California Air Resources Board Updated Health Endpoints Bulletin

1. Introduction

CARB is charged with protecting the public from the harmful effects of air pollution and developing programs and actions to fight climate change. In carrying out this mission, CARB develops and implements programs to achieve state and federal air quality standards and reviews benefits to the public. CARB evaluates, quantifies, and makes publicly available the benefits of actions to reduce air pollution to support plans and regulations. CARB's current approach to health analysis focuses on quantification of a small subset of morbidity and mortality health outcomes associated with air pollution. However, the body of research on air pollution's health effects has grown substantially in the last ten years, and CARB's health analysis needs to be updated in response to the advances in scientific knowledge.

In response to new research, the Board directed staff, in Resolution 20-13 (Health Evaluation of Air Quality and Climate Regulations and Programs) in April 2020 to update and expand health analysis tools, pollutants, and health endpoints to capture a broader and more comprehensive range of benefits from reductions in air pollution.[1]

This document covers the update to the health endpoints for $PM_{2.5.}$ Additional health endpoints for $PM_{2.5}$ and health endpoints for other pollutants may be developed or updated in the future. Health endpoints are adverse health outcomes (e.g., heart attacks, asthma attacks, hospitalizations) used for evaluating quantitative or qualitative health impacts from air pollution exposure. In December 2021, CARB held a public workshop proposing new and updated endpoints. Staff finalized the proposed endpoints and methodology, considering comments received both during and after the workshop. This document provides the final endpoints for $PM_{2.5}$, the scientific basis for choosing those endpoints, information on the valuation, and next steps in expanding CARB's health analysis. The endpoints described in this document will be used in subsequent CARB health analyses for plans and regulations.

[1] CARB, Health Evaluation of Air Quality and Climate Regulations and Programs: Resolution 20-13, April 2020. Retrieved March 15, 2022 from: *https://ww2.arb.ca.gov/sites/default/files/barcu/board/res/2020/res20-13.pdf*

2. Background

CARB currently analyzes the following four mortality and morbidity health endpoints for $PM_{2.5}$:

- Premature mortality (cardiopulmonary)
- Hospital admissions for cardiovascular illnesses
- Hospital admissions for respiratory illnesses
- Emergency room visits for asthma attacks

Staff estimate the change in the number of health outcomes (e.g. premature mortality/deaths) resulting from changes in direct $PM_{2.5}$ emissions and a portion of secondary $PM_{2.5}$ emissions.

While these endpoints represent important health outcomes experienced by the public, they reflect a small subset of the full suite of benefits to the public from reductions in air pollution. Other mortality and morbidity outcomes that impact the public and lead to societal and economic impacts include hospitalizations, emergency room visits, missed work and school days, and other burdens. A wealth of evidence demonstrates that air pollution can cause a wide range of health effects beyond the four endpoints listed above. For instance, the U.S. Environmental Protection Agency (EPA)'s 2019 Integrated Science Assessment (ISA) for Particulate Matter concluded that there are several health outcomes with either a "causal," "likely to be causal," or "suggestive of causal," relationship with long-term $PM_{2.5}$ exposure (**Table 1**).[2] Out of the eight categories of health outcomes listed in **Table 1**, CARB is currently only evaluating endpoints in three categories (mortality, a subset of cardiovascular effects, and a subset of respiratory effects).

[2] U.S. EPA. (2019). *Integrated Science Assessment (ISA) for Particulate Matter (December 2019)* (EPA/600/R-19/188). Retrieved March 15, 2022 from: *https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=347534#tab-3*

Table 1. Long-term and short-term $PM_{2.5}$ health outcomes and causality links (adapted from U.S. EPA[3])

Causality Links	Health outcomes from $PM_{2.5}$ exposure
Causal	Mortality* Cardiovascular Effects*
Likely to be causal	Respiratory Effects* Nervous Systems Effects (long-term only) Cancer (long-term only)
Suggestive of causal	Metabolic Effects Male and Female Reproduction and Fertility Effects Nervous Systems Effects (short-term only)
*CARB currently calculates this health endpoint	

The U.S. EPA determines the casual relationship using a formal causal framework drawn from a number of federal and international groups such as the National Academy of Sciences and the International Agency for Research on Cancer.[4] This framework considers aspects such as number of studies, consistency of study findings, biological plausibility, and uncertainties to determine the causal relationship (e.g., causal, likely to be causal, etc.). The U.S. EPA has a rigorous review process including a formal independent panel of scientific subject matter experts, the Clean Air Scientific Advisory Committee (CASAC), as well as the public.

As shown in **Table 1**, the U.S. EPA classifies endpoints in hierarchical levels, with "causal" and "likely to be causal" reflecting the most confident relationships between $PM_{2.5}$ and attributable health impacts. "Suggestive of causal" does not necessarily mean the outcome is less associated with air pollution exposure but may reflect a lack of or limited number of studies. In the future, CARB may consider incorporating additional levels of causation. In addition, CARB and other investigators are conducting research to better capture the extent of adverse public health impacts from air pollution (see "Ongoing/Next Steps").

In this memo, CARB presents updated and additional $PM_{2.5}$ -related health endpoints, which will be incorporated into the agency's routine health analysis. CARB is using scientific

[3] Ibid.
[4] U.S. EPA. *Preamble to The Integrated Science Assessments (ISA)*. U.S. Environmental Protection Agency, Washington, DC, EPA/600/R-15/067, 2015

evidence reviewed and documented in U.S. EPA health impact analysis and assessments.[5,6] (see the "Health Endpoints, Use of Endpoints and Supporting Studies" section).

CARB held a public workshop in December 2021 to discuss the endpoints. The recording and presentations slides are available online (*https://ww2.arb.ca.gov/events/evaluating-new-health-endpoints-use-carbs-health-analyses*). A summary of the public comments received after this workshop are provided in the "Summary of Submitted Public Comments to December 2021 Public Workshop" section.

3. Health Endpoints, Use of Endpoints and Supporting Studies

CARB is adding 11 health endpoints to the $PM_{2.5}$ health analysis methodology: three are updated endpoints, and eight are new endpoints (**Table 2**). All of these endpoints are currently in use by U.S. EPA, as reported in their analysis for the Cross-State Air Pollution Rule Update.[7] Additional endpoints may be considered in the future. CARB will use these endpoints in calculating health impacts of regulations and plans. For most health analysis, CARB uses these endpoints with a tool called "Incidents Per Ton" (IPT) to calculate the health impacts per ton of pollution reduced. This tool relates changes in emissions projected in specific years to changes in health outcomes for those years. The IPT method is based on approaches such as U.S. EPA's Environmental Benefits Mapping and Analysis Program (BenMAP).[8] More information on the IPT method is available on CARB's website.[9]

To calculate changes in health outcomes, CARB uses a "concentration-response" (CR) function. A CR function calculates a change in the health outcome in the population based on the change in the pollutant concentration to which that population is being exposed. CARB uses inputs to the CR function that are specific to each endpoint. These inputs are the baseline incidence rate (for illness or deaths) and the effect estimate (that calculates the incremental change in health effect) and are derived from epidemiological research. The baseline incidence rate is the number of events of illness or death, or the number of people experiencing that event in the population. Baseline incidence rates can be acquired from health databases such as those from state or federal agencies or also built into the U.S. EPA's BenMAP software.[10] The effect estimate for an endpoint is the incremental increase in health effect per unit of pollution (1 $\mu g/m^3$) and is specifically derived from epidemiological studies. The effect estimates are applicable to all types of $PM_{2.5}$ since currently there is no consensus

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[5] See U.S. EPA. (2019) *ISA for Particulate Matter*.

[6] U.S. EPA. (2021). *Technical Support Document (TSD) for the Final Revised Cross-State Air Pollution Rule Update for the 2008 Ozone Season NAAQS: Estimating PM2.5- and Ozone-Attributable Health Benefits* (EPA-HQ-OAR-2020-0272). Retrieved March 15, 2022 from: *https://www.epa.gov/sites/default/files/2021-03/documents/estimating_pm2.5-_and_ozone-attributable_health_benefits_tsd_march_2021.pdf*

[7] Ibid.

[8] U.S. EPA. (2019). Environmental Benefits Mapping and Analysis Program - Community Edition (BenMAP-CE). Retrieved March 15, 2022 from *https://www.epa.gov/benmap*

[9] CARB's Methodology for Estimating the Health Effects of Air Pollution. Retrieved March 18, 2022 from: *https://ww2.arb.ca.gov/resources/documents/carbs-methodology-estimating-health-effects-air-pollution*

[10] See U.S. EPA. (2019) BenMAP-CE.

among research studies on separate effect estimates for different sources and components of $PM_{2.5}$.[11] The studies described in this document include the effect estimate inputs to the CR function. These effect estimates and related endpoints will be included in CARB's health analysis methodology.

Table 3 lists the studies used by U.S. EPA to quantify the 11 endpoints, including the effect estimates. This list includes new endpoints from respiratory and cardiovascular effects, as well as a new cancer endpoint and two new nervous system effects. The U.S. EPA recently identified and quantified these endpoints in 2021.[12] All 11 of these endpoints were determined by U.S. EPA to have a "causal" or "likely causal" relationship with particulate matter as described in their 2019 ISA and summarized in **Table 1**.[13] Furthermore, additional evidence on the confirmed causal relationships is included in the U.S. EPA's 2021 draft supplement document to their ISA (currently under review).[14] Thus, the health endpoints to be included in CARB's health analysis methodology are based on a body of peer-reviewed health research. Each of these endpoints are described in more detail later in this section.

[11] See U.S. EPA. (2019) *ISA for Particulate Matter.*
[12] See U.S. EPA. (2021) *TSD.*
[13] See U.S. EPA. (2019) *ISA for Particulate Matter.*
[14] U.S. EPA. (2021). *Supplement to the 2019 Integrated Science Assessment for Particulate Matter (External Review Draft)* (EPA/600/R-21/198). Retrieved March 15 2022 from: *https://cfpub.epa.gov/ncea/isa/recordisplay.cfm?deid=352823*

Table 2. List of updated and new $PM_{2.5}$ health endpoints in CARB's health analysis methodology

Updated Endpoints	New Endpoints
Cardiovascular hospital admissions*	Cardiovascular ED Visits
Respiratory hospital admissions*	Acute Myocardial Infarction, Nonfatal
Respiratory ED visits**	Asthma Onset
	Asthma Symptoms / Exacerbation
	Work Loss Days
	Lung Cancer Incidence
	Alzheimer's Disease
	Parkinson's Disease

ED = emergency department

*CARB is currently calculating this endpoint but are updating the effect estimate to use a more recent study.

**CARB is currently calculating ED visits for specifically asthma and are updating this endpoint to include all respiratory diseases.

Table 3. List of health endpoints and summary of studies (adapted from U.S. EPA[15])

	Endpoint(s)	Study	Age Range	Location	Effect Estimate
Cardiovascular	Cardiovascular hospital admissions*	Bell et al. (2015)	Seniors (65-99)	US	0.00065
	Cardiovascular ED visits	Ostro et al. (2016)	All ages 0-99)	US (CA)	0.00061
	Acute myocardial infarction, nonfatal	4 studies: • Pope III et al. (2006) • Sullivan et al. (2005) • Zanobetti et al. (2009) • Zanobetti and Schwartz, (2006)	Adults (18-99)	US	4 studies: • 0.00481 • 0.00198 • 0.00225 • 0.0053
Respiratory	Respiratory hospital admissions*	Bell et al. (2015)	Seniors (65-99)	US	0.00025
	Respiratory ED visits**	Krall et al. (2017)	All ages (0-99)	US	4 locations: • 0.00055 • 0.00097 • 0.00083 • 0.00135
	Asthma onset	Tetreault et al. (2016)	Children (0-13)	Canada	0.04367
	Asthma symptoms	Rabinovitch et al. (2006)	Children (6-13)	US	0.002
	Work loss days	Ostro (1987)	Adults (18-64)	US	0.0046

ED = emergency department

*CARB is currently calculating this endpoint but are updating the effect estimate to use a more recent study.

**CARB is currently calculating ED visits for specifically asthma and are updating this endpoint to include all respiratory diseases.

Note: The full reference for each study in the table is provided in the section describing that endpoint

Table 4 (continued).

	Endpoint(s)	Study	Age Range	Location	Effect Estimate
Cancer	Lung cancer incidence	Gharibvand et al. (2017)	Adults (30-99)	US and Canada	0.03784
Nervous System Effects	Alzheimer's disease	Kioumourtzoglou et al. (2016)	Seniors (65-99)	US	0.13976
	Parkinson's disease	Kioumourtzoglou et al. (2016)	Seniors (65-99)	US	0.07696

While there are many epidemiological studies on all these endpoints, U.S. EPA identified one or more studies for each endpoint for the purpose of health analysis quantification. The studies were chosen based on U.S. EPA's set of criteria listed in **Table 5**. Each criterion had its own list of preferred study attributes, and the U.S. EPA considered these criteria collectively when evaluating studies. For instance, a study location in the US or Canada and a study size with a large population were preferred. More details about these criteria are provided by U.S. EPA in the aforementioned 2021 TSD.[16]

[15] See U.S. EPA. (2019) *ISA for Particulate Matter*.
[16] See U.S. EPA. (2021) *TSD*.

Table 5. Summary of U.S. EPA's criteria for selecting studies and risk estimates (adapted from U.S. EPA[17])

Criterion	Description of Preferred Attributes
Study Period	Longer period of time and more recent studies
Exposure Estimate	Exposures estimated using a combination of approaches (e.g., modeling, monitoring, etc.). Long-term/chronic exposure studies over short-term.
Study Type	For long-term epidemiological studies, cohort studies over case-control studies, and both are preferred over cross-sectional or ecological studies.
Population Attributes	Study populations that are representative of the greater affected population (diverse race/ethnicities, both sexes, broader age groups).
Study Location	US or Canada
Health Endpoints	Broad health endpoints over more specific endpoints.
Study Size	Relatively large sample sizes
Pollutant Concentrations	Evaluate air pollutant exposures that are close to or below current conditions.
Hazard/Risk Estimate	Use of multiple well-established statistical models
Lag Period	Strongest multi-day/distributed lag periods that are more biological plausible

CARB will use the studies identified by U.S. EPA for the quantification of the 11 health endpoints summarized in **Table 3**.[18] In addition, CARB may use other epidemiological studies, including those identified in the EPA 2021 TSD, to provide supplemental information on the 11 health endpoints or other endpoints quantified by CARB. CARB may also update the studies used for the quantification of health endpoints or add more health endpoints in future bulletins. The 11 endpoints are presented in more detail below. Some endpoints are grouped together because they utilize the same study (cardiovascular and respiratory hospital admissions; and hospitalizations for Alzheimer's and Parkinson's diseases). Most of the listed endpoints rely on studies using hospital data of coded diagnoses, and multiple

[17] See U.S. EPA. (2021) *TSD*.
[18] Ibid.

diseases are categorized under the cardiovascular and respiratory endpoints. CARB has noted the codes from the International Classification of Diseases, Ninth Revision (ICD-9) for each endpoint, with their specific definitions provided in **Table 6**, for reference.[19] Each endpoint listed below is noted as either being *Updated* or *New* for CARB's health analysis methodology (also summarized in **Table 2**). The endpoints will use the new or updated effect estimates in the studies noted for that endpoint.

3.1. Cardiovascular Hospital Admissions and Respiratory Hospital Admissions – Both Updated

Hospital admissions for cardiovascular disease and hospital admissions for respiratory disease both use the same quantification study. CARB currently calculates both endpoints in our regular analyses, but we are updating the study to Bell et al., 2015.[20] This study utilized a Medicare cohort (>65 years of age) from 1999-2010 that spanned the U.S. Because of its large cohort size, relatively long study period, and location in the U.S., this study was identified by the U.S. EPA as being robust for quantification of hospital admissions for both cardiovascular and respiratory outcomes.[21] The cardiovascular diseases included are ischemic heart disease, heart failure, and other cardiovascular outcomes (ICD-9 code 410, omitting 410.x2; 410-414; 426-427; 428; 429; 430-438; and 440-448), while the respiratory diseases included asthma, chronic obstructive pulmonary disease (COPD), respiratory infections, and others (ICD-9 codes 464-466, 480-487, 490-492, 493). Quantification of these endpoints provides the number of events (hospital admissions for either cardiovascular disease or respiratory disease), not the number of individuals admitted to the hospital for these diseases.

3.2. Cardiovascular Emergency Department (ED) Visits – New

Emergency Department (ED) visits differ from hospital admissions in that the former are often unscheduled visits that occur more frequently and are usually for less serious medical events.[22] The cardiovascular diseases included in this endpoint are similar to those in the hospital admissions endpoint and include ischemic heart disease, heart failure, and other cardiovascular-related outcomes (ICD-9 codes 390-459). To quantify this endpoint, CARB will use the Ostro et al., 2016 study selected by the U.S. EPA. Ostro et al., 2016 conducted a case cross-over analysis of eight cities in California, using the Office of Statewide Health

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[19] Centers for Disease Control and Prevention (CDC): National Center for Health Statistics. International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). Retrieved March 15, 2022 from: *https://www.cdc.gov/nchs/icd/icd9cm.htm*

[20] Bell, M. L., Son, J. Y., Peng, R. D., Wang, Y., & Dominici, F. (2015). Ambient PM2.5 and Risk of Hospital Admissions: Do Risks Differ for Men and Women? *Epidemiology*, 26(4), 575-579. doi:10.1097/ede.0000000000000310

[21] See U.S. EPA. (2021) *TSD*.

[22] Winquist A, Klein M, Tolbert P, Flanders WD, Hess J, Sarnat SE. Comparison of emergency department and hospital admissions data for air pollution time-series studies. *Environ Health*. 2012 Sep 21; 11:70. doi: 10.1186/1476-069X-11-70.

Planning and Development (OSHPD) data between 2005 and 2008.[23] Among the several epidemiological studies that U.S. EPA evaluated for quantifying this endpoint, this was the only study with short-term exposure specifically investigating cardiovascular ED visits.[24]

3.3. Acute Myocardial Infarction (AMI), Nonfatal – New

An Acute Myocardial Infarction (AMI) is also called a heart attack; this endpoint refers to hospitalizations from heart attacks (ICD-9 code 410) and does not include deaths resulting from heart attacks. Among the many epidemiological studies available on this endpoint, U.S. EPA identified several studies that met the robust criteria for quantification of impacts from $PM_{2.5}$. These studies included Sullivan et al., 2005 from King County, WA; Pope III et al., 2006, from Wasatch Range, UT; Zanobetti and Schwartz, 2006, from Boston, MA; and Zanobetti et al., 2009, which looked at 26 U.S. communities.[25,26,27,28] These studies spanned different areas across the U.S. and analyzed all adults (18-99 years old). Three of these studies used hospital discharge data for AMI, while Pope III et al., 2006 used data from angiographically characterized patients, which is known to be a more precise indicator of AMI.[29] If there are multiple robust studies for characterizing risks, U.S. EPA uses pooling methods to account for the information from these multiple studies, consistent with advice from the National Academies of Sciences.[30,31] The results from application of effect estimates in these four studies will be used together, or "pooled", in CARB's approach to estimate hospitalizations for nonfatal acute myocardial infarctions. The method for pooling is described in U.S. EPA's BenMAP manual.[32]

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[23] Ostro B, Malig B, Hasheminassab S, Berger K, Chang E, Sioutas C. Associations of Source-Specific Fine Particulate Matter with Emergency Department Visits in California. *Am J Epidemiol*. 2016 Sep 15;184(6):450-9. doi: 10.1093/aje/kwv343.

[24] See U.S. EPA. (2021) *TSD*.

[25] Sullivan J, Sheppard L, Schreuder A, Ishikawa N, Siscovick D, Kaufman J. Relation between short-term fine-particulate matter exposure and onset of myocardial infarction. *Epidemiology*. 2005 Jan;16(1):41-8. doi: 10.1097/01.ede.0000147116.34813.56.

[26] Pope CA 3rd, Muhlestein JB, May HT, Renlund DG, Anderson JL, Horne BD. Ischemic heart disease events triggered by short-term exposure to fine particulate air pollution. *Circulation*. 2006 Dec 5;114(23):2443-8. doi: 10.1161/CIRCULATIONAHA.106.636977.

[27] Zanobetti A, Schwartz J. Air pollution and emergency admissions in Boston, MA. *J Epidemiol Community Health*. 2006 Oct;60(10):890-5. doi: 10.1136/jech.2005.039834.

[28] Zanobetti A, Franklin M, Koutrakis P, Schwartz J. Fine particulate air pollution and its components in association with cause-specific emergency admissions. *Environ Health*. 2009 Dec 21; 8:58. doi: 10.1186/1476-069X-8-58.

[29] See U.S. EPA. (2021) *TSD*.

[30] Ibid.

[31] NRC (2002). Estimating the public health benefits of proposed air pollution regulations. 0309086094. National Academies Press.

[32] U.S. EPA. (2022). Environmental Benefits Mapping and Analysis Program - Community Edition: User's Manual. Retrieved March 22, 2022 from *https://www.epa.gov/sites/default/files/2015-04/documents/benmap-ce_user_manual_march_2015.pdf?VersionId=7BSmKllr0O6KccspW4pA.nMsu4EeLlrt*

3.4. Respiratory ED Visits – Updated

For previous analyses, CARB calculated ED visits specifically for asthma; however, CARB is updating this endpoint to include all respiratory diseases, which encompasses not just asthma, but also COPD, respiratory infections, and other respiratory outcomes (ICD-9 codes (460-465, 466, 477, 480-486, 491, 492, 493, 496, 786.07). As mentioned earlier, ED visits differ from hospital admissions in that the former are often unscheduled visits that occur more frequently and are usually for less serious medical events.[33] CARB is using Krall et al., 2017 to quantify this endpoint, which the U.S. EPA identified as a robust study since it covered a wide geographic area across four major U.S. cities (Atlanta, GA; Birmingham, AL; St. Louis, MO; and Dallas, TX) and included all ages (0-99-year-old individuals).[34]

3.5. Lung Cancer Incidence – New

CARB has not previously quantified cancer incidence as part of the health analysis. The U.S. EPA had determined that there is a "likely to be causal" relationship between cancer and long-term $PM_{2.5}$ exposure.[35] Also, an International Agency for Research on Cancer (IARC) Working Group concluded that outdoor air pollution, and specifically PM, is carcinogenic (cancer-causing).[36] Both the U.S. EPA and the IARC Working Group based their determinations on a wealth of epidemiological studies on humans as well as experimental studies on model organisms showing increased risks for tumor development and other carcinogenic effects with exposure to air pollution.[37,36] In addition, CARB found that diesel particulates were linked to lung cancer incidence based on a combination of human epidemiological and animal studies.[38,39] For this endpoint, "Lung cancer incidence" refers to diagnoses of lung cancer (ICD-O-3 codes C34.0-C34.9) and does not include deaths. Among the many studies available, U.S. EPA identified four lung cancer incidence studies that met its criteria but ultimately chose Gharibvand et al., 2017 for quantification because of its study population and location.[40] The authors analyzed a cohort of over 80,000 people (composed of females and males with non-smoking history) from the Adventist Health and Smog Study-2

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[33] See Winquist A et al. *Environ Health*. 2012.

[34] Krall JR, Mulholland JA, Russell AG, Balachandran S, Winquist A, Tolbert PE, Waller LA, Sarnat SE. Associations between Source-Specific Fine Particulate Matter and Emergency Department Visits for Respiratory Disease in Four U.S. Cities. *Environ Health Perspect*. 2017 Jan;125(1):97-103. doi: 10.1289/EHP271.

[35] See U.S. EPA. (2019) *ISA for Particulate Matter*.

[36] IARC. "Outdoor Air Pollution: Volume 109." In IARC Monographs on the Evaluation of Carcinogenic Risks to Humans. Lyon, France: International Agency for Research on Cancer, 2016. Retrieved March 15, 2022 from: *https://monographs.iarc.who.int/monographs-available/*

[37] See U.S. EPA. (2019) *ISA for Particulate Matter*.

[38] CARB. "Overview: Diesel Exhaust & Health." Retrieved March 15, 2022 from: *https://ww2.arb.ca.gov/resources/overview-diesel-exhaust-and-health*

[39] CARB. "Summary: Diesel Particulate Matter Health Impacts." Retrieved March 15, 2022 from: *https://ww2.arb.ca.gov/resources/summary-diesel-particulate-matter-health-impacts*

[40] See U.S. EPA. (2021) *TSD*.

(AHSMOG-2) across the U.S.[41] The quantification for this endpoint considers the lag or latency period between exposure and the onset of the cancer and considers adults at least 30 years of age. CARB will be using the effect estimate from Gharibvand et al., 2017.

3.6. Asthma Onset – New

While CARB has previously calculated ED visits for asthma, "asthma onset" itself is a new endpoint in CARB's methodology. Asthma is a disease that is characterized by inflammation of the airways, and "onset" refers to new diagnoses. The 2019 ISA also indicated asthma onset to be a key clinically relevant health endpoint when considering plausible biological pathways.[42] For quantification, U.S. EPA chose Tetreault et al., 2016, which looked at children (0-13 years of age) in Quebec, Canada, using medical administrative databases for hospital discharged diagnosis of asthma or reported asthma cases by physicians.[43] The U.S. EPA considered studies in Canada to be applicable to the U.S. because both countries have similar ambient $PM_{2.5}$ concentrations, pollutants transport between the two countries, and most Canadians live less than 100 miles from the U.S.[44] While there were other studies available on this endpoint, the U.S. EPA identified this study as being particularly robust because of its more recent time period and larger cohort size. Therefore, CARB will utilize the Tetreault study.

3.7. Asthma Symptoms/Exacerbation – New

While CARB has previously calculated ED visits for asthma, "asthma symptoms/exacerbation" is a new endpoint in our methodology. Asthma symptoms and exacerbation refers to the worsening of asthma, as measured by use of albuterol medication. Albuterol inhalers are considered to be a rescue medication and are a useful endpoint when considering asthma symptoms. Rabinovitch et al., 2006 followed asthmatic children (ages 6-13) in Denver, Colorado for two consecutive winters from 2001-2003 to capture the albuterol use frequency within a 24-hour period.[45] The authors also used hourly $PM_{2.5}$ concentration from the Colorado Department of Health Air Pollution Control Division's Tapered Element Oscillating Microbalance (TEOM) monitor as well as a Federal Reference Monitor (FRM) located next to the TEOM. The authors found that there was a consistent association between ambient $PM_{2.5}$ levels and increased albuterol use in asthmatic children. CARB will utilize the effect estimates from this study.

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[41] Gharibvand L, Shavlik D, Ghamsary M, Beeson WL, Soret S, Knutsen R, Knutsen SF. The Association between Ambient Fine Particulate Air Pollution and Lung Cancer Incidence: Results from the AHSMOG-2 Study. *Environ Health Perspect*. 2017 Mar;125(3):378-384. doi: 10.1289/EHP124.

[42] See U.S. EPA. (2019) *ISA for Particulate Matter*.

[43] Tétreault LF, Doucet M, Gamache P, Fournier M, Brand A, Kosatsky T, Smargiassi A. Childhood Exposure to Ambient Air Pollutants and the Onset of Asthma: An Administrative Cohort Study in Québec. *Environ Health Perspect*. 2016 Aug;124(8):1276-82. doi: 10.1289/ehp.1509838.

[44] See U.S. EPA. (2021) *TSD*.

[45] Rabinovitch N, Strand M, Gelfand EW. Particulate levels are associated with early asthma worsening in children with persistent disease. *Am J Respir Crit Care Med*. 2006 May 15;173(10):1098-105. doi: 10.1164/rccm.200509-1393OC.

3.8. Work loss days – New

Work loss days refers to the time unable to work due to health conditions. The U.S. EPA identified the Ostro 1987 study on work loss days as the most robust study for quantifying this endpoint because it was conducted at the nationwide level covering several thousand subjects; no other studies published since were identified for quantification.[46] The authors estimated the impacts of PM2.5 on the incidence of work loss days using a survey dataset of the working adult population (age range of 18-65, with 162 million survey results) living in U.S. metropolitan areas between 1976-1981.[47] CARB will be using this paper to quantify this endpoint. CARB also has an ongoing research contract evaluating the effects of air pollution on work loss days in California. The results of this study are expected next year, and CARB expects to workshop the results to inform any potential update this endpoint at that time.

3.9. Hospitalizations for Alzheimer's disease and hospitalizations for Parkinson's disease – Both New

Nervous system effects (Alzheimer's and Parkinson's) are new endpoints in CARB's methodology. The U.S. EPA determined there was a "likely to be causal" relationship between nervous system effects and long-term $PM_{2.5}$ exposure based on the increasing number of epidemiological as well as animal studies in the last decade.[48] These two health endpoints are neurodegenerative diseases, with Alzheimer's disease being a form of dementia and Parkinson's disease being a serious movement disorder. For the hospitalization endpoints for Alzheimer's disease and Parkinson's disease, U.S. EPA chose the paper by Kioumourtzoglou et al, published in 2016.[49] CARB will use this study for both endpoints. The authors investigated annual average $PM_{2.5}$ impacts on Alzheimer's and Parkinson's diseases among more than 9.8 million Medicare enrollees (65+ years old) in 50 northeastern U.S. cities during the 1999-2010 time period. The investigators analyzed annual follow up records and considered just the first case of hospital admission for Parkinson's disease (ICD-9, 332), and Alzheimer's disease (ICD-9, 331.0).

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[46] See U.S. EPA. (2021) *TSD*.

[47] Ostro, B. D. (1987). Air pollution and morbidity revisited: A specification test. *Journal of Environmental Economics and Management*, 14(1), 87-98. doi: https://doi.org/10.1016/0095-0696(87)90008-8

[48] See U.S. EPA. (2019) *ISA for Particulate Matter.*

[49] Kioumourtzoglou MA, Schwartz JD, Weisskopf MG, Melly SJ, Wang Y, Dominici F, Zanobetti A. Long-term PM2.5 Exposure and Neurological Hospital Admissions in the Northeastern United States. *Environ Health Perspect.* 2016 Jan;124(1):23-9. doi: 10.1289/ehp.1408973.

Table 6. Selected relevant codes from the International Classification of Diseases, Ninth Revision (ICD-9) (adapted from CDC[50])

ICD-9 Code	Disease
331.0	Alzheimer's disease
332	Parkinson's disease
390	Rhematic fever without mention of heart involvement
410	Acute myocardial infarction
411	Other acute and subacute forms of ischemic heart disease
412	Old myocardial infarction
413	Angina pectoris
414	Other forms of chronic ischemic heart disease
426	Conduction disorders
427	Cardiac dysrhythmias
428	Heart failure
429	Ill-defined descriptions and complications of heart disease
430-438	Cerebrovascular disease
440	Atherosclerosis
441	Aortic aneurysm and dissection
442	Other aneurysm
443	Other peripheral vascular disease
444	Arterial embolism and thrombosis
445	Atheroembolism
446	Polyarteritis nodosa and allied conditions

Table 7 (continued).

ICD-9 Code	Disease
447	Other disorders of arteries and arterioles
448	Disease of capillaries
460-466	Acute respiratory infections
477	Allergic rhinitis
480	Viral pneumonia
481	Pneumococcal pneumonia
482	Other bacterial pneumonia
483	Pneumonia due to other specified organism
484	Pneumonia in infectious diseases classified elsewhere
485	Bronchopneumonia, organism, unspecified
486	Pneumonia, organism unspecified
487	Influenza
490	Bronchitis, not specified as acute or chronic
491	Chronic bronchitis
492	Emphysema
493	Asthma
496	Chronic airway obstruction, not elsewhere classified
786.07	Wheezing

[50] See CDC: National Center for Health Statistics. ICD-9-CM.

4. Valuation

As part of updating the health endpoints, CARB will use new valuations for the health endpoints. Valuation refers to placing a monetary value on an estimated health incidence. Improvements in air quality will lower the risk of developing adverse health effects, resulting in fewer cases of the adverse health effects across society. Monetizing the benefits of reduced air pollution involves estimating society's willingness to pay (WTP) to avoid these adverse outcomes or estimating the observed Cost of Illness (COI) of the health endpoint.[51] CARB's process for valuing endpoints is largely based on U.S. EPA's methodology, but considers California demographic and economic data.

The statewide valuations of health benefits for specific endpoints associated with a proposed regulation or scenario are calculated by multiplying the value per incident by the statewide total number of incidents avoided. The value of the health benefits may be compared with other costs and benefits of a proposed regulation or scenario to better understand a regulation or plan's total impacts. **Table 6** provides the value per incident currently used in CARB analyses for categories of endpoints.

The savings for avoided hospitalizations and emergency room visits are based on a combination of typical costs associated with hospitalization and the willingness of surveyed individuals to pay to avoid adverse outcomes that occur when hospitalized. These include hospital charges, post-hospitalization medical care, out-of-pocket expenses, and lost earnings of both individuals and family members, lost recreation value, and lost household production (e.g., valuation of time-losses from inability to maintain the household or provide childcare).[52,53] Currently, valuation for hospitalizations draws on published estimates of California illness costs while the valuation for emergency department visits draws on national estimates.

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[51] COI includes the direct medical costs and lost earnings associated with illness. COI may understate the true economic value of reductions in risk of health effects, as it may not include other factors such as avoided pain and suffering. WTP estimates may include these other factors but may be less readily available.

[52] Chestnut, Lauraine G., et al. "The economic value of preventing respiratory and cardiovascular hospitalizations." Contemporary Economic Policy 24.1 (2006): 127-143. *https://onlinelibrary.wiley.com/doi/pdf/10.1093/cep/byj007?casa_token=HUk1nm6UtUgAAAAA:tDnCaydUWJFYfY1oWFn_D33oUcc6m4Haazv5c_wPNQGe9QP-f9Mw4EdBb3mUwoWXENC3qda1Xps4-w*

[53] Smith, David H., et al. "A national estimate of the economic costs of asthma." American journal of respiratory and critical care medicine 156.3 (1997): 787-793. https://www.atsjournals.org/doi/full/10.1164/ajrccm.156.3.9611072

Table 6. Valuation per Incident for Avoided Health Outcomes Currently Used in CARB Analyses

Outcome	Value per incident (2020$)
Avoided Cardiovascular Hospitalizations	$59,247
Avoided Acute Respiratory Hospitalizations	$51,678
Avoided Emergency Room Visits	$848

CARB will update and transparently document the valuations that are currently used and use new valuations for the newly added health endpoints. CARB's methodology will use the same valuation studies that are included in U.S. EPA's BenMAP.[54,55]

More information on the valuation of health endpoints and specific studies relied upon is provided in a recent U.S. EPA's analysis as part of the Cross-State Air Pollution Rule Update.[56] Using BenMAP, the estimates from these valuation studies will be used as inputs into CARB staff's analysis. This analysis will rely on the IPT estimation (see "Health Endpoints, Use of Endpoints and Supporting Studies" section) and incorporate California specific data on inflation, wages, income, and demographics, where applicable. This will provide a total valuation by endpoint for the specific scenario, which can then be normalized by the number of incidents to derive a value per incident for each endpoint.

5. At-Risk Populations

There is a growing body of literature showing some populations are more susceptible to air pollutants and are at higher risk of air pollution-related illnesses. Understanding health and exposure disparities is critical to reducing air pollution exposure and health risks among low income and communities of color. These communities are often heavily burdened by higher levels of pollution from traffic and other industrial sources.[57,58] They also often simultaneously

[54] U.S. EPA. (2019) BenMAP-CE.
[55] See U.S. EPA. (2021) *TSD*.
[56] Ibid.
[57] Apte, Joshua. "A Method to Prioritize Sources for Reducing High PM2.5 Exposures in Environmental Justice Communities in California." (CARB Contract Number 17RD006). Retrieved March 15, 2022 from: *https://ww3.arb.ca.gov/research/single-project.php?row_id=67021*
[58] Tessum CW, Paolella DA, Chambliss SE, Apte JS, Hill JD, Marshall JD. PM2.5 polluters disproportionately and systemically affect people of color in the United States. *Sci Adv*. 2021 Apr 28;7(18):eabf4491. doi: 10.1126/sciadv.abf4491

face other stressors such as poor nutrition, economic insecurity, and sub-optimal living conditions that adds to vulnerability to air pollution impacts.[59,60]

The U.S. EPA's ISA and ISA supplement documents discuss factors contributing to an increased risk of $PM_{2.5}$ related health effects including: life stage, race/ethnicity, and socioeconomic status.[61,62] For example, the U.S. EPA concludes that the evidence is adequate to show that nonwhite groups, in particular the black population, are at higher risk for air pollution-related health impacts based on exposure and health studies analyzing different race/ethnic groups. Based on this evidence, CARB may implement additional quantitative methods for evaluating health impacts by race or ethnicity. There is also adequate evidence showing that children are at increased risk.

In addition, the aforementioned U.S. EPA documents report a suggestive relationship between low socioeconomic status (SES) populations and increased risk for adverse health effects from $PM_{2.5}$ exposures in comparison with higher SES populations. All of the above factors as well as others are important in considering the health impacts from air pollution exposure. The research into the relationship between $PM_{2.5}$ health impacts and specific subpopulations continues to grow as well as the analytical tools to quantify these relationships. Moving forward, CARB may use epidemiological studies demonstrating health outcomes in specific sub-populations together with data on race and ethnicity to provide disaggregated health outcome information that better reflects vulnerabilities in sub-populations. While CARB does not currently have a method to incorporate localized data on at-risk populations, staff are also considering how to incorporate population vulnerability information from existing scientific evidence and tools that demonstrate health and exposure disparities at smaller spatial scales into our health analysis approach.

6. Summary of Submitted Public Comments to December 2021 Public Workshop and Responses

CARB held a public workshop titled "Evaluating New Health Endpoints for Use in CARB's Health Analyses" in December 2021, and written comments from the public were received post-workshop. Public commenters asked about the literature and data sources used for the health analysis methodology, including study selection for the updated/new health endpoints as well as the health, air quality, and emissions data. There were also questions about the agency's approval process for the updated/new endpoints. Also, CARB received suggestions for future directions of expanding the health analysis methodology, including adding other pollutants and additional economic analyses, as the commenter stated that economic impacts also affect health.

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[59] OEHHA. CalEnviroScreen. California Office of Environmental Health Hazard Assessment. Retrieved March 15, 2022 from: *https://oehha.ca.gov/calenviroscreen/about-calenviroscreen*

[60] Braveman P, Gottlieb L. The Social Determinants of Health: It's Time to Consider the Causes of the Causes. Public Health Reports. 2014;129(1_suppl2):19-31. doi:10.1177/00333549141291S206

[61] See U.S. EPA. (2019) *ISA for Particulate Matter.*

[62] See U.S. EPA. (2021) *Supplement to the 2019 ISA for Particulate Matter (External Review Draft).*

In the current identification of new and updated endpoints described in this memo, CARB is relying on research reviewed as part of U.S. EPA's recent update of health endpoints , which included a set of criteria (summarized in **Table 4**) to select studies for quantification of $PM_{2.5}$ health impacts, as reported in their 2021 TSD.[63] CARB is using available information and data (both quantitative and qualitative) from state agencies and U.S. EPA whenever possible. CARB is also undertaking research contracts to provide updated California-specific data and effect estimates that may be used going forward. This update of the health endpoints used in CARB's analysis methodology is part of a process that was initiated in line with Board direction in an April 2020 Board hearing and resolution. Since then, CARB has provided an opportunity for public comment on the proposed endpoints through a public workshop and comment period, and the methodology updates will be posted online on CARB's health analysis methodology website as well as referenced in the health assessment sections of future regulatory documents. Lastly, CARB appreciates the public input on additional directions to expand our methodology. CARB is actively working internally and through research contracts to evaluate additional pollutants, health outcomes, and causation categories.

7. Ongoing/Next Steps

The new and updated endpoints provided in this document are a first step in expanding the agency's health analysis. The endpoints will provide a more comprehensive analysis for CARB's plans and regulations. CARB will be pursuing additional updates and improvements in future bulletins, including consideration of additional causation categories for the endpoints and endpoints for additional pollutants. CARB will also continue to evaluate approaches to provide both quantitative and qualitative information on health outcomes in low-income communities and communities of color. As part of that process, CARB has contracted with several science advisors from public and private universities, who have backgrounds in epidemiology, environmental health, environmental justice, and exposure assessment. They are individually providing CARB staff with input on approaches to expand the agency's health analysis. CARB plans to hold a public meeting, where the advisors will discuss and provide recommendations on our health analysis work.

Additionally, for longer-term work, CARB is continuing to develop California-specific health endpoint data for use in our health analysis. For example, CARB has current and upcoming contracts and research for neurological and birth outcomes, asthma, and work loss days. Some of these contracts are investigating outcomes by race and ethnicity as feasible and depending on data availability. Staff are also evaluating possible methods for more local-scale analysis, and incorporating qualitative methods to discuss community factors affecting health, especially where CARB does not have quantitative methods. Further information on the ongoing contracts can be found on CARB's online research page (*https://ww2.arb.ca.gov/our-work/programs/research-planning/research-division-contracts*).

[63] See U.S. EPA. (2021) *TSD*.

All CARB's efforts to expand the health analysis endpoints and methodology, including the underlying research, will continue to rely on the best available science.

Please see the CARB health analysis webpage for further background on our health analysis work and future updates (*https://ww2.arb.ca.gov/resources/documents/carbs-methodology-estimating-health-effects-air-pollution*).