|---|---|---|
| Endpoint considered | Risk estimate | Q1) Justification | Q2) Need for evidence update/ adjustment? | Conclusions to A and B |
| PM2.5:<br>Low birth weight (LBW)(<2.5 kg ) in term births (i.e. after 37 weeks or more of gestation) | Pedersen et al. (2013)<br><br>1.18 (1.06 – 1.33) for ΔPM2.5 = 5μg/$m^3$ | Institutions do not consider this endpoint and the US EPA's most recent ISA (2009 updated in 2012) concluded that evidence of LT exposure to PM2.5 on reproductive and developmental outcomes is suggestive of a causal relationship (= 3rd level of strength on a 1-5 scale).<br><br>However, the US EPA also stressed out that recent evidence strengthens the interpretation that PM exposure may be causally related to reductions in birth weights. | Pedersen et al. (2013) study comes from the ESACAPE project (14 Europe-based mother-child cohorts; n= 50,151).<br><br>Alternative meta-analysis studies:<br>(i) Dadvand et al. (2013) – based on cohorts across 14 centers, 5 of which are in Europe<br>OR: 1.10 (1.03-1.18) - ΔPM2.5 = 10μg/$m^3$<br>Pros: huge sample size of 3 million singleton term births including 81,953 births from a center in Newcastle upon Tyne.<br><br>(ii) Stieb et al. (2012) - 6 studies:<br>OR: 1.05 (0.99-1.12) - ΔPM2.5 = 10μg/$m^3$<br>Cons: Out of the 6 included studies, includes one which is not specifically on term LBW<br><br>(iii) Sapkota et al. (2012) - 4 studies:<br>OR: 1.09 (0.90-1.32) - ΔPM2.5 = 10μg/$m^3$<br>Cons: 4 studies only; Pros: result based on term LBW study results only.<br><br>NB: All these 4 studies on term LBW and air pollution used estimates of exposure during the entire pregnancy period. | A) More appropriate in sensitivity analysis.<br><br>B) Since all 3 other recent meta-analysis studies found a pooled estimate of smaller magnitude, using results from Dadvand et al. (2013), which has a very large sample size, appears preferable. |

Table 1: Comparison of endpoints considered in HIA of Leeds-Bradford LEZ with latest guidelines/ evidence assessment in the UK, EU and US *(continued)*

| **HIA of Leeds-Bradford LEZ Cooper et al. (2014)** | | **Comparative analysis of HIA against latest guidelines / integrated science assessment (ISA) in the UK, EU and US** | | |
|---|---|---|---|---|
| Endpoint considered | Risk estimate | Q1) Justification | Q2) Need for evidence update/ adjustment? | Conclusions to A and B |
| PM2.5:<br>Pre-term birth (< 37 weeks of gestation) | Sapkota et al. (2012)<br><br>1.15 (1.14-1.16) for ΔPM2.5 = 10µg/m3 | Institutions do not consider this endpoint and US EPA's most recent ISAs (US EPA, 2009 and 2012) concluded that evidence on prematurity is not consistent.<br>On the other hand, EU and US guidelines for HIA include infant mortality, which is known to be associated with prematurity. | Sapkota et al. (2012) relied on 6 studies and combined estimates based on exposure during entire pregnancy<br><br>Stieb et al. (2012) (4 studies) reported a pooled estimate of similar magnitude (but with larger SE) when using the entire pregnancy period as duration of exposure: OR = 1.16 (1.07-1.27) - ΔPM2.5 = 10 µg/m$^3$ | A) May be more appropriate in sensitivity analysis.<br><br>B) No since Sapkota et al. (2012)'s result is in line with Stieb et al. (2012)'s findings |
| NO2:<br>Low birth weight (<2.5 kg) in term births (i.e. after 37 weeks or more of gestation) | Pedersen et al. (2013)<br><br>1.09 (1-1.19) for ΔNO2= 10µg/m3 | Not considered in UK and EU guidelines and US EPA (2015) concluded that existing evidence on birth outcomes is suggestive of a causal relationship (= 3rd level of strength of evidence on a 1-5 scale). | Pedersen et al. (2013) study comes from the ESCAPE project. (n = 61,452).<br><br>An alternative source of evidence is :<br>Stieb et al (2012) - 10 studies:<br>OR = 1.05 (1.00-1.09) - ΔNO2 =37.6 µg/m$^3$ (20ppb) | A) May be more appropriate in sensitivity analysis.<br><br>B) No, but need adjustment for overlap with PM effect |
| NO2:<br>Prevalence of children asthma | Takenoue et al. (2012)<br><br>1.13 (1.03-1.25) for ΔNO2= 18.8µg/m3 (10 ppb) | Not considered in UK guidelines, which so far focused on LT mortality effects.<br><br>The main argument for considering this endpoint is provided by the US EPA's latest ISA on NO2 (US EPA, 2015) which concludes that existing evidence is likely to reflect a causal relationship (2nd level of evidence strength on a 1-5 scale) between long-term NO2 exposure and asthma development in children. | Takenoue et al. (2012) pooled together estimates from prevalence and incidence studies (n=9).<br><br>To data, the most recent meta-analysis for asthma prevalence in children is provided by Favarato et al. (2014) - 18 studies:<br>OR: 1.06(1.00-1.11) - ΔNO2 =10 µg/m$^3$<br><br>In addition, Gasana et al. (2012) reported a pooled estimate of similar magnitude for asthma development: OR: 1.05 (1.00-1.11) - ΔNO2 =10 µg/m$^3$ | A) Yes;<br><br>B) Yes. Using Favarato et al. (2014)'s result may be preferable since:<br>- it is the latest study available and<br>- it focuses on prevalence only (thus is consistent with health endpoint used) |

Table 1: Comparison of endpoints considered in HIA of Leeds-Bradford LEZ with latest guidelines/ evidence assessments in the UK, EU and US *(continued).*

## APPENDIX B: Analysis of potential endpoints to add to the scope of adverse health endpoints associated with chronic exposure to PM and $NO_2$.

| **Potential endpoints to add to current HIA scope** | **Additional endpoints considered in current guidelines / regulatory impact assessment** | | | **CCL** |
|---|---|---|---|---|
| | **UK – COMEAP** | **EU – WHO HRAPIE** | **US – US EPA** | |
| PM10: prevalence of bronchitis in children | Not considered | - Considered in sensitivity analysis only.<br><br>- Apply Hoek et al. (2013) result: 1.06 (1.04-1.08) for ΔPM10= 10 µg/$m^3$ to 6-12 yrs old | - Considered in main analysis.<br><br>- Apply Dockery et al. (1996) result: 1.50 (0.91-2.47) ΔPM10= 14.9 µg/$m^3$ to (8-12 yrs old) | Risk of potential double counting with asthma development in children. Choice to focus on chronic bronchitis in adults only.<br>=> Not added |
| PM10: incidence of chronic bronchitis in adults | Not considered | - Considered in in sensitivity analysis only.<br><br>- AHSMOG and SAPALDIA study results combined:<br>1.12 (1.04-1.19) for ΔPM10= 10 µg/$m^3$ to 18 yrs old and above | - Considered in in sensitivity analysis only.<br><br>- Use Abbey et al. (1995) (ASHMOG study) 1.81 (0.98 - 3.25) ΔPM10= 45 µg/$m^3$ 27 yrs old and above | => To be added to scope, in light of general evidence of adverse effects on respiratory system.<br><br>=> To be considered in S.A.<br><br>=> Use of combined AHSMOG and SAPALDIA study results |
| PM10: infant death (0-1 yr old) | Not considered | - Considered in in sensitivity analysis only.<br><br>- Use Woodruff et al. (1997): 1.04(1.02-1.07) for ΔPM10= 10 µg/$m^3$ | - Considered in main analysis.<br><br>- Use Woodruff et al. (1997): 1.04(1.02-1.07) ΔPM10= 10 µg/$m^3$ | Risk of double counting with prematurity<br>=> Not added. |

Table 2: Analysis of potential endpoints to add to the scope of adverse health endpoints associated with chronic exposure to PM and $NO_2$.

| **Potential endpoints to add to current HIA scope** | **Potential endpoints to add to current HIA scope based on comparison with current Guidelines / ISA** | | | **CCL** |
|---|---|---|---|---|
| | **UK – COMEAP** | **EU – WHO HRAPIE** | **US – US EPA** | |
| $NO_2$: AC mortality in adults | Use 1.025 (1.01-1.04) per ΔNO2= 10 µg/m$^3$ Reduce effect size by up to 33% (by 16.6% for mean estimate) if policy also reduces PM concentrations | - Considered in in sensitivity analysis only<br><br>- For conc. > 20 µg/m$^3$, apply Hoek et al (2013) result: 1.055(1.03-1.08) for ΔNO2= 10 µg/m$^3$ and adjust for effect overlap with PM. | The US EPA (2015) concluded that existing evidence is suggestive of a causal relationship (3rd level of strength on a 1-5 scale) | => To be added to scope<br><br>=> Since UK guidelines were recently updated for this endpoint (as reflected in DEFRA's updated damages costs (DEFRA, 2015), to be added in main analysis.<br><br>=> Use of COMEAP's current interim recommendations for magnitude of effect size. |
| $NO_2$: prevalence of bronchitis symptoms in asthmatic children | Not considered | - Considered in in sensitivity analysis only.<br><br>- Use McConnell et al. (2003) result: 1.02(0.990-1.060) for ΔNO2= 1 µg/m$^3$ | Not considered | Specificity of population subgroup and difficulty to obtain data on background incidence.<br>=> Not added. |

Table 2: Analysis of potential endpoints to add to the scope of adverse health endpoints associated with chronic exposure to PM and $NO_2$ *(continued).*

## APPENDIX C: QALY and costs computations: summary of main differences with Lomas et al (2016)

As explained in the main document, computation of QALY gain - and by extension, health care resource impacts - associated with a reduction in cases of morbidity and mortality following air pollution reduction required to define four components:

1. Timing of disease development / adverse event occurrence
2. The reduction in life expectancy associated with each adverse event
3. The duration of the disease
4. The health-related quality of life (HRQoL) weight associated with each condition.

This section details the differences between the computations undertaken to generate QALY and costs estimates to populate the toolbox and previous work by Lomas et al (2016).

### 1. Use of adjusted age-constant HRQoL decrements associated with each disease.

Lomas et al. (2016) used HRQoL scores associated with each condition and applied the difference between these scores and the scores of the general population (Kind et al., 1999) to compute the HRQoL loss associated with each endpoint. The main issue is that the scores associated with each condition were unadjusted for a number of explanatory factors that drive health condition, such as age, co-morbidities, income etc.

Therefore, in order to improve the accuracy of the quality of life loss associated with each condition, quality of life decrements associated with each morbid condition adjusted for age, gender, race/ethnicity, comorbidity, income and education estimated by Sullivan et al. (2011) were used.

These age-constant decrements were then multiplied with the time period during which the individuals would be expected to suffer from the disease, e.g. remaining life expectancy for chronic conditions, in order to compute the QALY loss associated with each endpoint.

Adjusted quality of life decrements are substantially lower than the decrements that were obtained by Lomas et al (2016) by subtracting unadjusted disease-specific HRQoL scores to the HRQoL scores of the general population, especially for CHD and asthma. However, as described below, as alternative assumptions were used with regards to components 1 to 3, the QALY scores and health care cost impacts obtained from the present computations are not substantially different from Lomas et al. (2016).

## 2. Coronary Heart Disease

*2.1. Timing of event:*

Lomas et al. (2016) assumed that the excess risk of developing CHD due to air pollution exposure would occur only in individuals of age group 60+, for which the mean age is respectively 71 for male and 72 for female. However, based on the fact most heart attacks occur from age 45 onwards (NHS, 2015), this assumption appears quite conservative. For the present computations it was therefore assumed that the excess risk of developing CHD due to air pollution exposure would occur in individuals of age group 45+, i.e. with mean age of 62 years old for male and 63 years old for female.

*2.2. Life expectancy shortening associated with adverse events:*

As discussed in main document, component 2 is important to account for, in order to avoid double counting of quality of life loss associated with morbidity events. Lomas et al. (2016) assumed that, to the exception of prematurity, morbid endpoints would not shorten life expectancy. This assumption was deemed inappropriate for CHD, which is well-known to be associated with an increased risk of death (Whiteley et al., 2005; Mercedes et al 2010). Therefore, in the present computations, the shortened life expectancy of individuals with CHD was used.

The latter was computed by applying hazard ratios of excess death provided by Whiteley et al., (2005) to the baseline mortality rates of individuals of the general population who do not suffer from CHD, which were obtained from life-table computation using ONS data (ONS, 2015). On average, CHD was found to reduce life expectancy by 3.4 years for males and 2.6 years for females, in comparison with individuals without CHD. When compared with individuals of the general population, in which life expectancy was used as a reference to compute the QALY loss for other morbid endpoints, CHD was associated with a 2-year reduction in life expectancy for both genders.

*2.3. Disease duration:*

The period of time during which individuals suffer from quality of life decrements following the development of a chronic disease will depend on the timing of event and the life expectancy after event. For CHD, whilst the present analysis accounted for the fact that CHD shortens life expectancy, the age group at risk of event was extended from age 60+ to 45+, thus shifting the mean age at time of event from 71 to 62 for males and from 72 to 63 for females. As a result, the mean disease duration underpinning the present QALY and cost computations for CHD was extended by respectively 5 years for males and 6 years for females, in comparison with Lomas et al (2016).

*2.4. HRQoL weights:*

Sullivan et al (2011) provided decrements associated with acute myocardial infarction, old myocardial infarction, angina pectoris and other chronic ischemic heart disease. In order to obtain an overall score for the CHD condition, a weighted average of these decrements was computed. Weights were obtained from hospitalizations statistics, according to causes of coronary heart disease for England and Wales. Coronary Heart statistics (2012) estimates that, as at 2010/11, about 23% and 21% of CHD hospitalizations for males and 31% and 26% of CHD hospitalizations for females were due to respectively angina pectoris and acute myocardial infarction (with the rest being classified as "for other coronary disease").

Additionally, in order to account for the fact that the loss of quality of life after a myocardial infarction is expected to be partially regained a few months after the event, two HRQoL decrements were computed for respectively (i) the year of event onset and (ii) subsequent years.

*2.5. Costs:*

Costs were computed based on the same data sources as Lomas et al (2016). For CHD, a weighted approach (based on the same hospitalization data-based weights used to obtain the HRQoL decrement associated with CHD) for the two time periods was also used to compute the average cost associated with a CHD case in year 1 and subsequent years. This slightly contrasts with Lomas et al. (2015)'s approach, which assumed that 50% of CHD cases were due to myocardial infarction and 50% due to other coronary causes.

## 3. Children's asthma

Given that that the non-adjusted HRQoL score associated with asthma is relatively low (0.722), Lomas et al. (2016) assumed that only 25% of asthma cases - assumed to represent only those suffering from persistent and frequent episodic asthma - would suffer from quality of life loss. As the presently used adjusted HRQoL decrement is substantially smaller than the decrement implied by the HRQoL scores used by Lomas et al (2016) (see section 4.2.1.), it was assumed that all cases of asthma were associated with a quality of life decrement.

## 4. Adding chronic bronchitis as health endpoint

See main document.

## References:

See main document.