ANSES Opinion
Request No 2019-SA-0198

The Director General

Maisons-Alfort, 16 May 2025

Revised OPINION[1] of the French Agency for Food, Environmental and Occupational Health & Safety

on the establishment of respiratory TRVs for particulate matter in ambient air ($PM_{2.5}$ and PM_{10}) and black carbon in ambient air

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It also contributes to the protection of the health and welfare of animals, the protection of plant health and the evaluation of the nutritional characteristics of food.
It provides the competent authorities with all necessary information concerning these risks as well as the requisite expertise and scientific and technical support for drafting legislative and statutory provisions and implementing risk management strategies (Article L.1313-1 of the French Public Health Code).
Its opinions are published on its website. This opinion is a translation of the original French version. In the event of any discrepancy or ambiguity the French language text dated 16 May 2025 shall prevail.

On 9 November 2019, ANSES issued an internal request to establish TRVs for particulate matter (PM) and black carbon (BC) in ambient air.

1. BACKGROUND AND PURPOSE OF THE REQUEST

1.1. Background

Quantitative health risk assessments related to ambient air estimate the impacts and inform the population of potential health risks, for example as part of impact assessments of road infrastructure (Anses (2012) and of classified installations for the protection of the environment. To undertake such risk assessments, it is essential to take account of airborne particles and therefore to have health reference values (HRVs) such as toxicity reference values (TRVs).

[1] Cancels and replaces the Opinion of 25 September 2024. For the tracking of changes, see Appendix 1 of this Opinion

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No TRVs have been identified relating to ambient air particulate matter in the strict sense. The TRVs currently available only concern certain chemicals, such as transition metals (nickel, zinc, copper, etc.) that are present in ambient air particulate matter (Anses 2020; INERIS 2020). However, these TRVs are not specific to these metals as components of ambient air particulate matter. Additionally, no TRV exist for the carbon fraction of ambient air particulate matter. The closest TRV identified is a threshold TRV established by the US Environmental Protection Agency (EPA) in 2003 for the inhalation of diesel exhaust emissions, comprising gases and particles (US EPA 2003).

In the absence of TRVs, the current method has been to compare ambient air concentration data either with HRVs such as those established by the World Health Organization (WHO) or with regulatory values. These values provide benchmarks but are not TRVs and cannot be used to quantitatively assess health risks associated with a given exposure. This is because regulatory values may incorporate economic or technical considerations. From a strict health perspective, the numerous epidemiological studies in this field show that adverse health effects can occur at atmospheric concentrations below these regulatory values.

According to an online questionnaire-based survey conducted by ANSES in 2018 among a non-representative sample of TRV users in France, the majority of respondents (61.5%) reported the need for a TRV for ambient air particulate matter in a variety of contexts.

In addition, risk assessors and other stakeholders involved in the interpretation of air pollution data have expressed the need for reference values for other particulate indicators, such as black carbon and ultrafine particles. Although their health effects are documented, there are no health (like those of the WHO) or regulatory values for these pollutants. In 2018, ANSES classified “black carbon”[2], a component of the carbon fraction of ambient air particulate matter, and ultrafine particles as “priority pollutants [...] for monitoring”, recommending that a TRV be established. This recommendation was confirmed in 2019 by an assessment of the weight of the epidemiological and toxicological evidence, which observed high levels of evidence for the adverse health effects of ambient air particulate matter components, including ultrafine particles, black carbon and organic carbon (OC).

1.2. Purpose of the request

In light of the above, as part of the work programme for ANSES’s expert appraisal tasks on TRVs, and following favourable opinions expressed in 2018 by the Expert Committees on “Health reference values” (HRV Committee) and “Assessment of the risks related to air environments” (CES Air), ANSES issued an internal request to establish TRVs for ambient air particulate matter. More specifically, the aims were to determine whether it was feasible to establish respiratory TRVs for $PM_{2.5}$, PM_{10}, black carbon and ultrafine particles and, if so, to develop these TRVs.

In an initial Opinion published in January 2023, ANSES established a no-threshold long-term respiratory TRV for $PM_{2.5}$. This value was also applicable to PM_{10} exposure concentrations following conversion to $PM_{2.5}$ exposure concentrations. In that same Opinion, the Agency concluded that it was feasible to establish TRVs for black carbon based on epidemiological data. However, after examining the feasibility of establishing TRVs for ultrafine particles based

[2] The term “black carbon” encompasses various metrics of the carbon fraction of ambient air particulate matter: black carbon, elemental carbon (EC) and absorbance. More details are provided later in this Opinion.

on epidemiological data, the Agency concluded that it was not feasible for the time being. The feasibility study on ultrafine particles is now available in the report published online (Anses 2024c).

This follow-up Opinion from September 2024 incorporates and presents the results and conclusions set out in separate reports on:

- the establishment of short- and long-term respiratory TRVs for particulate matter measured by mass ($PM_{2.5}$ and PM_{10}) (Anses 2024a),
- the establishment of short- and long-term respiratory TRVs for black carbon (Anses 2024b).

2. ORGANISATION OF THE EXPERT APPRAISAL

The expert appraisal was carried out in accordance with French standard NF X 50-110 "Quality in Expert Appraisals – General requirements of Competence for Expert Appraisals (May 2003)".

The issues being appraised lie within the scope of the HRV Committee. ANSES entrusted the expert appraisal to the Working Group (WG) on "PM TRVs" from November 2019. The methodological and scientific aspects of the work were presented to the HRV Committee between July 2018 (preparatory phase) and May 2024. The work was presented for information to the CES Air between June 2018 (preparatory phase) and December 2023. Concerning $PM_{2.5}$ and PM_{10}, the work was adopted by the HRV Committee at its meeting on 16 December 2021 for long-term TRVs and at its meeting on 17 May 2024 for short-term TRVs. Concerning black carbon, the work was adopted by the HRV Committee at its meeting on 15 December 2023 for short- and long-term TRVs.

ANSES analyses interests declared by experts before they are appointed and throughout their work in order to prevent risks of conflicts of interest in relation to the points addressed in expert appraisals. Request No 2019-SA-0198 showed a risk of conflict of interest for two HRV Committee experts. Therefore, these experts did not take part in the review of the work relating to the request in question. The experts' declarations of interests are made public via the following website: https://dpi.sante.gouv.fr/.

The appraisal was based firstly on a review of the available institutional reports, to document general information on ambient air particulate matter (definition, sources and levels of exposure, available standards and guidance values for ambient air quality). The kinetic aspects of inhaled particles were described and the health effects of fine particles and black carbon in ambient air were summarised, based on the institutional reports (Anses 2019; HEI 2022; WHO 2013a, 2017; Santé Publique France 2019; Thurston *et al.* 2020; Thurston *et al.* 2017; US EPA 2003, 2019).

The method for establishing these TRVs was adapted from the approach described in ANSES's TRV development guide (Anses 2017), which is currently being revised (Anses, to be released). It was based on the use of epidemiological studies and aimed to determine a set of candidate TRV values for various health events from which the recommended TRV would be selected.

The main findings of this work are summarised in the following sections of this Opinion:

- Overview of ambient air particulate matter (Section 3.1)
- Summary of the health effects of ambient air particulate matter (Section 3.2)
- Method for establishing TRVs for $PM_{2.5}$, PM_{10} and black carbon in ambient air (Section 3.3)
- Establishment of the short-term TRV for $PM_{2.5}$ and PM_{10} in ambient air (Section 3.4)
- Establishment of the long-term TRV for $PM_{2.5}$ in ambient air (Section 3.5)
- Establishment of the short-term TRV for black carbon (Section 3.6)
- Establishment of the long-term TRV for black carbon (Section 3.7)
- Conclusions (Section 3.8)

3. ANALYSIS AND CONCLUSIONS OF THE HRV COMMITTEE AND THE WG

3.1. Overview of ambient air particulate matter

3.1.1. $PM_{2.5}$ and PM_{10}

In the environmental field, the current metrological conventions for the measurement of airborne particulate matter (PM) are based on mass concentration for PM fractions with median aerodynamic diameters of less than or equal to 10 µm (PM_{10}) and 2.5 µm ($PM_{2.5}$). These fractions are used for the regulatory monitoring of particulate concentrations in ambient air, as defined by European Directive 2008/50/EC of 21 May 2008, which is currently being revised. The reference method for sampling and analysing PM_{10} and $PM_{2.5}$ concentrations is based on the filtration collection method with gravimetric analysis. continuous-monitoring automated measurement systems (AMSs), for which equivalence has been validated, can also be used. These include methods based on the use of oscillating microbalances, beta radiation attenuation or *in situ* optical methods.

PM_{10} and $PM_{2.5}$ come from a multitude of emission sources and physico-chemical transformation processes in the atmosphere (Anses 2019). Emissions can result from natural phenomena (desert sand, sea salt, volcanic eruptions, forest fires, etc.) or human activities (industry, transport, agriculture, heating, etc.). Secondary particles form in the atmosphere through reactions involving precursor gases such as sulphur dioxide, nitrogen oxides and nitrates, volatile organic compounds and ammonia. PM_{10} and $PM_{2.5}$ include various organic and inorganic compounds such as black carbon, organic carbon, metals, minerals, endotoxins and pollen.

3.1.2. Black carbon

The carbon fraction of ambient air particulate matter does not have a precise chemical composition but is a complex mixture of various components with different optical and physical properties. It is categorised based on its ability to absorb light or its refractory nature (US EPA 2012). The terms used to identify the different aerosol carbon fractions are derived from the measurement methods used.

Black carbon (BC) is the component of particulate matter that absorbs light most strongly. It is defined as the carbon component of particulate matter that absorbs all wavelengths of solar

radiation. It is formed through incomplete combustion. Elemental carbon (EC), the main mass component of BC, is the most refractory constituent of the carbon fraction of particulate matter. It is the purest, solid form of the carbon contained in ambient air particulate matter and is characterised by its lack of volatility and its chemical inertness. Elemental carbon appears to have a structure very similar to that of the BC fraction. Organic carbon (OC) is a complex mixture of components containing carbon bonds with other elements such as hydrogen or oxygen. It can be formed through incomplete combustion or the oxidation of volatile organic compounds in the atmosphere. Soot, a complex mixture of mainly BC and OC, is a light-absorbing primary pollutant emitted during the incomplete combustion of fossil fuels, biofuels and biomass. Black smoke (BS) refers to the oldest standardised method for measuring soot, dating from the late 1960s. The word “absorbance” (Abs), derived from the absorption coefficient of optical measurements, has been used in more recent studies and refers to a measurement technique similar to black smoke, usually with a cut-off diameter of 2.5 µm.

Several studies have shown a strong correlation between the BC, EC and Abs metrics (Olstrup, Johansson et Forsberg 2016; Petzold *et al.* 2013; US EPA 2012). Nevertheless, the quantitative relationships between the metrics can vary widely in time and space. Over long period of time, the correlation between BC and EC is variable and depends on many factors, but one remains a good indicator of the other. Conversion factors can facilitate comparisons of health risks identified in epidemiological studies using different metrics. Over short-term period, conversions are not recommended because of the major influence of local time contexts (pollution events and seasons) on variations in daily concentrations and on compositions and correlations.

Unless otherwise specified, “black carbon” is used in the rest of this document as a generic term referring to all the metrics of interest in the establishment of the TRV, i.e. BC, EC and Abs, all three of which are commonly used in the epidemiological literature[3].

The sources of black carbon in ambient air are related to the incomplete combustion of fossil fuels or biomass for example from diesel engines, residential wood and coal combustion, power stations using heavy oil or coal, the burning of agricultural residues and forest fires (Anses 2019). Therefore, black carbon is a universal tracer of a variable mixture of particles from a wide range of combustion sources. When measured in the atmosphere, black carbon is always found in combination with other substances resulting from the combustion of carbon-based fuels, such as organic compounds (Janssen *et al.* 2012).

3.2. Summary of the health effects of ambient air particulate matter

3.2.1. Kinetics of inhaled particles

The inhalation, penetration, deposition, translocation, clearance and retention of particulate matter in the upper and lower airways are influenced by particle characteristics, such as size and hygroscopicity, as well as individual characteristics, such as sex, age and state of health. These kinetic aspects vary within the human population and can differ significantly between species.

Quantitative extrapolation of findings from animal studies to humans remains complex and uncertain, given the physiological and anatomical differences between rodents and primates.

[3] Black smoke is not a metric of interest due to the age of the data and the obsolescence of the measurement method, which dates back to the late 1960s.

Although these differences can be partially overcome by dosimetric models, they are not yet widely applied to the study of ambient air particulate matter and do not incorporate toxicodynamic aspects.

As black carbon is a component of inhaled particles, kinetic aspects relating to the deposition, translocation, clearance and retention of black carbon appear to be similar to those of particles.

3.2.2.Health effects

The health effects of particulate matter have been recognised for many years. Compared with the PM_{10} fraction, literature has emerged more recently on the finer $PM_{2.5}$ fraction, which is included in PM_{10}. There is also a growing body of literature on the effects of the components of particulate matter, particularly black carbon.

The conclusions of several institutional reports on the health effects of $PM_{2.5}$ and black carbon, based on epidemiological and experimental data, are summarised in Table 1.

Table 1. Summary of the conclusions of institutional reports on the health effects of exposure to fine particulate matter ($PM_{2.5}$) and black carbon (including the BC, EC and Abs metrics)

Exposure	Conclusions on the health effects of exposure to fine particulate matter ($PM_{2.5}$)					Conclusions on the health effects of exposure to black carbon (BC, EC or Abs)				Examples of health events identified
	WHO (2013a)	**Thurston *et al.* (2017 & 2020);**	**WHO (2017)**	***Santé Publique France* (2019)***	**US EPA (2019)**	**WHO (2013a)**	**Anses (2019)**	**US EPA (2019)**	**HEI (2022)**	
Respiratory health										
Short term	Positive associations	Convincing evidence	NA	Established causality, Group A	Likely to be causal relationship	Sufficient evidence	"Strong" evidence of effects	Positive associations	NA	Mortality from all respiratory causes, hospitalisations for specific respiratory causes (asthma, COPD), asthma exacerbations
Long term	Positive associations	Convincing evidence	Established causality	Established causality, Group B	Likely to be causal relationship	Sufficient evidence	"Moderate" evidence of effects	Positive associations	Low confidence in children	Mortality from all respiratory causes and specific causes, incidence of asthma in children, incidence of COPD, lung function development disorder and lung function decline
Cardiovascular health										
Short term	Causal relationship	Positive associations	NA	Established causality, Group A	Causal relationship	Sufficient evidence	"Strong" evidence of effects	Positive associations	NA	Hospitalisations for and mortality from cardiovascular causes (all causes or specific causes, such as ischaemic heart disease), increased blood pressure
Long term	Causal relationship	Positive associations	Established causality	Established causality, Group B	Causal relationship	Sufficient evidence	"Moderate" evidence of effects	Limited and inconsistent data	Low to moderate confidence	Mortality from all cardiovascular causes, incidence of stroke and coronary diseases (including heart attack), change in carotid intima-media thickness
All-cause mortality										
Short term	Consistent and robust associations	NA	NA	Established causality, Group A	Causal relationship	Sufficient evidence	"Moderate" evidence of effects	Positive associations	NA	Mortality from all non-accidental causes
Long term	Consistent and robust associations	NA	Established causality	Established causality, Group A	Causal relationship	Sufficient evidence	"Strong" evidence of effects	Positive associations	High confidence	Mortality from all non-accidental causes, reduced life expectancy
All-cause hospitalisations										
Short term	NA	NA	NA	NA	NA	NA	"Strong" evidence of effects	NA	NA	Hospitalisations for all non-accidental causes
Neurological health										

Exposure	Conclusions on the health effects of exposure to fine particulate matter ($PM_{2.5}$)					Conclusions on the health effects of exposure to black carbon (BC, EC or Abs)				Examples of health events identified
	WHO (2013a)	**Thurston *et al.* (2017 & 2020);**	**WHO (2017)**	***Santé Publique France* (2019)***	**US EPA (2019)**	**WHO (2013a)**	**Anses (2019)**	**US EPA (2019)**	**HEI (2022)**	
Short term	NA	NA	NA	NA	Suggestive of a causal relationship	NA	No publications identified	Positive associations in children	NA	Depressive or anxious states, (transient) deficits in cognitive or behavioural function, markers of brain inflammation
Long term	Emerging evidence, suggested effect	Positive associations, emerging evidence	NA	Established causality, Group B	Likely to be causal relationship	NA	"Moderate" evidence of effects	Positive associations in children	Positive associations	Incidence of Parkinson's disease, degradation of cognitive function and acceleration of cognitive decline, impaired neurodevelopment in children
Perinatal health										
Long term	Growing evidence	Emerging evidence	NA	Established causality, Group A	Suggestive of a causal relationship	NA	"Moderate" evidence of effects	Positive associations	Very low to moderate confidence	Low birth weight, prematurity, fertility
Cancer										
Long term	NA	Increased risk†	Established causality†	Established causality, Group A	Likely to be causal relationship †	NA	"Inadequate" evidence of effects	Insufficient level of evidence	Low confidence	Mortality from lung cancer, incidence and prevalence of lung cancer
Metabolic disorders										
Short term	NA	Emerging, insufficiently robust evidence	NA	NA	Suggestive of a causal relationship	NA	No publications identified	No publications identified	NA	Markers of glucose tolerance, insulin sensitivity and diabetes control
Long term	Emerging evidence, suggested effect	Emerging, insufficiently robust evidence	NA	Established causality, Group B	Suggestive of a causal relationship	NA	"Inadequate" evidence of effects	No publications identified	Low confidence	Cardiometabolic mortality, incidence and prevalence of diabetes and metabolic syndrome, development of obesity in children, markers of glucose homoeostasis

*Abs: absorbance; ANSES: French Agency for Food, Environmental and Occupational Health & Safety; BC; black carbon; COPD: chronic obstructive pulmonary disease; EC: elemental carbon; HEI: Health Effects Institute (United States); NA: not available; WHO: World Health Organization; US EPA: United States Environmental Protection Agency *Group A: the level of uncertainty associated with the transposability of the risk is low and there are sufficient data to allow for reliable quantification. Group B: there are uncertainties concerning the transposability of the risk and the availability of data for quantifying the effects is not necessarily guaranteed. † Conclusions based on lung cancer.*

3.3. Method for establishing short- and long-term TRVs for $PM_{2.5}$, PM_{10} and black carbon in ambient air

The method for establishing TRVs for ambient air particulate matter was based on the TRV development approach commonly used for individual chemicals, as described in the ANSES guide (Anses, to be released). This method has been used previously to characterise the excess incidence or mortality risk of cancer due to exposure to specific chemicals (e.g. trichlorethylene) or radionuclides (e.g. radon) (Goldbohm *et al.* 2006; NRC 1988; US EPA 2002). Adaptations were made for ambient air particulate matter due to the ubiquitous nature of exposure. **The establishment method described below, which consists of five stages (Figure 1), was applied separately for $PM_{2.5}$, PM_{10} and black carbon as well as for each duration of exposure (short term and long term).**

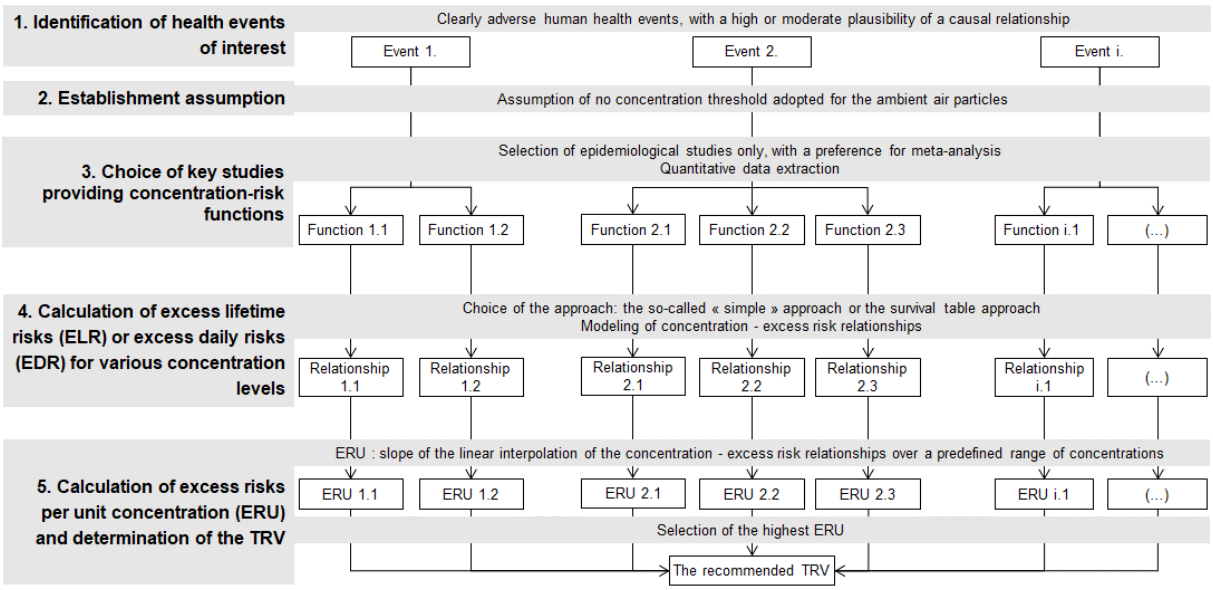


Figure 1. Approach used to establish respiratory TRVs for PM_{10}, $PM_{2.5}$ and black carbon in ambient air particulate matter

3.3.1. Identification of health events of interest

The adverse health events considered for the establishment of TRVs were identified based on those listed in the institutional reports mentioned above and had to meet the following two criteria: i) events corresponding to an adverse clinical event observed in humans, ii) events for which the plausibility of a causal relationship with exposure was classified as high or moderate by the WG.

An adverse clinical event is defined as in the WHO's pyramid of health effects associated with air pollution (WHO 2005), such as premature death and cardio-respiratory disease. Subclinical events, such as changes in biological parameters or functions (for example, biomarkers for the development of atherosclerosis or lung function development in children), were not considered when establishing the TRVs. Although studies analysing these subclinical events are essential for establishing biological plausibility, they are difficult to use for the quantitative prediction of human health risks due to the varying prognostic nature of these events and the lack of data on their distribution in the general population.

The WG's experts assigned one of three levels of plausibility (high, moderate, low) to causal relationships based on their expert judgement and the conclusions of the recent institutional reports cited above.

3.3.2.Establishment assumption

The assumption that there is no concentration threshold below which there is no adverse health effects was adopted for the establishment of these short- and long-term TRVs.

Indeed, observational studies in the general population analysing exposure to particulate matter have shown health effects even at the lowest concentrations found in the United States, Europe and Canada, for both annual and daily concentration levels. This no-threshold trend has been attributed to the wide distribution of individual susceptibility thresholds, which are potentially due to genetic factors, other environmental risk factors or pathological or behavioural states. At population level, these individual thresholds are smoothed out, resulting in no evidence of a threshold effect (Schwartz, Laden et Zanobetti 2002). The rational for establishing dose-response relationships without a concentration threshold is also described in the conceptual framework for risk assessment of the National Research Council (NRC) of the US National Academy of Sciences (NRC 2009), in which ambient air particulate matter is used as an example. Moreover, concentration-risk functions that do not assume a threshold concentration have already been used in the development of various decision-support tools related to atmospheric pollution, such as in quantitative health impact assessments (HEI 2020; WHO 2020; Santé Publique France 2019) and in guidance values and standards on ambient air quality (WHO 2021; US EPA 2021). Lastly, as black carbon is a major component of ambient air particulate matter, the conceptual basis supporting the no-threshold assumption is, in principle, valid for this component. Although fewer in number than for particulate matter, recent epidemiological studies showed that the health effects of black carbon persist at low concentration levels, with no evidence of a threshold.

3.3.3.Choice of key studies providing concentration-risk functions[4]

The references identified in a literature search in PubMed® and Scopus® were selected based on eligibility and inclusion criteria defined by the WG. Only epidemiological studies were considered due to the i) available epidemiological literature providing quantitative health risks in the general population for the health events of interest, and ii) limits of animal-human transposability.

The concentration-risk functions provided in the selected epidemiological studies were extracted. The key data of interest were the risk indicators reported in the publications, which quantified the relationship between exposure and one of the previously selected health events. Functions examining long-term exposure to black carbon were converted to an “equivalent-absorbance”, enabling comparisons between functions initially derived with different metrics (BC, EC or Abs).

Each extracted concentration-risk function was assigned a level of interest (high, moderate or low) for establishing a TRV based on i) a review of the full text and quality of the publication and ii) assessment criteria predefined by the WG describing the nature, robustness, power and external validity of the function. Studies and meta-analyses focusing on several geographical

[4] The term “concentration-risk function” is preferred in this Opinion over “dose-response relationship” because the work carried out was based on a body of epidemiological studies. This type of study generally relates pollutant concentrations in ambient air to an estimated health risk. This may be a relative risk (RR), an odds ratio (OR) or a hazard ratio (HR) for an increment of concentrations. The function linking this risk to the concentration is then assumed to be log-linear. It may also be derived from a mathematical model characterising the shape of the concentration-risk function, which may be non-linear (some examples are shape-constrained health impact function (SCHIF) models and spline functions).

locations in France or in several countries, including European countries, were preferred over single-location studies because they were considered more robust and more representative of the French population. The concentration-risk functions selected for the next steps were those with at least a moderate level of interest for the establishment of a TRV. Several functions could be selected for the same health event.

3.3.4.Calculation of excess risks for various concentration levels

- Definitions

Excess lifetime risk (ELR) is the lifetime probability of occurrence of a health event due to exposure throughout an individual's lifetime, which adds to the probability of occurrence of the event unrelated to this exposure, hereafter referred to as "background risk". ELR was used to derive the long-term TRV.

Excess daily risk (EDR) is the daily probability of occurrence of a health event due to exposure on the same day and/or in the few preceding days, which adds to the probability of occurrence of the event unrelated to this exposure. EDR was used to derive the short-term TRV.

- Approaches

Two approaches described in ANSES's development guide (Anses, to be released) for the establishment of no-threshold TRVs were used to derive excess risks (ELR or EDR) for different exposure levels: the "simple" approach and the survival table[5] approach. Both methods use the concentration-risk functions reported in epidemiological studies, but they do not use the same type of background risk data. The survival table approach requires data by age group for the health event. An adaptation, referred to as a "decremental" approach, was considered to calculate excess risks (ELR or EDR) with the effects of the exposure of interest removed from the background risk. This adaptation accounts for the absence of population groups not exposed to particulate matter in ambient air.

The decremental survival table approach was prioritized by the WG when the necessary data were available, as it provides more accurate results by incorporating competing risks and possible variations in risk over the course of a lifetime. The WG applied the simple decremental approach when the survival table approach was not i) feasible due to the lack of age-specific background data, ii) necessary because the health event occurs at a relatively young age(for example, low birth weight) or iii) necessary because of the short duration of exposure (a few days).

Since epidemiological studies in the general population were used, no time or allometric adjustments were required at this stage. Furthermore, as these epidemiological studies considered real-world exposure to ambient atmospheric concentrations, no extrapolation of concentration-risk relationships to lower concentrations was performed.

3.3.5. Calculation of excess risks per unit and determination of the TRV

TRV candidate values were derived for each health event and represented the excess risk per unit (ERU) of exposure concentration. The ERU is equal to the slope of the linear interpolation of the function representing the ELR (long term) or the EDR (short term) over a predefined range of concentrations. This range covered concentrations usually observed in metropolitan France, including the maximum values observed near road infrastructures. When the non-linear shape of the relationship between the concentration and the ELR or EDR was described,

[5] For ELR only.

the TRV was composed of two ERUs corresponding to divided concentration ranges. Each ERU was equal to the slope of the linear interpolation of the function over the divided range, plus the constant (intercept) from the second concentration range. No extrapolation of the relationship between the ELR or EDR and the concentration was carried out outside the predefined range as it was representative of the exposure of the population of interest (France) and aligned with the concentrations considered in the key epidemiological studies.

For each health event and duration of exposure, the most protective ERU value was selected as the candidate TRV value, provided it had the highest level of interest and was of sufficient quality. The candidate values were accompanied by a parametric function describing the relationship between the ELR (long term) or EDR (short term) and the concentration[6]. A confidence score from 1 to 5 was assigned to each candidate value, corresponding to the following confidence levels: low (= 1), moderate (= 2 or 3) or high (= 4 or 5) (ANSES development guide, to be released).

The recommended TRVs are equal to the most protective candidate values for health, for which:

- the associated concentration-risk function had the highest level of interest and
- the confidence score was among the highest.

3.4. Establishment of the short-term TRV for $PM_{2.5}$ and PM_{10} in ambient air

This section summarises the process used to determine the short-term respiratory TRV for exposure to $PM_{2.5}$ and PM_{10} in ambient air. The results for hospitalisations for cardiac causes (all ages), which was the health event ultimately used to derive the TRV, are detailed here. The results for other health events, representing all the other TRV candidate values, are set out in the collective expert appraisal report on $PM_{2.5}$ and PM_{10} (Anses 2024a).

3.4.1. Identification of health events of interest

Among the health events identified based on the conclusions in the institutional reports, the WG selected those with clinical relevance for which the plausibility of the causal relationship was classified as high or at least moderate:

- mortality from all non-accidental causes;
- for respiratory health: mortality from all respiratory causes, mortality from COPD[7], all respiratory hospitalisations and hospitalisations or emergency department visits for specific respiratory causes (asthma, COPD, respiratory infections);
- for cardiovascular health: mortality from all cardiovascular causes, mortality from specific cardiovascular causes (heart disease, ischaemic heart disease, myocardial infarction, stroke), all cardiovascular hospitalisations and hospitalisations or emergency department visits for specific cardiovascular causes (heart disease, ischaemic heart disease, myocardial infarction, heart failure, cardiac dysrhythmia, stroke).

[6] This parametric function can represent the shape of the relationship without resorting to linear interpolation; this is particularly relevant when the risk is non-linear.
[7] Chronic obstructive pulmonary disease.

3.4.2.Establishment assumption

The assumption that there is no concentration threshold with no adverse health effects was adopted for $PM_{2.5}$ and PM_{10} (see Section 3.3.2).

3.4.3.$PM_{2.5}$ / Choice of key studies providing concentration-risk functions

A total of 343 publications were identified in the literature search. After a selection process using criteria and procedures defined in advance by the WG, 29 publications were included, examining short-term exposure to $PM_{2.5}$ or PM_{10} in connection with one of the health events selected at the previous stage.

For $PM_{2.5}$, hospitalisations for cardiac causes (all ages) were investigated in two publications. The first publication was a meta-analysis encompassing risks estimated in 6 French cities over a period of three to four years (Lefranc *et al.* 2006) while the second was a more recent meta-analysis of risks estimated in 17 French cities over a period of nine years (Wagner *et al.* 2023).

Concentration-risk functions for $PM_{2.5}$ and hospitalisations for cardiac causes (all ages) are shown in Figure 2. The concentration-risk function with a “high” level of interest for deriving a TRV was selected for the rest of the approach.

Standardisation for the same concentration increment (10 µg·m^{-3}) was applied to enable comparisons. Lag: number of days between exposure and the health event. FR: French.

Figure 2. Relative risk (RR) and 95% confidence interval (CI) for hospitalisations for cardiac causes (all ages) for a 10 µg·m^{-3} increase in short-term exposure to $PM_{2.5}$

3.4.4. $PM_{2.5}$ / Calculation of excess risks

The “simple” decremental approach was used to calculate EDRs of hospitalisations for cardiac causes (all ages) (Figure 3).

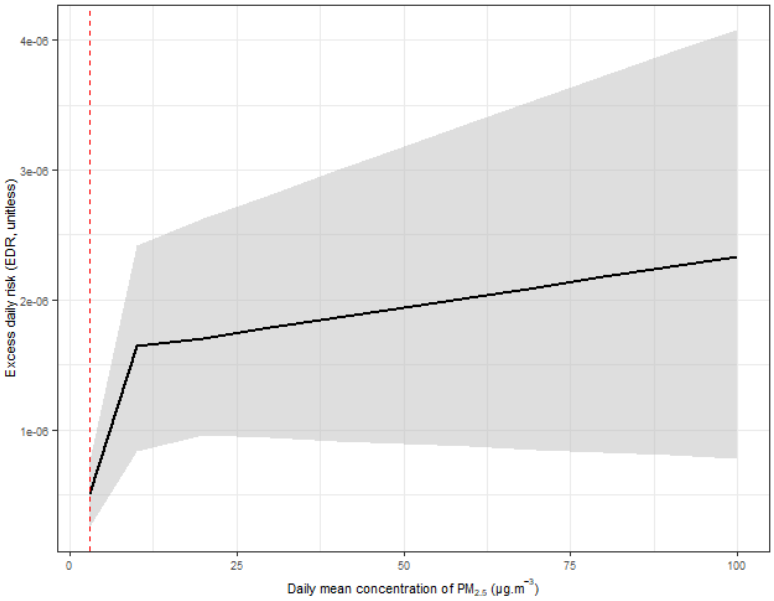


Figure 3: Excess daily risk (EDR, central estimate and confidence interval) <u>of hospitalisation for cardiac causes</u> as a function of daily concentration levels of $PM_{2,5}$, derived from the concentration-risk function of Wagner *et al.* (2023)

The function was determined using the piecewise linear model (Model 3) of Wagner et al. (2023) relating relative risk to concentration. The range of concentrations considered corresponded to the daily average concentrations observed in France.

The EDR derived using the concentration-risk function of Wagner *et al.* (2023) had the highest level of interest and was therefore selected by the WG. This function was taken from a study of several cities in metropolitan France and offered many advantages for deriving a TRV, compared with the function of Lefranc *et al.* (2006), mainly because it was based on a: 1) more recent study period, 2) larger number of cities (and *de facto* a more accurate RR that was easier to transpose to another population group) and 3) study of the shape of the concentration-risk relationship in addition to the linear model (piecewise linear, cubic spline). Moreover, the WG considered the study by Wagner *et al.* (2023) to be of good quality, given the low risk of bias.

3.4.5. $PM_{2.5}$ / Determination of candidate values and the TRV

All the candidate values for the short-term TRV for $PM_{2.5}$ are given in Appendix 2.

The short-term TRV for $PM_{2.5}$ is associated with the risk of hospitalisation for cardiac causes. The TRV corresponds to two different ERUs established for two $PM_{2.5}$[8] concentration ranges:

- an ERU of $1.65 \cdot 10^{-7}$ $(\mu g \cdot m^{-3})^{-1}$ for daily average [$PM_{2.5}$] concentrations less than or equal to 10 $\mu g \cdot m^{-3}$
- and an ERU of $7.69 \cdot 10^{-9}$ $(\mu g \cdot m^{-3})^{-1}$ + $1.56 \cdot 10^{-6}$ for daily average [$PM_{2.5}$] concentrations greater than 10 $\mu g \cdot m^{-3}$.

These are the most protective ERUs for health among all the candidate values, for which the level of interest of the associated concentration-risk function is the highest (“high”) and the confidence score is among the highest (4.8 out of 5).

[8] Two different ERUs established for two [$PM_{2.5}$] concentration ranges were selected given the shape of the relationship observed between the [$PM_{2.5}$] concentration and the EDR, and considering that average daily concentrations can often be observed in France in each of these two concentration ranges. Therefore, for a [$PM_{2.5}$] concentration less than or equal to 10 $\mu g \cdot m^{-3}$, EDR = $1.65 \cdot 10^{-7}$ x [$PM_{2.5}$], and for a [$PM_{2.5}$] concentration greater than 10 $\mu g \cdot m^{-3}$, EDR = $7.69 \cdot 10^{-9}$ x [$PM_{2.5}$] + $1.56 \cdot 10^{-6}$.

3.4.6.PM_{10} / Choice of key studies providing concentration-risk functions

A total of 343 publications were identified in the literature search. After a selection process using criteria and procedures defined in advance by the WG, 29 publications were included, examining short-term exposure to $PM_{2.5}$ or PM_{10} in connection with one of the health events selected at the previous stage.

For PM_{10}, hospitalisations for cardiac causes (all ages) were investigated in three publications. The first was a meta-analysis of two publications (Janssen *et al.* 2011). The second was a meta-analysis encompassing risks estimated in 8 French cities over a period of three to five years (Larrieu *et al.* 2007) while the third was a more recent meta-analysis of risks estimated in 17 French cities over a period of nine years (Wagner *et al.* 2023).

Concentration-risk functions for PM_{10} and hospitalisations for cardiac causes (all ages) are shown in Figure 4. The concentration-risk function with a “high” level of interest for deriving a TRV was selected for the rest of the approach.

Standardisation for the same concentration increment (10 µg·m^{-3}) was applied to enable comparisons. Lag: number of days between exposure and the health event. EU: European; FR: French; NA: not available.

Figure 4. Relative risk (RR) and 95% confidence interval (CI) for hospitalisations for cardiac causes (all ages) for a 10 µg·m^{-3} increase in short-term exposure to PM_{10}

3.4.7.PM_{10} / Calculation of excess risks

The “simple” decremental approach was used to calculate EDRs of hospitalisations for cardiac causes (all ages) (Figure 5).

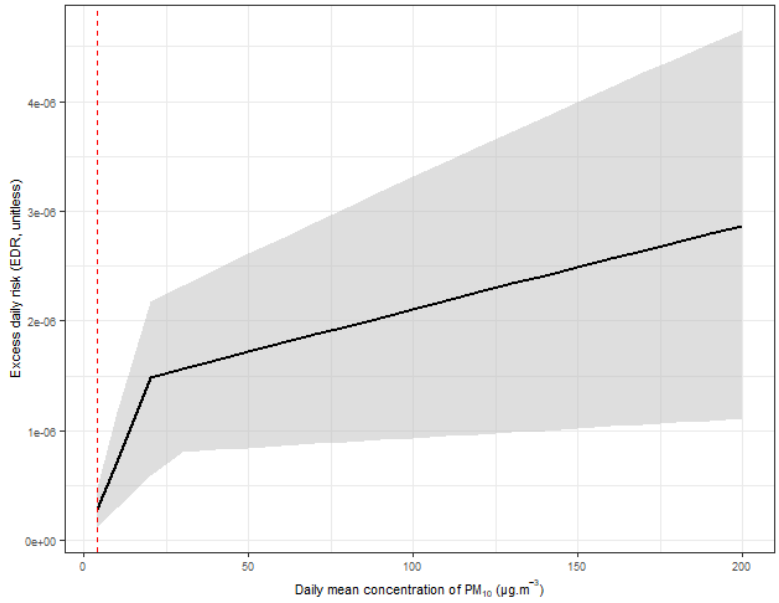


Figure 5: Excess daily risk (EDR, central estimate and confidence interval) <u>of hospitalisation for cardiac causes</u> as a function of daily concentration levels of PM_{10}, derived from the concentration-risk function of Wagner *et al.* (2023)

The function was determined using the piecewise linear model (Model 3) of Wagner et al. (2023) relating relative risk to concentration. The range of concentrations considered corresponded to the daily average concentrations observed in France.

The EDR derived using the concentration-risk function of Wagner *et al.* (2023) had the highest level of interest and was therefore selected by the WG. This function was taken from a study of several cities in metropolitan France and offered many advantages for deriving a TRV, compared with the function of Larrieu *et al.* (2007), mainly because it was based on a: 1) more recent study period, 2) larger number of cities (and *de facto* a more accurate RR that was easier to transpose to another population group) and 3) study of the shape of the concentration-risk relationship in addition to the linear model (piecewise linear, cubic spline). Moreover, the WG considered the study by Wagner *et al.* (2023) to be of good quality, given the low risk of bias.

3.4.8. PM_{10} / Determination of candidate values and the TRV

All the candidate values for the short-term TRV for PM_{10} are given in Appendix 3.

The short-term TRV for PM_{10} is associated with the risk of hospitalisation for cardiac causes. The TRV corresponds to two different ERUs established for two PM_{10}[9] concentration ranges:

- an ERU of $7.34 \cdot 10^{-8}$ $(\mu g \cdot m^{-3})^{-1}$ for daily average [PM_{10}] concentrations less than or equal to 20 $\mu g \cdot m^{-3}$
- and an ERU of $7.71 \cdot 10^{-9}$ $(\mu g \cdot m^{-3})^{-1}$ + $1.33 \cdot 10^{-6}$ for daily average [PM_{10}] concentrations greater than 20 $\mu g \cdot m^{-3}$.

These are the most protective ERUs for health among all the candidate values, for which the level of interest of the associated concentration-risk function is the highest (“high”) and the confidence score is among the highest (4.8 out of 5).

3.5. Establishment of the long-term TRV for $PM_{2.5}$ in ambient air

This section summarises the process used to determine the long-term respiratory TRV for exposure to $PM_{2.5}$ in ambient air. The results for mortality from all non-accidental causes, which was the health event ultimately used to derive the TRV, are detailed here. The results for other health events, representing all the other TRV candidate values, are set out in the collective expert appraisal report.

3.5.1.Identification of health events of interest

Among the health events identified based on the conclusions in the institutional reports, the WG selected those with clinical relevance for which the plausibility of the causal relationship was classified as high or at least moderate:

- mortality from all non-accidental causes and reduced life expectancy;
- for respiratory health: mortality from respiratory causes (all causes and specific causes: COPD, lower respiratory tract infections) and the incidence of chronic diseases (asthma in children and adults, COPD);
- for cardiovascular health: mortality from cardiovascular causes (all causes and specific causes: stroke and ischaemic heart disease), the incidence of cardiovascular events

[9] Two different ERUs established for two [PM_{10}] concentration ranges were selected given the shape of the relationship observed between the [PM_{10}] concentration and the EDR, and considering that average daily concentrations can often be observed in France in each of these two concentration ranges. Therefore, for a [PM_{10}] concentration less than or equal to 20 $\mu g \cdot m^{-3}$, EDR = $7.34 \cdot 10^{-8}$ x [PM_{10}], and for a [PM_{10}] concentration greater than 20 $\mu g \cdot m^{-3}$, EDR = $7.71 \cdot 10^{-9}$ x [PM_{10}] + $1.33 \cdot 10^{-6}$.

or diseases (stroke, ischaemic heart disease, coronary events, heart attack) and arterial hypertension;

- for cancer: the incidence of lung cancer, mortality from lung cancer;
- for perinatal health: low birth weight, prematurity and pre-eclampsia.

3.5.2. Establishment assumption

The assumption that there is no concentration threshold with no adverse health effects was adopted for $PM_{2.5}$ (see Section 3.3.2).

3.5.3. Choice of key studies providing concentration-risk functions

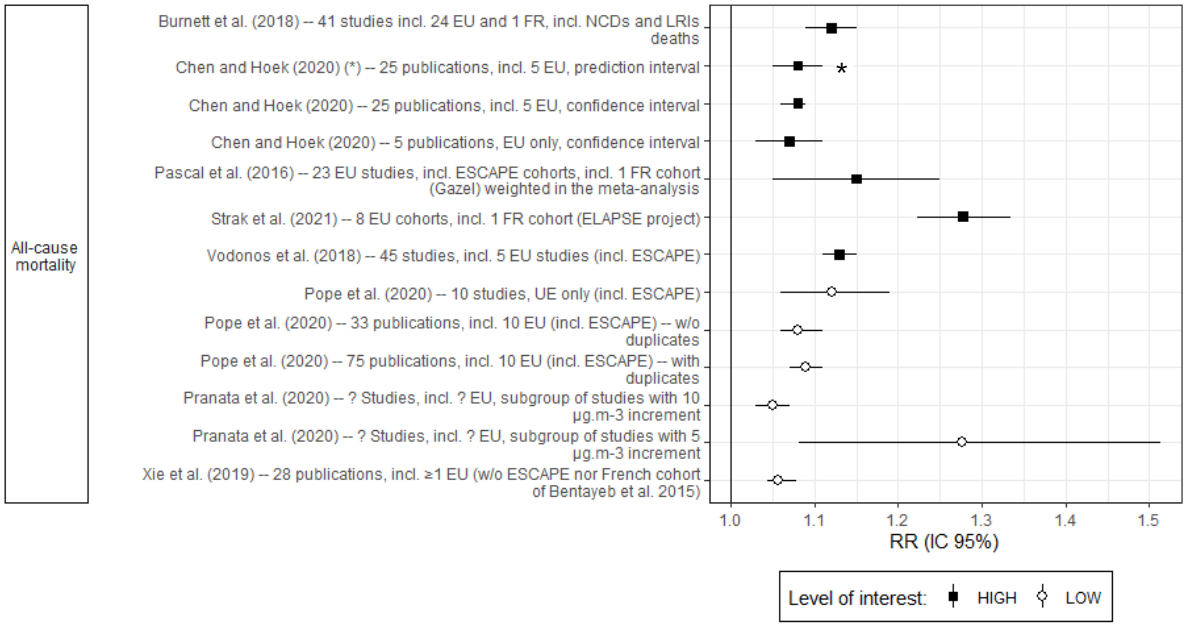
A total of 730 publications were identified for $PM_{2.5}$ in the literature search. After a selection process using criteria and procedures defined in advanced by the WG, 41 publications were included.

Mortality from all non-accidental causes was examined in eight publications in connection with long-term exposure to $PM_{2.5}$ (Burnett *et al.* 2018; Chen et Hoek 2020; Pascal *et al.* 2016; Pope *et al.* 2020; Pranata *et al.* 2020; Strak *et al.* 2021; Vodonos, Awad et Schwartz 2018; Xie *et al.* 2019). These were all meta-analyses of publications that included European studies as identified in a literature review, except Strak *et al.* (2021), which was a pooled analysis of eight European cohorts undertaken as part of the European ELAPSE[10] project.

Concentration-risk functions for mortality from all non-accidental causes (expressed as relative risks for a 10 $\mu g \cdot m^{-3}$ increase) are shown in Figure 6. Three publications also characterised the (non-linear) shape of the concentration-risk relationship (Burnett *et al.* 2018; Strak *et al.* 2021; Vodonos, Awad et Schwartz 2018). The six[11] concentration-risk functions with a "high" level of interest for deriving a TRV were selected for the rest of the approach.

[10] Effects of Low-level Air Pollution: a Study in Europe.

[11] Seven concentration-risk functions with a "high" level of interest are presented here. The function of Chen and Hoek (2020), who included 25 publications, is shown twice, first with its confidence interval and then with its prediction interval (the central estimate is the same). The analysis with the prediction interval was preferred over the one with the confidence interval.

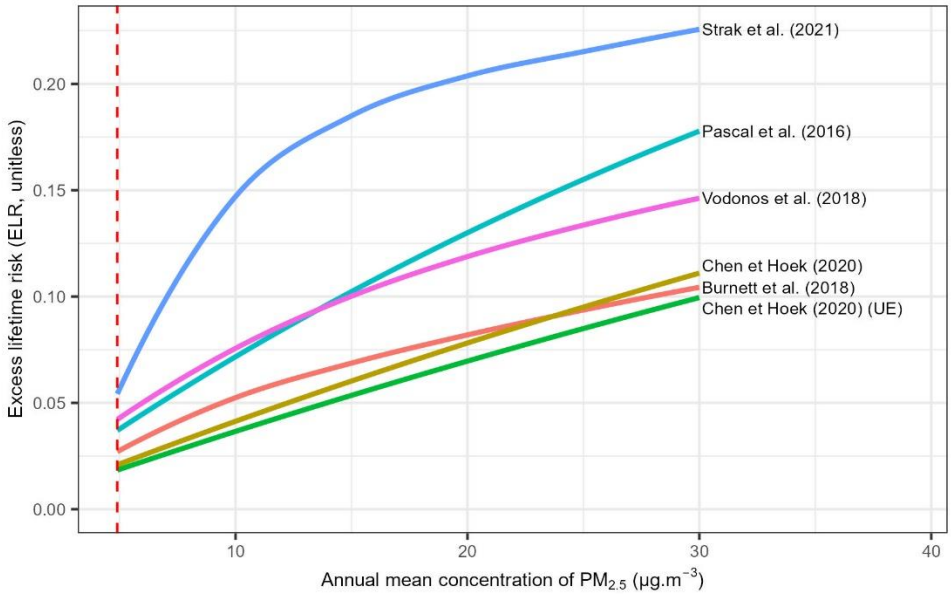


The RRs shown were standardised for the same increment (10 µg·m^{-3}) of long-term exposure to $PM_{2.5}$, thereby enabling comparisons. (*) Central RR estimate shown with its prediction interval (to be distinguished from the central estimate with the confidence interval). EU: European; FR: French; incl.: including; LRIs: lower respiratory infections; NCDs: non-communicable diseases; w/o: without.

Figure 6. Relative risk (RR) and 95% confidence interval (CI) for mortality from all non-accidental causes for a 10 µg·m^{-3} increase in long-term exposure to $PM_{2.5}$

3.5.4. Calculation of excess risks

Given the availability of data on background risk by age group for all-cause deaths, the survival table approach was used to calculate the ELRs associated with the concentration-risk functions for this health event (Figure 7).



Three functions include the non-linear shape of the relationship (Burnett et al. 2018; Strak et al. 2021; Vodonos, Awad et Schwartz 2018). The others assume a log-linear relationship. Burnett et al. (2018) also considered the change in the relationship as a function of age. The range of concentrations considered corresponded to the annual average concentrations observed in France (Pascal et al. 2016).

Figure 7. Excess lifetime risk (ELR, central estimate) of death from all non-accidental causes as a function of annual $PM_{2.5}$ concentration levels

The ELR derived using the concentration-risk function of Strak *et al.* (2021) is the most protective for health across the entire range of concentrations considered. The (non-linear) shape of the relationship between exposure to $PM_{2.5}$ and the risk of death from all non-accidental causes was also included, with the authors focusing specifically on low ambient concentrations. The analysis by Strak *et al.* (2021) had the advantage of considering only European cohorts, improving the transposability of the concentration-risk function to the French population, which was the population of interest in this work. The WG experts considered this analysis to be of good quality due to the standardisation of individual data between cohorts, the degree of adjustment for confounding factors and the sophisticated modelling of exposure (fine spatial and temporal resolution and good modelling performance).

Therefore, in light of the above, the ELR established using the concentration-risk function of Strak *et al.* (2021) was selected to derive the candidate TRV for the health event: mortality from all non-accidental causes.

3.5.5. Determination of candidate values and the TRV

All the candidate values for the long-term TRV for $PM_{2.5}$ are given in Appendix 4.

The selected TRV for ambient air particulate matter is the ERU of death from all non-accidental causes of $1.28 \cdot 10^{-2}$ $(\mu g \cdot m^{-3})^{-1}$ and the associated parametric function $ELR = 2.19 \cdot 10^{-5} \times [PM_{2.5}]^3 - 1.51 \cdot 10^{-3} \times [PM_{2.5}]^2 + 3.61 \cdot 10^{-2} \times [PM_{2.5}] - 8.83 \cdot 10^{-2}$. This is the most protective ERU for health among all the candidate values, for which the level of interest of the associated concentration-risk function is the highest ("high") and the confidence score is among the highest (4.8 out of 5). For mortality from all non-accidental causes, two interpolation slopes were constructed over the $PM_{2.5}$ concentration intervals [4.9 – 15.0 $\mu g \cdot m^{-3}$] and [15.0 – 30.0 $\mu g \cdot m^{-3}$], given the supra-linear shape of the relationship between concentration and ELR.

3.6. Establishment of the short-term TRV for black carbon

This section summarises the process used to determine the short-term respiratory TRV for exposure to black carbon in ambient air particulate matter. The results for cardiovascular hospitalisations, which was the health event ultimately selected to derive the TRV, are detailed here. Results for other health events, representing all the other candidate TRV, can be found in the expert appraisal report on black carbon (Anses 2024b).

3.6.1. Identification of health events of interest

Among the health events identified based on the conclusions of institutional reports, the WG selected those with clinical relevance, for which the plausibility of the causal relationship was classified as high or moderate:

- mortality from all non-accidental causes and hospitalisations for all non-accidental causes;
- for respiratory health: mortality from respiratory causes, respiratory hospitalisations, hospitalisations for specific respiratory causes (asthma, COPD, respiratory infections), asthma (symptom triggering, treatment) and wheezing;
- for cardiovascular health: mortality from cardiovascular causes, cardiovascular hospitalisations and hospitalisations for specific cardiovascular causes (stroke, ischaemic heart disease, congestive heart failure, heart attack and coronary events).

3.6.2. Establishment assumption

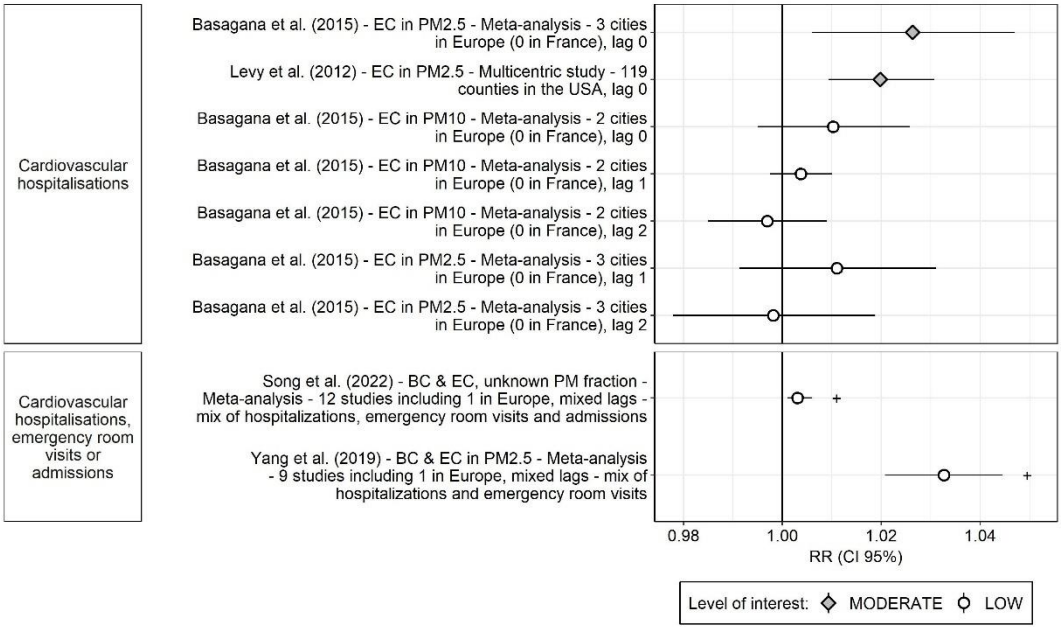
The assumption that there is no concentration threshold below which there is no adverse health effects was adopted for black carbon (see Section 3.3.2).

3.6.3. Choice of key studies providing concentration-risk functions

A total of 999 publications were identified in the literature search. After applying the selection criteria and procedures predefined by the WG, 30 publications were included. Of these, nine examined short-term exposure to black carbon in association with one of the selected health events.

Cardiovascular hospitalisations were examined in four publications (Basagaña *et al.* 2015; Levy *et al.* 2012; Song *et al.* 2022; Yang *et al.* 2019). The first two were multi-city studies whereas the last two were meta-analyses of nine to 12 publications (including the one by Basagaña *et al.* (2015)).

Concentration-risk functions for cardiovascular hospitalisations (expressed as relative risks for a 1 $\mu g \cdot m^{-3}$ increase in elemental carbon) are shown in Figure 8. The two concentration-risk functions with a "moderate" level of interest for deriving a TRV were selected for the next steps.

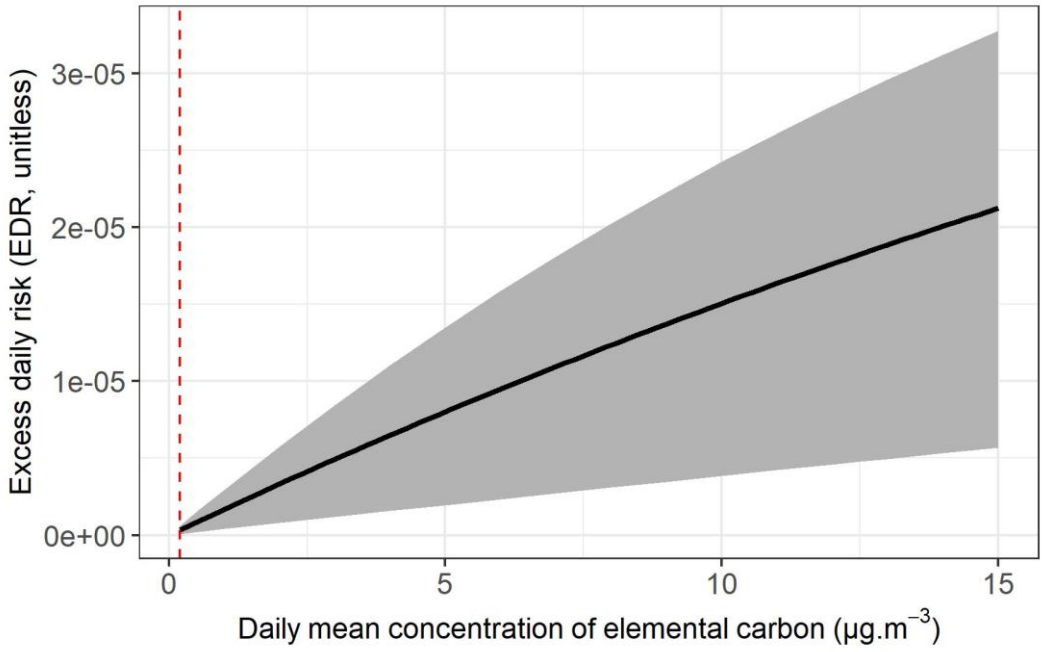


Standardisation for an increment of one concentration unit (1 $\mu g \cdot m^{-3}$) was applied to enable comparisons. + Mixture of metrics. BC: black carbon; EC: elemental carbon.

Figure 8. Relative risk (RR) and 95% confidence interval (CI) for cardiovascular hospitalisations for a 1 $\mu g \cdot m^{-3}$ increase in short-term exposure to "black carbon"

3.6.4. Calculation of excess risks

The "simple" decremental approach was used to calculate EDRs for cardiovascular hospitalisations. The EDR derived from the concentration-risk function of Basagaña *et al.* (2015) for elemental carbon in the $PM_{2.5}$ fraction at lag 0 (Figure 9) was the most protective for health across the entire range of concentrations. Moreover, the WG considered the study by Basagaña *et al.* (2015) to be of good quality, given the low risk of bias.



In black: central estimate. In grey: confidence interval.

Figure 9. Excess daily risk (EDR, central estimate and confidence interval) of cardiovascular hospitalisations as a function of concentration levels of "black carbon", derived from the concentration-risk function of Basagaña *et al.* (2015)

Therefore, the EDR established using the concentration-risk function of Basagaña *et al.* (2015) was selected to derive the candidate TRV for the health event: cardiovascular hospitalisations.

3.6.5. Determination of candidate values and the TRV

All the candidate values for the short-term TRV for black carbon are given in Appendix 5.

The short-term TRV for black carbon is the ERU of hospitalisation for all cardiovascular causes of $1.48 \cdot 10^{-6}$ $(\mu g \cdot m^{-3})^{-1}$ applicable to an elemental carbon exposure concentration. This is the most protective ERU for health among all the candidate values, for which the associated concentration-risk function had the highest level of interest ("moderate") and the confidence score is among the highest (4.5 / 5).

3.7. Establishment of the long-term TRV for black carbon

This section summarises the process used to determine the long-term respiratory TRV for exposure to black carbon in ambient air particulate matter. The results for mortality from all non-accidental causes, which was the health event ultimately selected to derive the TRV, are detailed here. Results for other health events, representing all the other candidate TRV, can be found in the expert appraisal report on black carbon (Anses 2024b).

3.7.1. Identification of health events of interest

Among the health events identified based on the conclusions of institutional reports, the WG selected those with clinical relevance, for which the plausibility of the causal relationship was classified as high or moderate:

- mortality from all non-accidental causes and reduced life expectancy;

- for respiratory health: mortality from respiratory causes (all causes and specific causes: COPD), the incidence of asthma in children, the incidence of asthma in adults and the incidence of COPD;
- for cardiovascular health: mortality from cardiovascular causes (all causes and specific causes: cerebrovascular, stroke, coronary diseases including heart attack and ischaemic heart disease), the incidence of coronary diseases (including heart attack) and the incidence of stroke;
- for perinatal health: low birth weight.

3.7.2.Establishment assumption

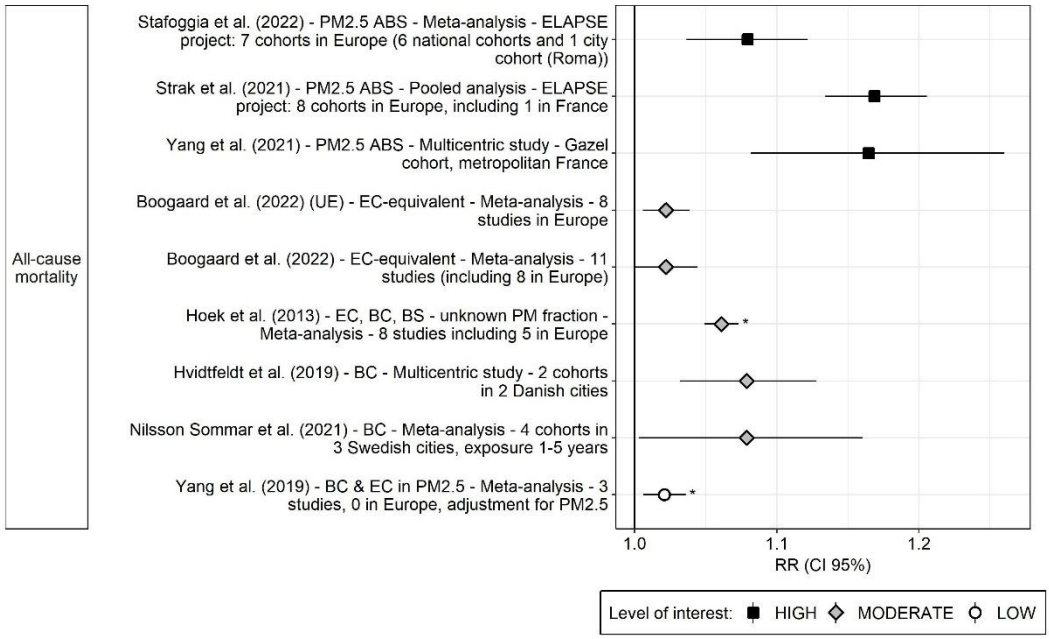
The assumption that there is no concentration threshold below which there is not adverse health effects was adopted for black carbon (see Section 3.3.2).

3.7.3.Choice of key studies providing concentration-risk functions

A total of 999 publications were identified in the literature search. After applying the selection criteria and procedures predefined by the WG, 30 publications were included. Of these, 23 examined long-term exposure to black carbon in association with one of the selected health events.

Mortality from all non-accidental causes was examined in eight publications including three multicentre studies (Hvidtfeldt *et al.* 2019; Strak *et al.* 2021; Yang *et al.* 2021) and five meta-analyses (Boogaard *et al.* 2022; Hoek *et al.* 2013; Nilsson Sommar *et al.* 2021; Stafoggia *et al.* 2022; Yang *et al.* 2019), all including European locations.

Concentration-risk functions for mortality from non-accidental causes (expressed as relative risks for a $1 \cdot 10^{-5}$ m^{-1} increase in equivalent-absorbance) are shown in Figure 10.



*Standardisation for an increment of one concentration unit ($1 \cdot 10^{-5}$) of absorbance or equivalent-abs was applied to enable comparisons. * The risks could not be converted to equivalent-abs because a mixture of metrics was used by the authors, with no possibility of transformation; the risk is therefore expressed for an increment of 1 $\mu g \cdot m^{-3}$. Abs: absorbance; BC: black carbon; BS: black smoke; EC: elemental carbon; ELAPSE: Effects of Low-Level Air Pollution: A Study in Europe; PM: particulate matter.*

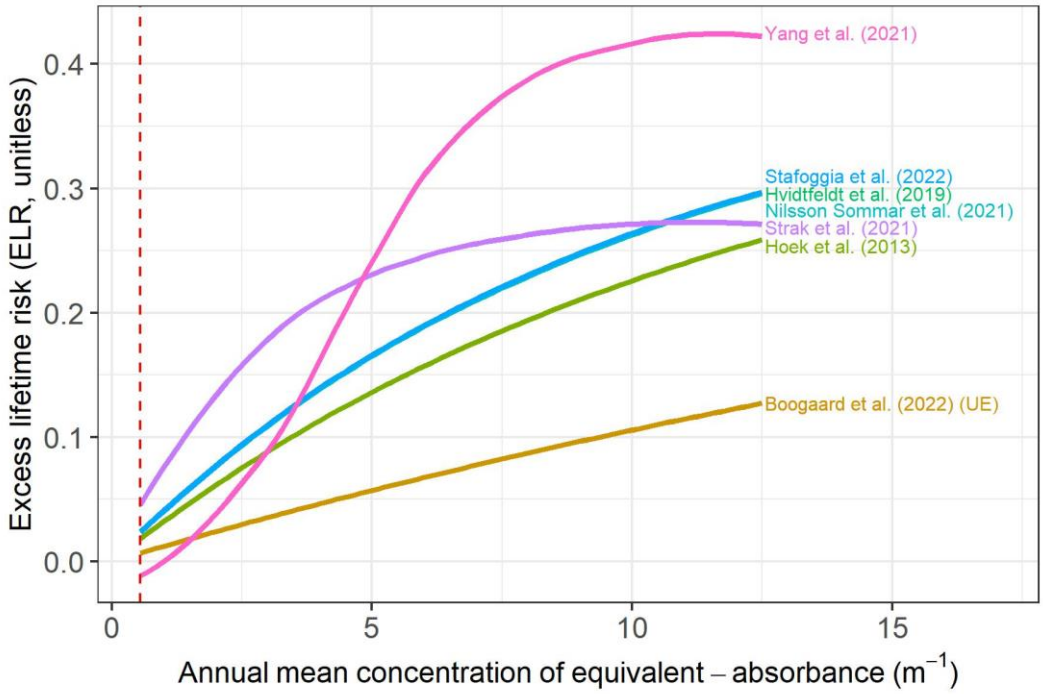
Figure 10. Relative risk (RR) and 95% confidence interval (CI) for mortality from all non-accidental causes for a $1 \cdot 10^{-5}$ increase in long-term exposure to black carbon

Seven[12] concentration-risk functions with a sufficient level of interest (i.e., at least "moderate") for deriving a TRV were selected for the next steps. Three publications characterised the non-linear shape of the concentration-risk relationship (Stafoggia *et al.* 2022; Strak *et al.* 2021; Yang *et al.* 2021).

3.7.4.Calculation of excess risks

Given the availability of age-specific background data for all-cause deaths, the decremental survival table approach was used for this health event (Figure 11).

[12] Of the two publications extracted from Boogaard *et al.* (2022), the one from the secondary analysis that only included European locations was prioritized in the next steps as it was assumed to be more representative of the target (French) population and had a narrower confidence interval around the central risk estimate.



Two functions included the non-linear shape of the relationship between concentration and risk (Strak et al. 2021; Yang et al. 2021); the others assumed a log-linear relationship. The concentration-risk functions were converted into equivalent-abs when possible; only the function of Hoek et al. (2013) could not be converted. Three functions had the same central estimates, which is why the corresponding ELRs overlap in the figure (Hvidfeldt et al. 2019; Nilsson Sommar et al. 2021; Stafoggia et al. 2022).

Figure 11. Excess lifetime risk (ELR, central estimate) of death from all non-accidental causes as a function of annual average black carbon concentrations expressed as equivalent-absorbance

The ELR derived from the concentration-risk function of Strak *et al.* (2021) was the most protective for health in the lower part of concentration range (≤ $5 \cdot 10^{-5}$ m^{-1}), which is most frequently observed in urban areas in France. The non-linear shape of the relationship between exposure to black carbon and the risk of all-cause mortality was also reported by Strak et al., even for populations exposed to low ambient concentration levels (≤ $3 \cdot 10^{-5}$ m^{-1}). However, it is important to note that this involves extrapolation of the concentration-risk function to higher levels. Moreover, Strak *et al.* (2021) only considered European cohorts, which allows for good transposability of the function to the French population. Lastly, this analysis was considered of high quality by the WG due to the standardisation of individual data between cohorts, the high degree of adjustment for confounding factors and the sophisticated modelling of exposure (fine spatial and temporal resolution and good performance).

It should be noted that the ELR derived from the concentration-risk function of Yang *et al.* (2021) was the most protective for a population exposed to higher annual concentrations (≥ $5 \cdot 10^{-5}$ m^{-1}), typical of specific, one-off situations such as proximity to road infrastructures with heavy traffic. Higher uncertainty is expected around ELRs derived for concentration ranges ≥ $8 \cdot 10^{-5}$ m^{-1}, as these are underrepresented in epidemiological studies describing concentration-risk functions.

Therefore, the ELR established using the concentration-risk function of Strak *et al.* (2021) was selected to derive the candidate TRV for the health event: mortality from all non-accidental causes.

3.7.5. Determination of candidate values and the TRV

All the candidate values for the long-term TRV for black carbon are given in Appendix 6.

The long-term TRV for black carbon is the ERU of death from all non-accidental causes of $5.29 \cdot 10^{-2}$ $(.10^{-5}$ $m^{-1})^{-1}$ and the associated parametric function $ELR = 2.86 \cdot 10^{-4} \times [abs]^3 - 8.24 \cdot 10^{-3} \times [abs]^2 + 8.00 \cdot 10^{-2} \times [abs] + 4.49 \cdot 10^{-3}$. This is the most protective ERU for health among all the candidate values, for which the plausibility of causality was high, the associated concentration-risk function had the highest level of evidence ("high") and the confidence score was among the highest (4.6 out of 5).

3.8. Conclusions

The TRVs developed for $PM_{2.5}$ are based on a wide range of aerosols present in the atmosphere. For particulate pollution with a specific physico-chemical composition (e.g. aerosol particles enriched with metals or minerals from industrial sources), the HRV Committee emphasizes that TRVs dedicated to these chemical particulates should be used whenever available. These should be applied in addition to and separately from the TRV proposed here for $PM_{2.5}$ in ambient air.

For each pollutant ($PM_{2.5}$, PM_{10} or black carbon), it should be noted that the short-term and the long-term TRVs should be used independently and the results of their application should be interpreted separately. This distinction is necessary because long-term effects partly incorporate short-term effects, and vice versa.

Similarly, TRVs for black carbon, $PM_{2.5}$ and PM_{10} should be used separately. $PM_{2.5}$ and PM10 encompass particulate matter in general, including black carbon and other components. Black carbon, however, serves as a universal indicator of particulate matter from various combustion sources. Therefore, in the presence of particulate pollution from a combustion process (such as road traffic or wood heating), the TRVs for black carbon can be used in addition to those for $PM_{2.5}$ and PM_{10}.

As a reminder, the term "black carbon" is used generically in the present document to refer to various metrics: black carbon, elemental carbon and the absorption coefficient (absorbance). The TRVs were based on black carbon concentrations expressed as elemental carbon (short term) and absorbance (long term), as these metrics were commonly used in the epidemiological studies. The WG and HRV Committee reiterate that conversion factors are available for converting concentrations between the three black carbon metrics. However, as these factors can vary in time and across locations, it is advisable to use, whenever possible, a conversion factor specific to the measurement method, the geographical area and the time period.

ERUs and parametric functions have been developed for health events beyond those used to establish the TRVs (Appendix 2, 3, 4, 5 and 6). They can be used similarly to TRV in a quantitative health risk assessment targeting these events, taking care to avoid double counting when aggregating certain health outcomes (for example, deaths from all cardiovascular causes and deaths from ischaemic heart disease). To assess the health risk associated with exposure during childhood or prenatal exposure, ERUs and parametric functions related to the incidence of asthma in children and low birth weight can be used.

Lastly, the TRV can be used to calculate an excess risk associated with exposure to a predefined concentration of $PM_{2.5}$, PM_{10} or black carbon.

3.8.1.Short-term and long-term TRVs for $PM_{2.5}$ and PM_{10} in ambient air

The HRV Committee recommends using two respiratory TRVs, i.e. a short-term and a long-term respiratory TRV, for $PM_{2.5}$ (Table 2). For PM_{10}, the HRV Committee recommends using a short-term TRV; for long-term exposure, it recommends converting this into a $PM_{2.5}$ concentration and then applying the long-term TRV developed for $PM_{2.5}$. These are the most protective ERUs for which the level of interest of the associated concentration-risk function is the highest. A high confidence level was assigned to these TRVs.

For an annual average concentration of $PM_{2.5}$ greater than 15 $\mu g \cdot m^{-3}$, the long-term TRV could overestimate the risk due to the (non-linear) shape of the relationship between concentration and risk over this range. To refine the calculation for this range, the ERU can be replaced with the parametric function.

It was decided not to develop a respiratory TRV for long-term exposure to PM_{10} because:

- the health effects of $PM_{2.5}$ are generally better substantiated than those of PM_{10} in the recent literature,
- the reported risks associated with long-term exposure to PM_{10} for all-cause mortality, mortality from ischaemic heart disease, mortality from all respiratory causes and mortality from lung cancer are of a lower magnitude than those reported for $PM_{2.5}$ (Chen et Hoek 2020),
- and the $PM_{2.5}$ fraction included in the PM_{10} fraction is strongly correlated with the latter in ambient air and enables relevant factors to be used for concentration conversion.

For an annual average PM_{10} concentration ($[PM_{10}]$), it is advisable to convert it into an annual average $PM_{2.5}$ concentration ($[PM_{2.5}]$) using the $[PM_{2.5}]$:$[PM_{10}]$ ratio specific to the geographical area being assessed, or any other more sophisticated model, and then to use the recommended long-term TRV for $PM_{2.5}$ (Table 2). In France, local ratios can be provided by approved air quality monitoring associations.

More generally, the WHO (2021) states that a $[PM_{2.5}]$:$[PM_{10}]$ ratio of 0.5 to 0.8 is valid for most situations. In 2013, the WHO project HRAPIE recommended using a $[PM_{2.5}]$:$[PM_{10}]$ ratio of 0.65, considered as an average for the European population, to convert concentration-risk functions for PM_{10} into $PM_{2.5}$ (WHO 2013b). These different values can be used in the absence of concentration data specific to the geographical area being assessed.

To date, there is no consensus or recommendations on acceptable levels of health risk associated with exposure to ambient air particulate matter. The acceptable risk levels traditionally considered for carcinogenic chemicals are 10^{-5} or 10^{-6}. For information, for ionising radiation and radon in air, 70 years of exposure to the regulatory limit value for public exposure[13] would correspond to an estimated level of cancer risk of around 10^{-3} to 10^{-2}, based on the available exposure-risk relationships (Hunter *et al.* 2015; ICRP 2022) and assuming a no-threshold linear relationship between exposure and risk.

For ambient air particulate matter, the lowest $PM_{2.5}$ concentrations observed in France are associated with a risk level of around 10^{-4} for lung cancer, low birth weight and asthma, and of

[13] For ionising radiation, the effective dose limit for public exposure set out in Article 12 of Directive 2013/59/Euratom is 1 mSv per year. For radon in air, Article 74 of this same directive sets a reference level not to be exceeded for the annual average activity concentration in air of 300 $Bq \cdot m^{-3}$.

around 10^{-3} for premature death, compared with a background concentration[14] of 5 $\mu g \cdot m^{-3}$. For information, the levels of excess lifetime risk of premature death, corresponding to exposure to a $PM_{2.5}$ concentration equivalent to the interim target values recommended by the WHO in 2021, vary from $8.6 \cdot 10^{-2}$ (for the WHO IT-4 value of 10 $\mu g \cdot m^{-3}$) to $20.7 \cdot 10^{-2}$ (for the WHO IT-1 value of 35 $\mu g \cdot m^{-3}$) compared to a background concentration of 5 $\mu g \cdot m^{-3}$.

[14] Background concentration: concentration level in the absence of the exposure of interest in the risk assessment. The background concentration can be determined, for example, based on the initial state of the air environment (e.g. before the start of industrial operations), a comparison with a local control environment, or local or national benchmarks indicating ranges of usual values in the non-degraded environment.

In the absence of modelling data enabling the proportion of anthropogenic pollution (related to human activity) in France to be estimated, the reference level without anthropogenic pollution used by *Santé Publique France* is 5 $\mu g \cdot m^3$ for $PM_{2.5}$ (5^{th} percentile of the distribution of concentrations of the pollutant) (*Santé Publique France* 2021). This level is used here as the background concentration.

Table 2. Respiratory TRVs for $PM_{2.5}$ and PM_{10} in ambient air

Pollutant	Type of TRV	Effect (key study)	Concentration-Excess risk or equivalent concentration(s) function	TRV
$PM_{2.5}$	Short-term TRV	Hospitalisations for cardiac causes (I00-I52) Wagner *et al.* (2023): pooled analysis of 17 French cities, lag 0-1	Piecewise linear function (relative risk)*	**For $[PM_{2.5}] \leq 10$ µg·m^{-3}:** **ERU = $1.65 \cdot 10^{-7}$ (µg·m^{-3})$^{-1}$** **For $[PM_{2.5}] > 10$ µg·m^{-3}:** **ERU = $7.69 \cdot 10^{-9}$ (µg·m^{-3})$^{-1}$ + $1.56 \cdot 10^{-6}$** (daily average $[PM_{2.5}]$)
				Confidence level: High
	Long-term TRV	Deaths from all non-accidental causes Strak *et al.* (2021): pooled analysis of eight European cohorts as part of the ELAPSE project	Non-linear function (hazard ratio)**	**ERU = $1.28 \cdot 10^{-2}$ (µg·m^{-3})$^{-1}$** *To refine, use the following parametric function:* **ELR = $2.19 \cdot 10^{-5}$ x $[PM_{2.5}]^3$ - $1.51 \cdot 10^{-3}$ x $[PM_{2.5}]^2$ + $3.61 \cdot 10^{-2}$ x $[PM_{2.5}]$ - $8.83 \cdot 10^{-2}$** (annual average $[PM_{2.5}]$)
				Confidence level: High
PM_{10}	Short-term TRV	Hospitalisations for cardiac causes (I00-I52) Wagner *et al.* (2023): pooled analysis of 17 French cities, lag 0-1	Piecewise linear function (relative risk)*	**For $[PM_{10}] \leq 20$ µg·m^{-3}:** **ERU = $7.34 \cdot 10^{-8}$ (µg·m^{-3})$^{-1}$** **For $[PM_{10}] > 20$ µg·m^{-3}:** **ERU = $7.71 \cdot 10^{-9}$ (µg·m^{-3})$^{-1}$ + $1.33 \cdot 10^{-6}$** (daily average $[PM_{10}]$)
				Confidence level: High
	Long-term TRV			No long-term TRV established # *# It is advisable to convert the PM_{10} exposure concentration ($[PM_{10}]$) into a $PM_{2.5}$ concentration ($[PM_{2.5}]$) using the $[PM_{2.5}]$:$[PM_{10}]$ ratio specific to the geographical area being assessed, or any another more sophisticated model, and then to use the recommended long-term TRV for $PM_{2.5}$*

*ERU: excess risk per unit; ELAPSE: Effects of Low-Level Air Pollution: A Study in Europe; ELR: excess lifetime risk; Lag: number of days between exposure and the health event; $[PM_{2.5}]$: atmospheric concentration of $PM_{2.5}$; $[PM_{10}]$: atmospheric concentration of PM_{10}. * Model 3. ** Shape-constrained health impact function (SCHIF), "ensemble" model.*

3.8.2. Short-term and long-term TRVs for black carbon in ambient air

The HRV Committee recommends using two TRVs established for black carbon, a short-term and a long-term respiratory TRVs (Table 3). These are the most protective ERUs, with the highest level of interest of the associated concentration-risk function. A high confidence level was assigned to these TRVs.

Table 3. Respiratory TRVs for black carbon in ambient air particulate matter

Type of TRV	Effect (key study)	Concentration-Excess risk or equivalent concentration(s) function	TRV
Short-term TRV	Cardiovascular hospitalisations Basagaña *et al.* (2015): meta-analysis of studies in three cities in Spain and Italy	Relative change in the risk ($\%_{change}$)	**ERU = $1.48 \cdot 10^{-6}$ ($\mu g \cdot m^{-3}$)$^{-1}$** (daily average [EC])
			Confidence level: High
Long-term TRV	Deaths from all non-accidental causes Strak *et al.* (2021): pooled analysis of eight European cohorts as part of the ELAPSE project	Non-linear hazard ratio function*	**ERU = $5.29 \cdot 10^{-2}$ (10^{-5} m^{-1})$^{-1}$** *To refine, use the following parametric function:* **ELR = $2.86 \cdot 10^{-4}$ x [Abs]^3 - $8.24 \cdot 10^{-3}$ x [Abs]^2 + $8.00 \cdot 10^{-2}$ x [Abs] + $4.49 \cdot 10^{-3}$** (annual average [Abs])
			Confidence level: High

*[Abs]: level of light absorbance in the atmosphere; [EC]: atmospheric concentration of elemental carbon (in the $PM_{2.5}$ fraction); ERU: excess risk per unit; ELAPSE: Effects of Low-Level Air Pollution: A Study in Europe; ELR: excess lifetime risk. * Shape-constrained health impact function (SCHIF), "ensemble" model.*

For an annual average concentration of black carbon between $5.00 \cdot 10^{-5}$ and $12.50 \cdot 10^{-5}$ m^{-1}, the long-term TRV could overestimate the risk due to the (non-linear) shape of the relationship between concentration and risk over this range. To refine the calculation for this range, the ERU can be replaced with the parametric function. However, for concentrations greater than $12.50 \cdot 10^{-5}$ m^{-1}, it is not advisable to use the parametric function due to major uncertainties concerning the shape of the relationship between concentration and risk.

The WG and HRV Committee reiterate that conversion factors are available for converting concentrations between the three black carbon metrics. However, as these factors can vary in time and across locations, it is advisable to use, whenever possible, a conversion factor specific to the measurement method, the geographical area and the time period.

4. AGENCY CONCLUSIONS AND RECOMMENDATIONS

The French Agency for Food, Environmental and Occupational Health & Safety endorses the conclusions and recommendations of the HRV Committee on the establishment of respiratory TRVs for various indicators of ambient air particulate matter: the $PM_{2.5}$ fraction, the PM_{10} fraction and black carbon in ambient air particulate matter.

This Opinion supplements the ANSES Opinion published in January 2023, which proposed a no-threshold long-term TRV for $PM_{2.5}$ – which remains unchanged – adding the establishment of short-term respiratory TRVs for $PM_{2.5}$ and PM_{10} and the establishment of short- and long-term respiratory TRVs for black carbon. With regard to ultrafine particles, the earlier feasibility study, which concluded that the establishment of TRVs was not feasible to date based on epidemiological studies, is not discussed in this Opinion. The Agency is continuing to carry out work to propose a TRV based on this feasibility study and new epidemiological and toxicological publications.

ANSES reiterates that the TRVs recommended here for $PM_{2.5}$ and PM_{10} concern environmental conventions for the measurement of ambient air particulate matter[15], without considering specific physico-chemical compositions. They are supplemented by TRVs for black carbon, an indicator of various combustion sources, which was added in the recast of the European Directive on ambient air quality (under the terms “black carbon” and “elemental carbon”) among the pollutants of emerging concern, such as ultrafine particles and the oxidative potential of particulate matter. These TRVs should be used separately in risk calculations (e.g. without adding together the excess risks calculated with the $PM_{2.5}$ TRV and with the black carbon TRV). In the event of particulate pollution with a specific physico-chemical composition (e.g. aerosol particles enriched with metals or minerals from industrial sources), the use of these TRVs should also be supplemented by risk calculations using the TRVs dedicated to the chemical particulates in question, separate from calculations using the $PM_{2.5}$, PM_{10} or black carbon TRVs.

The proposed TRVs have been established to be applicable in the concentration ranges generally observed in France and Europe.

Similarly, the proposed TRVs are based on French mortality and morbidity data. Therefore, the recommended values would have been different if another geographical scale had been considered. For example, for the long-term TRV for $PM_{2.5}$, the use of mortality data across the European Union would lead to an ERU of $1.59 \cdot 10^{-2}$ $(\mu g \cdot m^{-3})^{-1}$ instead of the value recommended here of $1.28 \cdot 10^{-2}$ $(\mu g \cdot m^{-3})^{-1}$.

Lastly, ANSES points out that $PM_{2.5}$, PM_{10} and black carbon are correlated with each other and with other pollutants in ambient air. The recommended values may therefore reflect the health effects of these indicators of particulate pollution, as well as some of the effects of the other correlated pollutants.

These values are intended to provide a useful tool for stakeholders involved in interpreting air pollution data. They will provide a way to assess particulate matter and black carbon in ambient air, using an approach comparable to that for chemicals, by expressing a quantification of the health risk, bearing in mind that the values usually used to establish acceptable risk levels[16] for chemicals are not directly transposable.

[15] In contrast to the measurement methods used in occupational health
[16] Expressed as individual excess risk (IER) or ELR

Nevertheless, the proposed TRVs will help to go beyond the simple comparison of concentration data with available guidance or regulatory values for PM_{10} and $PM_{2.5}$ (there are no guidance or regulatory values for black carbon).

The Agency will bring this expert appraisal work to the attention of its counterpart agencies in Europe, in particular in connection with changes in the regulations on air quality monitoring in Europe as announced by the revision of Directive 2008/50/EC.

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KEYWORDS

Carbone suie, carbone élémentaire, inhalation, particules, pollution de l'air ambiant, valeur toxicologique de référence, VTR.

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APPENDIX 1 – TRACKING OF UPDATES TO THE OPINION

Date	Page	Description of the change
12/01/2023	**-**	**Initial version concerning the recommendation of respiratory TRVs for long-term exposure to particulate matter in ambient air ($PM_{2.5}$) and the feasibility of establishing TRVs for black carbon and ultrafine particles.**
02/01/2023-26/03/2024	/	**Chapter 1 Background and purpose of the request** Section 1.1 Background: addition of text relating to black carbon and ultrafine particles (last paragraph of Section 1.1) Section 1.2 Purpose of the request: addition and amendment of text relating to the new purpose of the request **Chapter 2 Organisation of the expert appraisal**: addition of text concerning the adoption of the new work by the HRV Committee (short-term TRVs for $PM_{2.5}$ and PM_{10}, short- and long-term TRVs for black carbon), replacement of Table 1 on the method of examining the request (initial version) with text **Chapter 3 Analysis and conclusions of the HRV Committee and WG** Deletion of Section 3.1.2. Ultrafine particles (initial version) Section 3.1.2. Black carbon: amendment of the first paragraph to introduce the concept of the carbon fraction of particles and to provide metrological clarifications Section 3.2.1. Kinetics of inhaled particles: addition of the last paragraph on black carbon Section 3.2.2. Health effects: deletion of the text on ultrafine particles, replacement of Table 2 (initial version) – Summary of the health effects of long-term exposure to fine particulate matter ($PM_{2.5}$) with Table 1 – Summary of the conclusions of institutional reports on the health effects of exposure to fine particulate matter ($PM_{2.5}$) and black carbon (including the BC, EC and Abs metrics) Section 3.2.3. Sensitive population groups (initial version): deletion of this section Section 3.3. Method for establishing short- and long-term TRVs for $PM_{2.5}$, PM_{10} and black carbon in ambient air: addition and amendment of text and amendment of figures to include short-term TRVs and black carbon TRVs Section 3.4. Establishment of the short-term TRV for $PM_{2.5}$ and PM_{10} in ambient air: addition of this section Section 3.5. Feasibility of establishing TRVs for black carbon and ultrafine particles in ambient air: deletion of the initial version

Date	Page	Description of the change
		Section 3.6. Establishment of the short-term TRV for black carbon: addition of this section Section 3.7. Establishment of the long-term TRV for black carbon: addition of this section Section 3.8. Conclusions: Addition of the first paragraph providing information on the use of the $PM_{2.5}$, PM_{10} and black carbon TRVs Section 3.8.1. Short-term and long-term TRVs for $PM_{2.5}$ and PM_{10} in ambient air: addition and amendment of text and amendment of figures to include the short-term TRVs, extrapolation of the long-term TRV for $PM_{2.5}$ to PM_{10} and comparisons of the risk levels associated with $PM_{2.5}$ with the WHO guidance values and with the acceptable risk levels for ionising radiation and radon in air Section 3.6.2. on extrapolation of the long-term TRV for $PM_{2.5}$ to PM_{10}: deletion of the initial version Section 3.6.3. on the feasibility of recommending TRVs for black carbon and for ultrafine particles: deletion of the initial version **Chapter 4 Agency conclusions and recommendations** Updating of the conclusions and recommendations following the update of the previous Opinion of 12 January 2023, summarising the conclusions of this previous Opinion with regard to the feasibility of establishing TRVs for black carbon and for ultrafine particles.
25/09/2024	**-**	**Completed version concerning the establishment of respiratory TRVs for particulate matter in ambient air ($PM_{2.5}$ and PM_{10}) and black carbon in ambient air**
07/02/2025	/	**Chapter 3 Analysis and conclusions of the HRV Committee and the WG** Section 3.1.2. Black carbon: deletion of the sentence "*Primary emissions of black carbon play a key role in the formation of secondary organic aerosols (a major component of $PM_{2.5}$)*" Section 3.2.2. Health effects, Table 1 : - deletion of the text "*for the category of effect" in the column heading "Conclusions on the health effects of exposure to black carbon (BC, EC or Abs) for the category of effect*". - deletion of the text "*reported*" in the cell on the HEI (2022) conclusion on long-term neurological health "*Positive associations reported*". Section 3.3.4. Calculation of excess risks for various concentration levels: replacement of the text "*Excess daily risk (EDR) is the <u>additional</u> probability of occurrence of a health event due to an*

Date	Page	Description of the change
		exposure <u>of interest</u> on the same day of and/or in the few days preceding this occurrence, combined with the probability of occurrence of the event unrelated to this exposure." by "*Excess daily risk (EDR) is the <u>daily</u> probability of occurrence of a health event due to exposure on the same day of and/or in the few days preceding this occurrence, which adds to the probability of occurrence of the event unrelated to this exposure.*" Section 3.4.3. Choice of key studies providing concentration-risk functions, Figure 2: deletion of footnote "*NA: not available*", inclusion of footnote "*FR: French*" Section 3.4.4. $PM_{2.5}$ / Calculation of excess risks, Figure 3: replacement of the figure on the PM_{10} – EDR of hospitalisation for cardiac causes by the figure on the $PM_{2.5}$ - EDR of hospitalisation for cardiac causes. Section 3.4.6. PM_{10} / Choice of key studies providing concentration-risk functions, Figure 4: inclusion of footnotes "*EU: European; FR: French".* Section 3.4.7. PM_{10} / Calculation of excess risks, Figure 5: replacement of "$PM_{2.5}$" by "PM_{10}" in the title of the abscissa axis. Section 3.5.3. Choice of key studies providing concentration-risk functions, Figure 6: inclusion of footnotes "*EU: European; FR: French; incl.: including; LRIs: lower respiratory infections; NCDs: non-communicable diseases; w/o: without*". Section 3.6.4. Calculation of excess risk: moving of the paragraph "*The EDR derived from the concentration-risk function of Basagaña et al. … given the low risk of bias.*" before figure 9.

APPENDIX 2 – SUMMARY OF THE CANDIDATE VALUES FOR ESTABLISHING THE SHORT-TERM TRV FOR $PM_{2.5}$

Health event	**Plausibility of the causal relationship**	**Key reference selected**	**Level of interest**	**ERU in $(\mu g \cdot m^{-3})^{-1}$ over the $PM_{2.5}$ concentration range of 3 to 100 $\mu g \cdot m^{-3}$ [95% confidence interval of the ERU] (R^2) ***		**Parametric function describing the EDR value as a function of $[PM_{2.5}]$ from 3 to 100 $\mu g \cdot m^{-3}$**	**ERU confidence level (/5)**
Hospitalisations for pneumonia (<19 years)	Moderate	Nhung *et al.* (2017)	Moderate	$6.04 \cdot 10^{-7}$ [$1.34 \cdot 10^{-7}$; $1.00 \cdot 10^{-6}$] (R^2 = 1.0)		EDR = $6.04 \cdot 10^{-7}$ * [PM2.5]	HIGH (4.1)
Hospitalisations for cardiac causes (>65 years)	High	Atkinson *et al.* (2014)	Moderate	$5.02 \cdot 10^{-7}$ [$4.86 \cdot 10^{-8}$; $8.54 \cdot 10^{-7}$] (R^2 = 1.0)		EDR = $5.02 \cdot 10^{-7}$ * [PM2.5]	HIGH (4.3)
All cardiovascular hospitalisations (>65 years)	High	Atkinson *et al.* (2014)	Moderate	$2.80 \cdot 10^{-7}$ [$1.41 \cdot 10^{-7}$; $4.09 \cdot 10^{-7}$] (R^2 = 1.0)		EDR = $2.80 \cdot 10^{-7}$ * [PM2.5]	HIGH (4.3)
Hospitalisations for ischaemic heart disease (>65 years)	High	Lefranc *et al.* (2006)	Moderate	$1.82 \cdot 10^{-7}$ [$9.95 \cdot 10^{-8}$; $2.53 \cdot 10^{-7}$] (R^2 = 1.0)		EDR = $1.82 \cdot 10^{-7}$ * [PM2.5]	HIGH (4.4)
Hospitalisations for heart failure (>65 years)	High	Atkinson *et al.* (2014)	Moderate	$1.74 \cdot 10^{-7}$ [$6.05 \cdot 10^{-8}$; $2.64 \cdot 10^{-7}$] (R^2 = 1.0)		EDR = $1.74 \cdot 10^{-7}$ * [PM2.5]	HIGH (4.2)
Hospitalisations for cardiac causes	**High**	**Wagner *et al.* (2023)**	**High**	**$[PM_{2.5}] \in [3\text{-}10]$ $\mu g \cdot m^{-3}$** **$1.65 \cdot 10^{-7}$** **[$8.41 \cdot 10^{-8}$; $2.44 \cdot 10^{-7}$]** **(R^2 = 1.0)**	**$[PM_{2.5}] \in]10\text{-}100]$ $\mu g \cdot m^{-3}$** **$7.69 \cdot 10^{-9}$ $(\mu g \cdot m^{-3})^{-1}$ + $1.56 \cdot 10^{-6}$** **[$-2.23 \cdot 10^{-9}$ $(\mu g \cdot m^{-3})^{-1}$ + $1.00 \cdot 10^{-6}$;** **$1.83 \cdot 10^{-8}$ $(\mu g \cdot m^{-3})^{-1}$ + $2.26 \cdot 10^{-6}$]** **(R^2 = 1.0)**	**$[PM2.5] \in [3\text{-}10]$ $\mu g \cdot m^{-3}$** **EDR = $1.65 \cdot 10^{-7}$ * [PM2.5]** **$[PM2.5] \in [10\text{-}100]$ $\mu g \cdot m^{-3}$** **EDR = $7.69 \cdot 10^{-9}$ * [PM2.5] + $1.56 \cdot 10^{-6}$**	**HIGH (4.8)**
All respiratory hospitalisations (>65 years)	High	Atkinson *et al.* (2014)	Moderate	$7.91 \cdot 10^{-8}$ [$-7.82 \cdot 10^{-8}$; $2.15 \cdot 10^{-7}$] (R^2 = 1.0)		EDR = $7.91 \cdot 10^{-8}$ * [PM2.5]	HIGH (4.0)
All respiratory hospitalisations	High	Wagner *et al.* (2023)	High	$[PM_{2.5}] \in [3\text{-}20]$ $\mu g \cdot m^{-3}$ $6.00 \cdot 10^{-8}$ [$3.92 \cdot 10^{-8}$; $8.04 \cdot 10^{-8}$] (R^2 = 1.0)	$[PM_{2.5}] \in]20\text{-}100]$ $\mu g \cdot m^{-3}$ $-2.21 \cdot 10^{-8}$ $(\mu g \cdot m^{-3})^{-1}$ + $1.64 \cdot 10^{-6}$ [$-3.58 \cdot 10^{-8}$ $(\mu g \cdot m^{-3})^{-1}$ + $1.67 \cdot 10^{-6}$; $-2.48 \cdot 10^{-8}$ $(\mu g \cdot m^{-3})^{-1}$ + $1.85 \cdot 10^{-6}$] (R^2 = 1.0)	$[PM2.5] \in [3\text{-}20]$ $\mu g \cdot m^{-3}$ EDR = $6.00 \cdot 10^{-8}$ * [PM2.5] $[PM2.5] \in [20\text{-}100]$ $\mu g \cdot m^{-3}$ EDR = $-2.21 \cdot 10^{-8}$ * [PM2.5] + $1.64 \cdot 10^{-6}$	HIGH (4.9)
All cardiovascular hospitalisations	High	Atkinson *et al.* (2014)	Moderate	$5.76 \cdot 10^{-8}$ [$1.11 \cdot 10^{-8}$; $1.02 \cdot 10^{-7}$] (R^2 = 1.0)		EDR = $5.76 \cdot 10^{-8}$ * [PM2.5]	HIGH (4.3)

Health event	Plausibility of the causal relationship	Key reference selected	Level of interest	ERU in $(\mu g \cdot m^{-3})^{-1}$ over the $PM_{2.5}$ concentration range of 3 to 100 $\mu g \cdot m^{-3}$ [95% confidence interval of the ERU] (R^2) *		Parametric function describing the EDR value as a function of $[PM_{2.5}]$ from 3 to 100 $\mu g \cdot m^{-3}$	ERU confidence level (/5)
Mortality from all non-accidental causes	High	Wagner *et al.* (2023)	High	$\underline{[PM_{2.5}] \in [3\text{-}10]\ \mu g \cdot m^{-3}}$ $4.90 \cdot 10^{-8}$ $[1.67 \cdot 10^{-8}; 7.71 \cdot 10^{-8}]$ (R^2 = 1.0)	$\underline{[PM_{2.5}] \in]10\text{-}100]\ \mu g \cdot m^{-3}}$ $3.56 \cdot 10^{-9}\ (\mu g \cdot m^{-3})^{-1} + 4.46 \cdot 10^{-7}$ $[2.43 \cdot 10^{-9}\ (\mu g \cdot m^{-3})^{-1} + 1.61 \cdot 10^{-7}; 5.02 \cdot 10^{-9}\ (\mu g \cdot m^{-3})^{-1} + 7.13 \cdot 10^{-7}]$ (R^2 = 1.0)	$\underline{[PM2.5] \in [3\text{-}10]\ \mu g \cdot m^{-3}}$ EDR = $4.90 \cdot 10^{-8}$ * [PM2.5] $\underline{[PM2.5] \in [10\text{-}100]\ \mu g \cdot m^{-3}}$ EDR = $3.56 \cdot 10^{-9}$ * [PM2.5] + $4.46 \cdot 10^{-7}$	HIGH (4.9)
Hospitalisations for ischaemic heart disease	High	Lefranc *et al.* (2006)	Moderate	$3.20 \cdot 10^{-8}$ $[-1.54 \cdot 10^{-9}; 5.94 \cdot 10^{-8}]$ (R^2 = 1.0)		EDR = $3.20 \cdot 10^{-8}$ * [PM2.5]	HIGH (4.3)
Hospitalisations for heart failure	High	Shah *et al.* (2013)	Moderate	$2.02 \cdot 10^{-8}$ $[1.40 \cdot 10^{-8}; 2.68 \cdot 10^{-8}]$ (R^2 = 1.0)		EDR = $2.02 \cdot 10^{-8}$ * [PM2.5]	HIGH (4.3)
Mortality from all cardiovascular causes	High	Wagner *et al.* (2023)	High	$\underline{[PM_{2.5}] \in [3\text{-}10]\ \mu g \cdot m^{-3}}$ $1.66 \cdot 10^{-8}$ $[4.95 \cdot 10^{-9}; 2.75 \cdot 10^{-8}]$ (R^2 = 1.0)	$\underline{[PM_{2.5}] \in]10\text{-}100]\ \mu g \cdot m^{-3}}$ $4.87 \cdot 10^{-10}\ (\mu g \cdot m^{-3})^{-1} + 1.57 \cdot 10^{-7}$ $[-1.66 \cdot 10^{-10}\ (\mu g.m^{-3})^{-1} + 6.81 \cdot 10^{-8}; 1.71 \cdot 10^{-9}\ (\mu g.m^{-3})^{-1} + 2.54 \cdot 10^{-7}]$ (R^2 = 1.0)	$\underline{[PM_{2.5}] \in [3\text{-}10]\ \mu g \cdot m^{-3}}$ EDR = $1.66 \cdot 10^{-8}$ * [PM2.5] $\underline{[PM_{2.5}] \in]10\text{-}100]\ \mu g \cdot m^{-3}}$ EDR = $4.87 \cdot 10^{-10}$ * [PM2.5] + $1.57 \cdot 10^{-7}$	HIGH (5.0)
Mortality from all cardiac causes (>74 years)	Moderate	Pascal *et al.* (2014)	Moderate	$9.10 \cdot 10^{-9}$ $[0.00; 1.72 \cdot 10^{-8}]$ (R^2 = 1.0)		EDR = $9.10 \cdot 10^{-9}$ * [PM2.5]	HIGH (4.6)
Hospitalisations for stroke	Moderate	Shah *et al.* (2015)	Moderate	$5.09 \cdot 10^{-9}$ $[4.65 \cdot 10^{-9}; 5.53 \cdot 10^{-9}]$ (R^2 = 1.0)		EDR = $5.09 \cdot 10^{-9}$ * [PM2.5]	HIGH (4.1)
Mortality from ischaemic heart disease	Moderate	Atkinson *et al.* (2014)	Moderate	$2.35 \cdot 10^{-9}$ $[5.32 \cdot 10^{-10}; 3.82 \cdot 10^{-9}]$ (R^2 = 1.0)		EDR = $2.35 \cdot 10^{-9}$ * [PM2.5]	HIGH (4.2)
Emergency department visits for asthma (<18 years)	High	Host *et al.* (2018)	Moderate	$1.85 \cdot 10^{-9}$ $[3.17 \cdot 10^{-10}; 2.68 \cdot 10^{-9}]$ (R^2 = 1.0)		EDR = $1.85 \cdot 10^{-9}$ * [PM2.5]	HIGH (4.3)
Mortality from all respiratory causes	Moderate	Liu *et al.* (2019)	High	$5.31 \cdot 10^{-10}$ $[3.77 \cdot 10^{-10}; 6.53 \cdot 10^{-10}]$ (R^2 = 1.0)		EDR = $5.31 \cdot 10^{-10}$ * [PM2.5]	HIGH (4.6)

Health event	Plausibility of the causal relationship	Key reference selected	Level of interest	ERU in $(\mu g \cdot m^{-3})^{-1}$ over the $PM_{2.5}$ concentration range of 3 to 100 $\mu g \cdot m^{-3}$ [95% confidence interval of the ERU] (R^2) *	Parametric function describing the EDR value as a function of [$PM_{2.5}$] from 3 to 100 $\mu g \cdot m^{-3}$	ERU confidence level (/5)
Mortality from stroke	Moderate	Orellano *et al.* (2020)	High	$4.58 \cdot 10^{-10}$ [$7.84 \cdot 10^{-11}$; $8.18 \cdot 10^{-10}$] ($R^2 = 1.0$)	EDR = $4.58 \cdot 10^{-10}$ * [PM2.5]	HIGH (4.4)
Hospitalisations for chronic obstructive pulmonary disease (>65 years)	Moderate	Atkinson *et al.* (2014)	Moderate	$2.80 \cdot 10^{-10}$ [$1.26 \cdot 10^{-10}$; $4.19 \cdot 10^{-10}$] ($R^2 = 1.0$)	EDR = $2.80 \cdot 10^{-10}$ * [PM2.5]	HIGH (4.2)

*Values presented in the table in decreasing order of ERU. In bold: the row of the table corresponding to the ERU used to establish the TRV. * The ERU unit ("$\mu g \cdot m^{-3})^{-1}$") is indicated in the table when this includes a constant (intercept), to be able to identify the slope factor for the constant. When the ERU unit is not stated, it is the slope factor. [$PM_{2.5}$]: average daily concentration of $PM_{2.5}$; EDR: excess daily risk; ERU: excess risk per unit = excess daily risk per $PM_{2.5}$ concentration unit; R^2: coefficient of determination of the linear regression line. The closer R^2 is to 1, the better the linear fit. For the parametric function relating EDR to [$PM_{2.5}$], all the coefficients of determination of the linear regression curve are equal to 1.0, rounded to the first decimal place.*

APPENDIX 3 – SUMMARY OF THE CANDIDATE VALUES FOR ESTABLISHING THE SHORT-TERM TRV FOR PM_{10}

Health event	**Plausibility of the causal relationship**	**Key reference selected**	**Level of interest**	**ERU in $(\mu g \cdot m^{-3})^{-1}$ over the PM_{10} concentration range of 4 to 200 $\mu g \cdot m^{-3}$ [95% confidence interval of the ERU] (R^2) ***		**Parametric function describing the EDR value as a function of [PM_{10}] from 4 to 200 $\mu g \cdot m^{-3}$**	**ERU confidence level (/5)**
All cardiovascular hospitalisations (>65 years)	High	Larrieu *et al.* (2007)	Moderate	$2.30 \cdot 10^{-7}$ [$1.12 \cdot 10^{-7}$; $3.40 \cdot 10^{-7}$] (R^2 = 1.0)		EDR = $2.30 \cdot 10^{-7}$ * [PM10]	HIGH (4.3)
Hospitalisations for cardiac causes (>65 years)	High	Larrieu *et al.* (2007)	Moderate	$2.12 \cdot 10^{-7}$ [$1.05 \cdot 10^{-7}$; $2.95 \cdot 10^{-7}$] (R^2 = 1.0)		EDR = $2.12 \cdot 10^{-7}$ * [PM10]	HIGH (4.3)
Hospitalisations for ischaemic heart disease (>65 years)	High	Larrieu *et al.* (2007)	Moderate	$1.15 \cdot 10^{-7}$ [$6.99 \cdot 10^{-8}$; $2.79 \cdot 10^{-7}$] (R^2 = 1.0)		EDR = $1.15 \cdot 10^{-7}$ * [PM10]	HIGH (4.4)
All respiratory hospitalisations (>65 years)	High	Lefranc *et al.* (2006)	Moderate	$7.70 \cdot 10^{-8}$ [$-6.92 \cdot 10^{-8}$; $2.14 \cdot 10^{-7}$] (R^2 = 1.0)		EDR = $7.70 \cdot 10^{-8}$ * [PM10]	HIGH (4.4)
Hospitalisations for cardiac causes	**High**	**Wagner *et al.* (2023)**	**High**	**[PM10] ∈ [4-20] µg·m^{-3}** **$7.34 \cdot 10^{-8}$** **[$2.96 \cdot 10^{-8}$; $1.11 \cdot 10^{-7}$]** **(R^2 = 1.0)**	**[PM10] ∈ [20-200] µg·m^{-3}** **$7.71 \cdot 10^{-9}$ $(\mu g \cdot m^{-3})^{-1} + 1.33 \cdot 10^{-6}$** **[$2.08 \cdot 10^{-9}$ $(\mu g.m^{-3})^{-1} + 7.12 \cdot 10^{-7}$; $1.38 \cdot 10^{-8}$ $(\mu g.m^{-3})^{-1} + 1.93 \cdot 10^{-6}$]** **($R^2$ = 1.0)**	**[PM10] ∈ [4-20] µg·m^{-3}** **EDR = $7.34 \cdot 10^{-8}$ * [PM10]** **[PM10] ∈ [20-200] µg·m^{-3}** **EDR = $7.71 \cdot 10^{-9}$ * [PM10] + $1.33 \cdot 10^{-6}$**	**HIGH (4.8)**
All cardiovascular hospitalisations	High	Larrieu *et al.* (2007)	Moderate	$4.36 \cdot 10^{-8}$ [$6.56 \cdot 10^{-9}$; $7.19 \cdot 10^{-8}$] (R^2 = 1.0)		EDR = $4.36 \cdot 10^{-8}$ * [PM10]	HIGH (4.3)
All respiratory hospitalisations	High	Wagner *et al.* (2023)	High	[PM10] ∈ [4-50] µg·m^{-3} $3.15 \cdot 10^{-8}$ [$1.53 \cdot 10^{-8}$; $9.42 \cdot 10^{-8}$] (R^2 = 1.0)	[PM10] ∈ [50-200] µg·m^{-3} $-5.37 \cdot 10^{-8}$ $(\mu g \cdot m^{-3})^{-1} + 4.40 \cdot 10^{-6}$ [$-8.46 \cdot 10^{-8}$ $(\mu g.m^{-3})^{-1} + 5.74 \cdot 10^{-6}$; $1.17 \cdot 10^{-8}$ $(\mu g.m^{-3})^{-1} + 1.64 \cdot 10^{-6}$] ($R^2$ = 1.0)	[PM10] ∈ [4-50] µg·m^{-3} EDR = $3.15 \cdot 10^{-8}$ * [PM10] [PM10] ∈ [50-200] µg·m^{-3} EDR = $-5.37 \cdot 10^{-8}$ * [PM10] + $4.40 \cdot 10^{-6}$	HIGH (4.9)
Hospitalisations for ischaemic heart disease	High	Larrieu *et al.* (2007)	Moderate	$2.52 \cdot 10^{-8}$ [$1.15 \cdot 10^{-8}$; $3.66 \cdot 10^{-8}$] (R^2 = 1.0)		EDR = $2.52 \cdot 10^{-8}$ * [PM10]	HIGH (4.3)
Mortality from all non-accidental causes	High	Wagner *et al.* (2023)	High	[PM10] ∈ [4-30] µg·m^{-3} $1.79 \cdot 10^{-8}$ [$1.03 \cdot 10^{-8}$; $2.49 \cdot 10^{-8}$] (R^2 = 1.0)	[PM10] ∈ [30-200] µg·m^{-3} $1.19 \cdot 10^{-9}$ $(\mu g \cdot m^{-3})^{-1} + 4.87 \cdot 10^{-7}$ [$-1.65 \cdot 10^{-9}$ $(\mu g \cdot m^{-3})^{-1} + 4.46 \cdot 10^{-7}$; $4.39 \cdot 10^{-9}$ $(\mu g \cdot m^{-3})^{-1} + 6.13 \cdot 10^{-7}$] ($R^2$ = 1.0)	[PM10] ∈ [4-30] µg·m^{-3} EDR = $1.79 \cdot 10^{-8}$ * [PM10] [PM10] ∈ [30-200] µg·m^{-3}	HIGH (4.9)

Health event	Plausibility of the causal relationship	Key reference selected	Level of interest	ERU in $(\mu g \cdot m^{-3})^{-1}$ over the PM_{10} concentration range of 4 to 200 $\mu g \cdot m^{-3}$ [95% confidence interval of the ERU] (R^2) *		Parametric function describing the EDR value as a function of $[PM_{10}]$ from 4 to 200 $\mu g \cdot m^{-3}$	ERU confidence level (/5)
						EDR = $1.19 \cdot 10^{-9}$ * [PM10] + $4.87 \cdot 10^{-7}$	
Emergency department visits for asthma	High	Zheng *et al.* (2015)	Moderate	$1.17 \cdot 10^{-8}$ [$4.50 \cdot 10^{-9}$; $1.83 \cdot 10^{-8}$] (R^2 = 1.0)		EDR = $1.17 \cdot 10^{-8}$ * [PM10]	HIGH (4.1)
Mortality from all cardiac causes (>74 years)	Moderate	Pascal *et al.* (2014)	Moderate	$9.86 \cdot 10^{-9}$ [$2.17 \cdot 10^{-9}$; $1.62 \cdot 10^{-8}$] (R^2 = 1.0)		EDR = $9.86 \cdot 10^{-9}$ * [PM10]	HIGH (4.6)
Mortality from ischaemic heart disease (>74 years)	Moderate	Pascal *et al.* (2014)	Moderate	$9.34 \cdot 10^{-9}$ [$-6.68 \cdot 10^{-10}$; $1.70 \cdot 10^{-8}$] (R^2 = 1.0)		EDR = $9.34 \cdot 10^{-9}$ * [PM10]	HIGH (4.4)
Mortality from all cardiovascular causes	High	Wagner *et al.* (2023)	High	$\underline{[PM10] \in [4\text{-}30]\ \mu g \cdot m^{-3}}$ $5.64 \cdot 10^{-9}$ [$2.72 \cdot 10^{-9}$; $7.58 \cdot 10^{-9}$] (R^2 = 1.0)	$\underline{[PM10] \in [30\text{-}200]\ \mu g \cdot m^{-3}}$ $-5.07 \cdot 10^{-10}$ $(\mu g \cdot m^{-3})^{-1} + 1.89 \cdot 10^{-7}$ [$-1.51 \cdot 10^{-9}$ $(\mu g \cdot m^{-3})^{-1} + 1.66 \cdot 10^{-7}$; $5.85 \cdot 10^{-10}$ $(\mu g \cdot m^{-3})^{-1} + 1.99 \cdot 10^{-7}$] ($R^2$ = 1.0)	$\underline{[PM10] \in [4\text{-}30]\ \mu g \cdot m^{-3}}$ EDR = $5.64 \cdot 10^{-9}$ * [PM10] $\underline{[PM10] \in [30\text{-}200]\ \mu g \cdot m^{-3}}$ EDR = $-5.07 \cdot 10^{-10}$ * [PM10] + $1.89 \cdot 10^{-7}$	HIGH (5.0)
Hospitalisations for stroke	Moderate	Yang *et al.* (2014)	Moderate	$3.25 \cdot 10^{-9}$ [$4.81 \cdot 10^{-10}$; $5.81 \cdot 10^{-9}$] (R^2 = 1.0)		EDR = $3.25 \cdot 10^{-9}$ * [PM10]	HIGH (4.0)
Hospitalisations for asthma	High	Zheng *et al.* (2015)	Moderate	$2.43 \cdot 10^{-9}$ [$1.81 \cdot 10^{-9}$; $3.22 \cdot 10^{-9}$] (R^2 = 1.0)		EDR = $2.43 \cdot 10^{-9}$ * [PM10]	HIGH (4.3)
Mortality from all cardiac causes	Moderate	Pascal *et al.* (2014)	Moderate	$1.29 \cdot 10^{-9}$ [0.00; $2.40 \cdot 10^{-9}$] (R^2 = 1.0)		EDR = $1.29 \cdot 10^{-9}$ * [PM10]	HIGH (4.6)
Hospitalisations for myocardial infarction	Moderate	Mustafić *et al.* (2012)	Moderate	$1.25 \cdot 10^{-9}$ [$1.24 \cdot 10^{-10}$; $1.59 \cdot 10^{-9}$] (R^2 = 1.0)		EDR = $1.25 \cdot 10^{-9}$ * [PM10]	HIGH (4.1)
Mortality from all respiratory causes	Moderate	Orellano *et al.* (2020)	High	$6.27 \cdot 10^{-10}$ [$1.24 \cdot 10^{-10}$; $1.08 \cdot 10^{-9}$] (R^2 = 1.0)		EDR = $6.27 \cdot 10^{-10}$ * [PM10]	HIGH (4.7)
Mortality from ischaemic heart disease	Moderate	Pascal *et al.* (2014)	Moderate	$6.04 \cdot 10^{-10}$ [$-3.33 \cdot 10^{-10}$; $1.38 \cdot 10^{-9}$] (R^2 = 1.0)		EDR = $6.04 \cdot 10^{-10}$ * [PM10]	HIGH (4.4)

Health event	Plausibility of the causal relationship	Key reference selected	Level of interest	ERU in $(\mu g \cdot m^{-3})^{-1}$ over the PM_{10} concentration range of 4 to 200 $\mu g \cdot m^{-3}$ [95% confidence interval of the ERU] (R^2) *	Parametric function describing the EDR value as a function of $[PM_{10}]$ from 4 to 200 $\mu g \cdot m^{-3}$	ERU confidence level (/5)
Mortality from stroke	Moderate	Orellano *et al.* (2020)	High	$2.79 \cdot 10^{-10}$ $[1.42 \cdot 10^{-10}; 4.11 \cdot 10^{-10}]$ ($R^2 = 1.0$)	EDR = $2.79 \cdot 10^{-10}$ * [PM10]	HIGH (4.9)

*Values presented in the table in decreasing order of ERU. In bold: the row of the table corresponding to the ERU used to establish the TRV. * The ERU unit ("$\mu g \cdot m^{-3})^{-1}$") is indicated in the table when this includes a constant (intercept), to be able to identify the slope factor for the constant. When the ERU unit is not stated, it is the slope factor. $[PM_{10}]$: average daily concentration of PM_{10}; EDR: excess daily risk; ERU: excess risk per unit = excess daily risk per PM_{10} concentration unit; R^2: coefficient of determination of the linear regression line. The closer R^2 is to 1, the better the linear fit. For the parametric function relating EDR to $[PM_{10}]$, all the coefficients of determination of the linear regression curve are equal to 1.0, rounded to the first decimal place.*

APPENDIX 4 – SUMMARY OF THE CANDIDATE VALUES FOR ESTABLISHING THE LONG-TERM TRV FOR $PM_{2.5}$

Health event	Plausibility of the causal relationship	Key reference selected	Level of interest	ERU value in $(\mu g \cdot m^{-3})^{-1}$ [95% confidence interval] over the $PM_{2.5}$ concentration range of 4.9 to 30 $\mu g \cdot m^{-3}$ (R^2)		Parametric function describing the ELR value as a function of the $[PM_{2.5}]$ concentration from 4.9 to 30 $\mu g \cdot m^{-3}$	ERU confidence level (/5)
Mortality from all non-accidental causes	**High**	Strak *et al.* (2021)	**High**	**4.9 to 15 $\mu g \cdot m^{-3}$** **$1.28 \cdot 10^{-2}$** **[$9.37 \cdot 10^{-3}$; $1.77 \cdot 10^{-2}$]** **(R^2 = 1.0)**	**15 to 30 $\mu g \cdot m^{-3}$** **$2.67 \cdot 10^{-3}$ $(\mu g \cdot m^{-3})^{-1}$ + $1.47 \cdot 10^{-1}$** **[$2.20 \cdot 10^{-3}$ $(\mu g \cdot m^{-3})^{-1}$ + $1.14 \cdot 10^{-1}$; $2.89 \cdot 10^{-3}$ $(\mu g \cdot m^{-3})^{-1}$ + $2.00 \cdot 10^{-1}$]** **(R^2 = 1.0)**	**ELR = $2.19 \cdot 10^{-5}$ x $[PM_{2.5}]^3$ - $1.51 \cdot 10^{-3}$ x $[PM_{2.5}]^2$ + $3.61 \cdot 10^{-2}$ x $[PM_{2.5}]$ - $8.83 \cdot 10^{-2}$**	**High (4.8)**
Incidence of asthma in adults	Moderate	Liu *et al.* (2021)	Moderate	$4.62 \cdot 10^{-3}$ [$3.26 \cdot 10^{-3}$; $1.81 \cdot 10^{-2}$] (R^2 = 0.8)		ELR = $1.46 \cdot 10^{-6}$ x $[PM_{2.5}]^3$ - $1.58 \cdot 10^{-4}$ x $[PM_{2.5}]^2$ + $7.47 \cdot 10^{-3}$ x $[PM_{2.5}$ + $1.38 \cdot 10^{-3}$	Moderate (3.6)
Incidence of asthma in children	High	Khreis *et al.* (2017)	High	$3.87 \cdot 10^{-3}$ [$1.59 \cdot 10^{-3}$; $4.99 \cdot 10^{-3}$] (R^2 = 0.9)		ELR = $7.94 \cdot 10^{-7}$ x $[PM_{2.5}]^3$ - $9.80 \cdot 10^{-5}$ x $[PM_{2.5}]^2$ + $5.73 \cdot 10^{-3}$ x $[PM_{2.5}$ + $5.60 \cdot 10^{-4}$	High (4.7)
Mortality from all cardiovascular causes	High	Strak *et al.* (2021)	High	$1.99 \cdot 10^{-3}$ [$9.92 \cdot 10^{-4}$; $2.52 \cdot 10^{-3}$] (R^2 = 0.8)		ELR = $2.80 \cdot 10^{-6}$ x $[PM_{2.5}]^3$ - $2.23 \cdot 10^{-4}$ x $[PM_{2.5}]^2$ + $6.39 \cdot 10^{-3}$ x $[PM_{2.5}]$ - $1.60 \cdot 10^{-2}$	High (4.9)
Low birth weight	Moderate	Pedersen *et al.* (2013)	High	$1.64 \cdot 10^{-3}$ [$7.05 \cdot 10^{-4}$; $2.11 \cdot 10^{-3}$] (R^2 = 0.9)		ELR = $2.82 \cdot 10^{-7}$ x $[PM_{2.5}]^3$ - $3.71 \cdot 10^{-5}$ x $[PM_{2.5}]^2$ + $2.27 \cdot 10^{-3}$ x $[PM_{2.5}$ + $1.55 \cdot 10^{-4}$	High (4.3)
Incidence of stroke	High	Brunekreef *et al.* (2021)	High	$1.37 \cdot 10^{-3}$ [$2.38 \cdot 10^{-4}$; $2.37 \cdot 10^{-3}$] (R^2 = 0.9)		ELR = $1.15 \cdot 10^{-6}$ x $[PM_{2.5}]^3$ - $1.09 \cdot 10^{-4}$ x $[PM_{2.5}]^2$ + $3.84 \cdot 10^{-3}$ x $[PM_{2.5}]$ - $1.17 \cdot 10^{-2}$	High (4.9)
Incidence of lung cancer	Moderate	Hvidtfeldt *et al.* (2021)	High	$9.56 \cdot 10^{-4}$ [$2.16 \cdot 10^{-4}$; $1.54 \cdot 10^{-3}$] (R^2 = 0.8)		ELR = $1.13 \cdot 10^{-6}$ x $[PM_{2.5}]^3$ - $9.21 \cdot 10^{-5}$ x $[PM_{2.5}]^2$ + $2.78 \cdot 10^{-3}$ x $[PM_{2.5}]$ - $6.37 \cdot 10^{-3}$	High (4.6)
Mortality from ischaemic heart disease	Moderate	Strak *et al.* (2021)	High	$4.20 \cdot 10^{-4}$ [$1.58 \cdot 10^{-4}$; $7.08 \cdot 10^{-4}$] (R^2 = 1.0)		ELR = $2.23 \cdot 10^{-7}$ x $[PM_{2.5}]^3$ - $2.12 \cdot 10^{-5}$ x $[PM_{2.5}]^2$ + $8.89 \cdot 10^{-4}$ x $[PM_{2.5}]$ - $2.04 \cdot 10^{-3}$	High (4.5)
Mortality from all respiratory causes	Moderate	Strak *et al.* (2021)	High	$3.05 \cdot 10^{-4}$ [$-1.96 \cdot 10^{-4}$; $6.88 \cdot 10^{-4}$] (R^2 = 0.8)		ELR = $2.66 \cdot 10^{-7}$ x $[PM_{2.5}]^3$ - $2.65 \cdot 10^{-5}$ x $[PM_{2.5}]^2$ + $9.04 \cdot 10^{-4}$ x $[PM_{2.5}]$ - $2.65 \cdot 10^{-3}$	High (4.8)

Health event	**Plausibility of the causal relationship**	**Key reference selected**	**Level of interest**	**ERU value in $(\mu g \cdot m^{-3})^{-1}$ [95% confidence interval] over the $PM_{2.5}$ concentration range of 4.9 to 30 $\mu g \cdot m^{-3}$ (R^2)**		**Parametric function describing the ELR value as a function of the $[PM_{2.5}]$ concentration from 4.9 to 30 $\mu g \cdot m^{-3}$**	**ERU confidence level (/5)**
Mortality from COPD	Moderate	Strak *et al.* (2021)	High	4.9 to 15 $\mu g \cdot m^{-3}$ $2.67 \cdot 10^{-4}$ $[-7.41 \cdot 10^{-7} + 9.71 \cdot 10^{-5}; 3.46 \cdot 10^{-4} + 1.90 \cdot 10^{-3}]$ ($R^2 = 1.0$)	15 to 30 $\mu g \cdot m^{-3}$ $7.61 \cdot 10^{-5} (\mu g \cdot m^{-3})^{-1} + 2.83 \cdot 10^{-3}$ $[-4.38 \cdot 10^{-6} (\mu g \cdot m^{-3})^{-1} + 9.71 \cdot 10^{-5}; 3.47 \cdot 10^{-5} (\mu g \cdot m^{-3})^{-1} + 6.37 \cdot 10^{-3}]$ ($R^2 = 1.0$)	$ELR = 2.54 \cdot 10^{-7} \times [PM_{2.5}]^3 - 2.04 \cdot 10^{-5} \times [PM_{2.5}]^2 + 5.91 \cdot 10^{-4} \times [PM_{2.5}] - 1.24 \cdot 10^{-3}$	High (4.6)
Mortality from lower respiratory tract infection	Moderate	Burnett *et al.* (2018)	Moderate	$1.19 \cdot 10^{-4}$ $[6.60 \cdot 10^{-5}; 1.59 \cdot 10^{-4}]$ ($R^2 = 1$)		$ELR = -3.39 \cdot 10^{-8} \times [PM_{2.5}]^3 - 5.19 \cdot 10^{-7} \times [PM_{2.5}]^2 + 1.73 \cdot 10^{-4} \times [PM_{2.5}] - 4.44 \cdot 10^{-4}$	High (4.1)

COPD: chronic obstructive pulmonary disease; ELR: excess lifetime risk (except for the incidence of asthma in children where excess risk is calculated over the period <1-19 years, and for low birth weight, where excess risk is calculated for exposure throughout pregnancy); ERU: excess risk per unit; R^2: coefficient of determination of the linear regression line used to calculate the ERU. For the parametric function relating ELR to $[PM_{2.5}]$, all the coefficients of determination of the polynomial regression curve are equal to 1.0, rounded to the first decimal place.

APPENDIX 5 – SUMMARY OF THE CANDIDATE VALUES FOR ESTABLISHING THE SHORT-TERM TRV FOR BLACK CARBON

Health event	Plausibility of the causal relationship	Key reference selected	Level of interest	ERU value in $(\mu g \cdot m^{-3})^{-1}$ [95% confidence interval] over the elemental carbon concentration range of 0.2 to 15.0 $\mu g \cdot m^{-3}$ (R^2)	Parametric function describing the EDR value as a function of the elemental carbon [EC] concentration from 0.2 to 15.0 $\mu g \cdot m^{-3}$	ERU confidence level (/5)
Cardiovascular hospitalisations	**High**	**Basagaña *et al.* (2015)[A]**	**Moderate**	**$1.48 \cdot 10^{-6}$ [$3.83 \cdot 10^{-7}$; $2.35 \cdot 10^{-6}$] (R^2 = 1.00)**	**EDR = $1.48 \cdot 10^{-6}$ x [EC]**	**4.5**
Respiratory hospitalisations	High	Basagaña *et al.* (2015)[B]	Moderate	$7.44 \cdot 10^{-7}$ [$2.96 \cdot 10^{-8}$; $1.30 \cdot 10^{-6}$] (R^2 = 1.00)	EDR = $7.44 \cdot 10^{-7}$ x [EC]	4.4
Emergency department visits for asthma	Moderate	Bi *et al.* (2023)[C]	Moderate	$2.20 \cdot 10^{-7}$ [$6.01 \cdot 10^{-8}$; $3.45 \cdot 10^{-7}$] (R^2 = 0.99)	EDR = $2.20 \cdot 10^{-7}$ x [EC]	4.4
All-cause mortality	High	Achilleos *et al.* (2017)[D]	Moderate	$7.61 \cdot 10^{-8}$ [$2.95 \cdot 10^{-8}$; $1.21 \cdot 10^{-7}$] (R^2 = 1.00)	EDR = $7.61 \cdot 10^{-8}$ x [EC]*	4.2
Mortality from cardiovascular causes	High	Basagaña *et al.* (2015)[E]	Moderate	$3.06 \cdot 10^{-8}$ [$1.79 \cdot 10^{-10}$; $5.72 \cdot 10^{-8}$] (R^2 = 1.00)	EDR = $3.06 \cdot 10^{-8}$ x [EC]	4.3
Mortality from respiratory causes	High	Basagaña *et al.* (2015)[F]	Moderate	$2.22 \cdot 10^{-8}$ [$6.80 \cdot 10^{-9}$; $3.35 \cdot 10^{-8}$] (R^2 = 0.99)	EDR = $2.22 \cdot 10^{-8}$ x [EC]	4.2

*A: elemental carbon in the $PM_{2.5}$ fraction at lag 0. B: elemental carbon in the $PM_{2.5}$ fraction at lag 1. C: elemental carbon over cumulative lag 0-7, all ages. D: mixture of elemental carbon and black carbon, mixed lags. E: elemental carbon in the PM_{10} fraction at lag 2. F: elemental carbon in the PM_{10} fraction at lag 1. * The EC metric is considered relevant because most of the studies included in the meta-analysis by Achilleos et al. examined this metric. EC: elemental carbon; EDR: excess daily risk; ERU: excess risk per unit; R^2: coefficient of determination of the linear regression line used to calculate the ERU.*

APPENDIX 6 – SUMMARY OF THE CANDIDATE VALUES FOR ESTABLISHING THE LONG-TERM TRV FOR BLACK CARBON

Health event	**Plausibility of the causal relationship**	**Key reference selected**	**Level of interest**	**ERU value in $(10^{-5}\ m^{-1})^{-1}$ [95% confidence interval] over the determined concentration range, in equivalent-absorbance [abs] (R^2)**		**Parametric function describing the ELR value as a function of the equivalent-absorbance [abs] concentration from $0.55 \cdot 10^{-5}$ to $12.50 \cdot 10^{-5}\ m^{-1}$**	**ERU confidence level (/5)**
Asthma incidence in adults	Moderate	Liu *et al.* (2021)	Moderate	From $0.55 \cdot 10^{-5}$ to $5.00 \cdot 10^{-5}\ m^{-1}$: $6.79 \cdot 10^{-2}$ [$4.85 \cdot 10^{-2}$; $7.98 \cdot 10^{-2}$] ($R^2 = 0.82$)	From $5.00 \cdot 10^{-5}$ to $12.50 \cdot 10^{-5}\ m^{-1}$: $8.14 \cdot 10^{-3}$ [abs] + $2.66 \cdot 10^{-1}$ [$1.35 \cdot 10^{-2}$ [abs] + $1.65 \cdot 10^{-1}$; $4.15 \cdot 10^{-3}$ [abs] + $3.20 \cdot 10^{-1}$] ($R^2 = 0.91$)	ELR = $-4.00 \cdot 10^{-5}$ x $[abs]^4$ + $1.39 \cdot 10^{-3}$ x $[abs]^3$ - $1.86 \cdot 10^{-2}$ x $[abs]^2$ + $1.23 \cdot 10^{-1}$ x [abs]	3.9
All-cause mortality	**High**	**Strak *et al.* (2021)**	**High**	**From $0.55 \cdot 10^{-5}$ to $5.00 \cdot 10^{-5}\ m^{-1}$: $5.29 \cdot 10^{-2}$ [$4.64 \cdot 10^{-2}$; $6.01 \cdot 10^{-2}$] ($R^2 = 0.87$)**	**From $5.00 \cdot 10^{-5}$ to $12.50 \cdot 10^{-5}\ m^{-1}$: $5.09 \cdot 10^{-3}$ [abs] + $2.15 \cdot 10^{-1}$ [$5.91 \cdot 10^{-4}$ [abs] + $2.15 \cdot 10^{-1}$; $5.50 \cdot 10^{-3}$ [abs] + $2.36 \cdot 10^{-1}$] ($R^2 = 0.82$)**	**ELR = $2.86 \cdot 10^{-4}$ x $[abs]^3$ - $8.24 \cdot 10^{-3}$ x $[abs]^2$ + $8.00 \cdot 10^{-2}$ x [abs] + $4.49 \cdot 10^{-3}$**	**4.6**
Mortality from cardiovascular causes	Moderate	Yang *et al.* (2021)	Moderate	From $0.55 \cdot 10^{-5}$ to $5.00 \cdot 10^{-5}\ m^{-1}$: $1.54 \cdot 10^{-2}$ [$-1.11 \cdot 10^{-2}$; $2.23 \cdot 10^{-2}$] ($R^2 = 0.92$)	From $5.00 \cdot 10^{-5}$ to $12.50 \cdot 10^{-5}\ m^{-1}$: $2.94 \cdot 10^{-3}$ [abs] + $5.80 \cdot 10^{-2}$ [$-2.24 \cdot 10^{-2}$ [abs] + $6.26 \cdot 10^{-2}$; $6.08 \cdot 10^{-4}$ [abs] + $9.00 \cdot 10^{-2}$] ($R^2 = 0.94$)	ELR = $5.77 \cdot 10^{-5}$ x $[abs]^3$ – $1.84 \cdot 10^{-3}$ x $[abs]^2$ + $2.12 \cdot 10^{-2}$ x [abs] + $2.17 \cdot 10^{-3}$	4.2
Incidence of stroke	Moderate	Wolf *et al.* (2021)	Moderate	From $0.55 \cdot 10^{-5}$ to $12.50 \cdot 10^{-5}\ m^{-1}$: $5.94 \cdot 10^{-3}$ [$3.62 \cdot 10^{-3}$; $8.24 \cdot 10^{-3}$] ($R^2 = 0.65$)		ELR = $3.46 \cdot 10^{-5}$ x $[abs]^3$ – $1.08 \cdot 10^{-3}$ x $[abs]^2$ + $1.29 \cdot 10^{-2}$ x [abs] + $1.65 \cdot 10^{-3}$	4.1
Low birth weight	Moderate	Pedersen *et al.* (2013)	Moderate	From $0.55 \cdot 10^{-5}$ to $12.50 \cdot 10^{-5}\ m^{-1}$: $5.42 \cdot 10^{-3}$ [$-4.99 \cdot 10^{-3}$; $6.75 \cdot 10^{-3}$] ($R^2 = 0.81$)		ELR = $1.88 \cdot 10^{-5}$ x $[abs]^3$ – $6.98 \cdot 10^{-4}$ x $[abs]^2$ + $1.03 \cdot 10^{-2}$ x [abs] + $4.83 \cdot 10^{-4}$	4.2
Mortality from ischaemic heart disease	Moderate	Strak *et al.* (2021)	High	From $0.55 \cdot 10^{-5}$ to $12.50 \cdot 10^{-5}\ m^{-1}$: $2.15 \cdot 10^{-3}$ [$1.29 \cdot 10^{-3}$; $2.46 \cdot 10^{-3}$] ($R^2 = 0.90$)		ELR = $2.34 \cdot 10^{-6}$ x $[abs]^3$ – $1.90 \cdot 10^{-4}$ x $[abs]^2$ + $3.96 \cdot 10^{-3}$ x [abs] – $1.42 \cdot 10^{-3}$	4.4
Mortality from respiratory causes	High	Strak *et al.* (2021)	High	From $0.55 \cdot 10^{-5}$ to $12.50 \cdot 10^{-5}\ m^{-1}$: $1.90 \cdot 10^{-3}$ [$1.13 \cdot 10^{-3}$; $2.29 \cdot 10^{-3}$] ($R^2 = 0.74$)		ELR = $1.06 \cdot 10^{-5}$ x $[abs]^3$ – $3.31 \cdot 10^{-3}$ x $[abs]^2$ + $4.07 \cdot 10^{-3}$ x [abs] + $8.87 \cdot 10^{-5}$	4.3
Mortality from COPD	High	Strak *et al.* (2021)	High	From $0.55 \cdot 10^{-5}$ to $5.00 \cdot 10^{-5}\ m^{-1}$: $1.40 \cdot 10^{-3}$ [$5.53 \cdot 10^{-4}$; $1.86 \cdot 10^{-3}$] ($R^2 = 0.94$)	From $5.00 \cdot 10^{-5}$ to $12.50 \cdot 10^{-5}\ m^{-1}$: $3.16 \cdot 10^{-4}$ [abs] + $5.12 \cdot 10^{-3}$ [$3.52 \cdot 10^{-4}$ [abs] + $1.03 \cdot 10^{-3}$; $1.57 \cdot 10^{-4}$ [abs] + $7.55 \cdot 10^{-3}$] ($R^2 = 0.95$)	ELR = $4.62 \cdot 10^{-6}$ x $[abs]^3$ – $1.54 \cdot 10^{-4}$ x $[abs]^2$ + $1.90 \cdot 10^{-3}$ x [abs] + $1.41 \cdot 10^{-4}$	4.3

Health event	Plausibility of the causal relationship	Key reference selected	Level of interest	ERU value in $(10^{-5}\ m^{-1})^{-1}$ [95% confidence interval] over the determined concentration range, in equivalent-absorbance [abs] (R^2)	Parametric function describing the ELR value as a function of the equivalent-absorbance [abs] concentration from $0.55 \cdot 10^{-5}$ to $12.50 \cdot 10^{-5}\ m^{-1}$	ERU confidence level (/5)
Asthma incidence in children	Moderate	Gehring *et al.* (2015)	High	From $0.55 \cdot 10^{-5}$ to $12.50 \cdot 10^{-5}\ m^{-1}$: $8.03 \cdot 10^{-4}$ [0.00; $9.01 \cdot 10^{-4}$] ($R^2 = 0.55$)	ELR = $5.09 \cdot 10^{-6}$ x $[abs]^3$ - $1.62 \cdot 10^{-4}$ x $[abs]^2$ + $1.86 \cdot 10^{-3}$ x [abs] + $1.83 \cdot 10^{-4}$	4.6

COPD: chronic obstructive pulmonary disease; ELR: excess lifetime risk; ERU; excess risk per unit; R^2: coefficient of determination of the linear regression line used to calculate the ERU.