9.11 World Trade Center Health Program

Evaluation of Scientific Evidence Supporting the Addition of Ischemic Heart Disease to the List of WTC-Related Health Conditions

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I. EXECUTIVE SUMMARY

At the direction of the Administrator of the World Trade Center (WTC) Health Program (Administrator), the WTC Health Program Science Team (Science Team) reviewed eight petitions — **Petitions 024, 042, 046, 047, 051, 056, 058,** and **067** — requesting the addition of various cardiovascular conditions falling under the general category of ischemic heart disease (IHD) to the List of WTC-Related Health Conditions (the List). In related actions, the Administrator previously evaluated "cardiovascular disease" and "atherosclerosis" in **Petition 004**[1] and **Petition 012**,[2] respectively; these two previous evaluations resulted in findings of *insufficient evidence* to add their respective health conditions to the List.

The Science Team evaluated the scientific evidence of a causal association between 9/11 exposures and IHD in accordance with the *Policy and Procedures for Adding Non-Cancer Health Conditions to the List of WTC-Related Health Conditions (Policy and Procedures)* [NIOSH 2026a]. A literature review of peer-reviewed, published, epidemiologic studies of IHD published between September 2001 and June 2026 identified 14 high-quality studies reporting on the risk of IHD in 9/11-exposed populations.

The Science Team evaluated the information from these 14 high-quality studies identified in the review of the literature, including 3 studies identified in the previous literature reviews conducted for **Petition 004** and **Petition 012**, individually and together, to characterize the available scientific evidence of a causal association between 9/11 exposures and IHD. The Science Team concludes that there is a limited likelihood of causal association between 9/11 exposures and IHD (Category III).[3]

II. BACKGROUND

Pursuant to the James Zadroga 9/11 Health and Compensation Act of 2010,[4] an interested party may petition the Administrator of the WTC Health Program (Program) for the addition of a health condition to the List of conditions eligible for treatment in the Program.[5,6] To petition the Program, petitioners must submit, in writing, their name, contact information, and signature of the interested party requesting the addition of a health condition to the List; a statement of intent to petition for the addition of a health condition to the List; the name or description of the health condition; and reasons for adding the health condition to the List, including the medical basis for the association between the September 11, 2001, terrorist attacks and the health condition.[7] These requirements are further explained in the *Policy and Procedures for Handling Submissions and Petitions to Add a Health Condition to the List of WTC-Related Health Conditions (Policy and Procedures for Handling Submissions and Petitions)* [NIOSH 2026b]. Submissions that meet all requirements are considered valid petitions.

1 *See* Federal Register, Vol. 79, No. 87, Tuesday, May 6, 2014, 25766-25717, https://www.govinfo.gov/content/pkg/FR-2014-05-06/pdf/2014-10434.pdf.
2 *See* Federal Register, Vol. 81, No. 240, Wednesday, December 14, 2016, 90295-90297, https://www.govinfo.gov/content/pkg/FR-2016-12-14/pdf/2016-29816.pdf.
3 *See Policy and Procedures*, Section V.C. [NIOSH 2026a].
4 Title I of Pub. L. 111-347, as amended by Pub. L. 114-113, Pub. L. 116-59, Pub. L. 117-328, Pub. L. 118-31, and Pub. L. 119-75; codified at 42 U.S.C. §§ 300mm – 300mm-64.
5 42 U.S.C. § 300mm-22(a)(6)(B).
6 The current List of WTC-Related Health Conditions is found in WTC Health Program regulations in Title 42 of the Code of Federal Regulations (CFR) Part 88 (42 C.F.R. § 88.15).
7 *See* 42 C.F.R. § 88.16(a)(1).

A. Petition 024

On October 3, 2019, the Administrator received a submission requesting the addition of "cardiovascular disease, including myocardial infarction, CABG (coronary artery bypass graft) and angioplasty" to the List. Upon review, the submission was found to be valid and assigned an ordinal number as **Petition 024**.

B. Petition 042

On January 23, 2023, the Administrator received a submission requesting the addition of "cardiovascular disease" to the List. Upon review, the submission was found to be valid and assigned an ordinal number as **Petition 042**.

C. Petition 046

On June 15, 2023, the Administrator received a submission requesting the addition of "cardiomyopathy" to the List. Upon review, the submission was found to be valid and assigned an ordinal number as **Petition 046**.

D. Petition 047

On September 3, 2023, the Administrator received a submission requesting the addition of "myocardial infraction [*sic*], unstable angina, obstructive coronary artery disease, ischemic cardiomyopathy, ischemic congestive heart failure, arrythmias (due to any of the above), stroke, and peripheral vascular disease" to the List. Upon review, the submission was found to be valid and assigned an ordinal number as **Petition 047**.

The Administrator exercised his discretion to separate the scientific evaluation of the eight conditions provided in **Petition 047** into three separate evaluations:[8] (1) "myocardial infraction (*sic*), unstable angina, obstructive coronary artery disease, ischemic cardiomyopathy, ischemic congestive heart failure, arrythmias (due to any of the above);" (2) "stroke;"[9] and (3) "peripheral vascular disease."[10]

The Administrator directed that the first group of health conditions will be evaluated in the current evaluation, under **Petition 047**. The second health condition is stroke and will be evaluated in a separate evaluation under a new ordinal number as **Petition 048**. The third health condition, peripheral artery disease, will be evaluated in a separate evaluation under a new ordinal number as **Petition 048a**.[11]

8 To ensure a comprehensive scientific evaluation of each of the specific health conditions requested in **Petition 047**, each of which are associated with a large volume of peer-reviewed, published, scientific studies, the Administrator directed the Science Team to review the scientific evidence for the requested health conditions in three separate evaluations pertaining to conditions: (1) affecting oxygen supply to the heart (i.e., ischemia); (2) affecting blood supply to the brain (i.e., ischemic and hemorrhagic stroke); and (3) affecting the peripheral artery system. *See infra*, note 10.

9 The Administrator understands the term "stroke," also known as a cerebral vascular accident or brain attack, to be a group of health conditions within a category called cerebrovascular diseases and to be a distinct subcategory of cardiovascular diseases. Stroke is generally described as a sudden onset of loss of focal neurological function caused by ischemia/infarction and/or hemorrhage in the relevant part of the brain, retina, or spinal cord. See Hankey [2017].

10 The Administrator understands the term "peripheral vascular disease" to mean the health condition known as "peripheral artery disease." *See* Campia et al. [2019].

11 *See Policy and Procedures for Handling Submissions and Petitions,* Section VII.C.2. [NIOSH 2026b].

E. Petition 051

On November 1, 2023, the Administrator received a submission requesting to add "cardiovascular diseases including coronary artery disease, myocardial infarction, stroke, congestive heart failure" to the List. Upon review, the submission was found to be valid and assigned an ordinal number as **Petition 051**. The Administrator directed that those portions of the submission valid for stroke be evaluated in a separate evaluation as **Petition 051a** along with **Petition 048**.

F. Petition 056

On January 6, 2025, the Administrator received a submission requesting the addition of "coronary artery disease (CAD)" to the List. Upon review, the submission was found to be valid and assigned an ordinal number as **Petition 056**.

G. Petition 058

On January 31, 2025, the Administrator received a submission requesting the addition of "cardiovascular disease, cardiomyopathy, atrial fibrillation" to the List. Upon review, the submission was found to be valid and assigned an ordinal number as **Petition 058**.

H. Petition 067

On September 3, 2025, the Administrator received a submission requesting the addition of "ischemic cardiomyopathy" to the List. Upon review, the submission was found to be valid and assigned an ordinal number as **Petition 067**.

I. Previous Petitions

The Administrator previously evaluated cardiovascular disease (CVD) and atherosclerosis for potential addition to the List. **Petition 004**, requesting the addition of "heart attack," was received on March 7, 2014, and interpreted by the Administrator to mean "cardiovascular disease." The Administrator's determination that the available evidence did not have the potential to provide a basis for a decision on whether to add CVD to the List was published in the *Federal Register* on May 6, 2014.[12]

On April 11, 2016, the Administrator received two submissions, combined into **Petition 012**, to add "atherosclerosis" to the List. The Administrator's determination that the available evidence did not have the potential to provide a basis for a decision on whether to add atherosclerosis to the List was published in the *Federal Register* on December 14, 2016.[13] The findings from these two previous evaluations are discussed in Sections VIII.B.1. and VIII.C.1. below.

12 *See supra*, note 1.
13 *See supra*, note 2.

III. PURPOSE

The purpose of this evaluation is to assess the scientific evidence from peer-reviewed, published, epidemiologic studies of IHD[14] in the 9/11-exposed population,[15] to determine whether sufficient evidence of a causal association between 9/11-related exposures, including exposure to 9/11 agents,[16] and the requested health condition exists to support adding the condition to the List. This evaluation is being provided to the Administrator to inform the Administrator's determination regarding **Petitions 024, 042, 046, 047, 051, 056, 058,** and **067** in accordance with the WTC Health Program's *Policy and Procedures* [NIOSH 2026a].

IV. REVIEW OF MEDICAL BASIS INFORMATION PROVIDED BY THE PETITIONERS

The validity of each petition was established by the Program in accordance with Program regulations and the *Policy and Procedures for Handling Submissions and Petitions* [NIOSH 2026a]. The Program examined the references provided with each submission to determine whether they included a medical basis for the association between the September 11, 2001, terrorist attacks and the health condition requested to be added to the List. *See* **Table 1a**. Across the eight petitions, 17 distinct studies provided by the petitioners in support of their petitions were determined to be sufficient medical basis for initiating this evaluation. *See* **Table 1b**.

A. Petition 024

Petition 024 provided one study as medical basis, Cohen et al. [2019], which was sufficient medical basis. Cohen et al. [2019] is a peer-reviewed, published longitudinal cohort study designed to assess whether 9/11 exposures were associated with elevated CVD risk, including but not limited to myocardial infarction (MI), stroke, unstable angina, coronary artery surgery or angioplasty, congestive heart failure, CVD death, stable angina, and cardiomyopathy in Fire Department of New York (FDNY) firefighters. Positive associations were observed between CVD and 9/11 exposures related to time of arrival and length of response. For a discussion of Cohen et al. [2019], *see* Section VIII.C.2.e.

B. Petition 042

Petition 042 provided 12 studies as medical basis. Five of the 12 studies were determined to provide sufficient medical basis [Alper et al. 2017; Remch et al. 2018; Cohen et al. 2019; Sloan et al. 2021; Mears et al. 2022].

14 The term "IHD" is defined in Section V. and in Table 3.

15 9/11-exposed population means those persons who can reasonably be assumed to have been exposed to hazards resulting from the September 11, 2001, terrorist attacks, including those 9/11 agents identified in the Program's *Development of the Inventory of 9/11 Agents (Inventory)*, within the geographic areas identified in the WTC Health Program's eligibility criteria; such populations may include, but are not limited to, WTC Health Program members. The *Inventory* includes a catalog of chemical, physical, biological, and other hazards that may have been present at the disaster areas. *See* NIOSH [2018].

16 9/11 agents are chemical, physical, biological, or other agents or hazards reported in a published, peer-reviewed, exposure assessment study of responders, recovery workers, or survivors who were present in the New York City disaster area, or at the Pentagon site, or the Shanksville, Pennsylvania site, as those locations are defined in 42 C.F.R. § 88.1, as well as those hazards not identified in a peer-reviewed, published, exposure assessment study, but which are reasonably assumed to have been present at any of the three sites. Known 9/11 agents are established in the *Inventory* [NIOSH 2018].

Alper et al. [2017] is a peer-reviewed, published longitudinal study of WTC Health Registry (WTCHR) enrollees who had acute exposure to WTC dust/debris or experienced a traumatic injury on September 11, 2001, and four self-reported health outcomes, including the cardiovascular diseases angina/MI; being injured on 9/11 was found strongly predictive of angina/MI, but angina/MI was not associated with intense dust cloud exposure.

Remch et al. [2018] is a peer-reviewed, published longitudinal study of WTC members who were first responders on or after September 11, 2001, examining whether post-traumatic stress disorder (PTSD) is a risk factor for MI and stroke combined. The study reported hazard ratios (HRs) for several 9/11 exposure measures and the MI/stroke outcome. Some of the HRs were increased and some were not, but none were statistically significant after adjustment for the presence of PTSD.

Cohen et al. [2019] is discussed above under **Petition 024**.

Sloan et al. [2021] is a peer-reviewed, published prospective cohort study designed to examine the annual and cumulative incidence of CVD, including coronary artery disease (CAD), MI, stroke, and congestive heart failure, among the WTC Health Program general responder cohort (GRC); it reported increased CVD risk in males and females exposed to the WTC dust cloud compared to those that were not exposed to the dust cloud (i.e., arrived on or after September 12, 2001). For discussion of four of these studies [Alper et al. 2017; Remch et al. 2018; Cohen et al. 2019; Sloan et al. 2021], *see* Section VIII.C.2.b., d., e., and h.

The remaining study, Mears et al. [2022], is a non-systematic review[17] study that summarized health effects arising from 9/11-related exposures, including cardiovascular effects in WTC rescue and recovery workers and survivors of the attacks. Mears et al. [2022] provided no original research findings and did not provide the methodology it used to identify the studies cited in its review, the methodology they used to draw conclusions, or the methodology used to assess the certainty of those conclusions. However, Mears et al. [2022] included citations to other studies which were found to provide sufficient medical basis, so it is also considered sufficient medical basis.[18] Mears et al. [2022] concluded that the long-term health effects, including cardiovascular effects, arising from 9/11 exposures remain unclear and that more study is needed. Nonetheless, Mears et al. [2022] was reviewed by the Science Team for relevant information for the evaluation.

Seven studies submitted with **Petition 042** were determined not to provide sufficient medical basis [Moline et al. 2016; Iyengar et al. 2017; Koshy et al. 2017; Tanwar et al. 2019; Veerappan et al. 2020; Park et al. 2022; Iyengar-Kapuganti et al. 2022]. Of these seven studies, two studies involved cardiometabolic effects in 9/11-exposed populations [Moline et al. 2016; Koshy et al. 2017]; three were toxicologic studies that evaluated the effect of WTC dust exposure in animal models [Tanwar et al. 2019; Veerappan et al. 2020; Park et al. 2022]; one was a study that evaluated the association between obstructive sleep apnea (OSA),

17 A systematic review collects and synthesizes all available, relevant evidence which brings together all existing primary studies for review and differs from other types of literature reviews in several major ways. Systematic review requires a transparent, reproducible methodology which indicates how studies were identified and the criteria upon which they were included or excluded. Systematic reviews provide methods for data extraction, data analysis, and quality assessment. In contrast, a non-systematic review does not provide a methodology that can be used to reproduce findings, nor inclusion and exclusion criteria, methods for data extraction, analysis, nor quality assessment. *See* Page et al. [2021].

18 *See* [NIOSH 2026b], Sections II. (definition of "scientific source") and VI.D.

a health condition already on the List, and left ventricular diastolic function [Iyengar-Kapuganti et al. 2022]; and one study was a conference poster presented at a meeting of the American College of Cardiology describing a study of particulate matter (PM) exposure and cardiovascular risk (i.e., estimated risk of developing IHD within the subsequent 10 years) among New York Police Department (NYPD) responders [Iyengar et al. 2017]. These seven studies did not examine the association between 9/11 exposures and CVD within the 9/11-exposed population and therefore were not eligible for further review. However, information from these seven studies was considered in the synthesis of biological plausibility, coherence, and analogy. *See* Section IX.B.4.

C. Petition 046

Petition 046 provided one study as medical basis, Cohen et al. [2019], described above, which was determined to provide sufficient medical basis and is discussed in Section VIII.C.2.e.

D. Petition 047

Petition 047 provided 33 studies as medical basis. These 33 studies covered several cardiovascular and cerebrovascular health conditions, including "MI, unstable angina, obstructive coronary artery disease, ischemic cardiomyopathy, ischemic congestive heart failure, arrythmias (due to any of the above), stroke, and peripheral vascular disease."[19]

Sufficient Medical Basis Studies. Fourteen of the 33 studies submitted with **Petition 047** provided sufficient medical basis [Brook et al. 2010; Newby et al. 2015; Kaufman et al. 2016; Alper et al. 2017; Cohen et al. 2017; Thurston et al. 2017; Cascio and Long 2018; Jordan et al. 2018; Remch et al. 2018; Cohen et al. 2019; EPA 2019; Newman et al. 2020; Sloan et al. 2021; Li et al. 2023].

Four of these studies, Alper et al. [2017], Remch et al. [2018], Cohen et al. [2019], and Sloan et al. [2021] are described above. These 4 studies plus 2 additional studies, Jordan et al. [2018] and Li et al. [2023] — a total of 6 of the 14 sufficient medical basis studies — are identified as high-quality studies and are discussed in Section VIII.C.2.b. through e., h., and i.

Jordan et al. [2018] is a cohort study that evaluated heart disease mortality (i.e., rheumatic heart disease, hypertension with heart disease, ischemic heart disease, chronic disease of the endocardium, cardiomyopathy, conductive disorder, and other diseases of the heart) occurring between 2003 and 2014 among WTCHR members. The study found that higher levels of exposure to WTC dust were positively associated but not-significantly with heart disease mortality in responders and survivors. Li et al. [2023] is a longitudinal cohort study of mortality in FDNY, WTCHR, and GRC responders followed over 15 years which

19 As noted in Section II.D. above, the Administrator exercised his discretion to separate the scientific evaluation of IHD (**Petition 047**) from stroke (**Petition 048**) and peripheral artery disease (**Petition 048a**). Ten studies submitted with **Petition 047** were found to provide sufficient medical basis for "stroke" [Brook et al. 2010; Newby et al. 2015; Cohen et al. 2017; Thurston et al. 2017; Cascio and Long 2018; Cohen et al. 2019; EPA 2019; Newman et al. 2020; Sloan et al. 2021; Yu et al. 2021]. The relevant medical basis for stroke will be discussed separately in the scientific evaluation for **Petition 048**. Seven studies submitted as medical basis for **Petition 047** provided sufficient medical basis for peripheral artery disease [Brook et al. 2010; Newby et al. 2015; Thurston et al. 2017; Cascio and Long 2018; Cohen et al. 2019; EPA 2019; Serra et al. 2021]. The relevant medical basis for peripheral artery disease will be discussed separately in the scientific evaluation for **Petition 048a**.

found a non-significantly elevated risk of heart disease-related mortality in GRC responders and certain WTCHR enrollees (i.e., those WTCHR enrollees who were not FDNY or GRC members) who first arrived between September 11 and 12, 2001, compared with those who arrived after September 17, 2001. Risk of heart disease-related mortality was significantly elevated among those WTCHR enrollees (non-FDNY/non-GRC) who arrived between September 13 and 17, 2001.

Eight of the 17 studies found to provide sufficient medical basis [Brook et al. 2010; Newby et al. 2015; Kaufman et al. 2016; Cohen et al. 2017; Thurston et al. 2017; Cascio and Long 2018; EPA 2019; Newman et al. 2020] described increased CVD risks associated with air pollution exposure, including PM with an aerodynamic diameter < 2.5 micrometers (μm) in diameter ($PM_{2.5}$). $PM_{2.5}$ is listed as a 9/11 agent in the *Development of the Inventory of 9/11 Agents (Inventory)* [NIOSH 2018].[20] These eight studies are briefly summarized below; however, because these studies did not examine health conditions in 9/11-exposed populations and did not examine exposure conditions experienced on September 11, 2001, they are not considered further in this evaluation.

Brook et al. [2010] presented a scientific statement from the American Heart Association (AHA) concluding that the available evidence supports a causal relationship between exposure to $PM_{2.5}$ and increased cardiovascular morbidity and mortality. The AHA further determined that $PM_{2.5}$ exposure should be regarded as a modifiable risk factor contributing to cardiovascular and related deaths. The paper also briefly discussed other 9/11 agents such as nitrogen oxide and dioxide (NO_x), carbon monoxide (CO), and ozone (O_3), associated with CVD.

Newby et al. [2015] is a scientific review conducted by the European Society of Cardiology (ESC) evaluating the evidence linking air pollution (whose components include the 9/11 agents $PM_{2.5}$, fine PM with a nominal mean aerodynamic diameter less than or equal to 10 μm (PM_{10}), ozone, nitrogen dioxide [NO_2], volatile organic compounds [including benzene], carbon monoxide [CO], and sulfur dioxide [SO_2]) to CVD. The ESC concluded that air pollution increases the risk of CVD and related morbidity and mortality. It also outlined potential biological mechanisms underlying this relationship and determined that air pollution should be considered a modifiable risk factor for CVD.

Kaufman et al. [2016] reported results from a 10-year prospective cohort study involving 6,795 participants in the Multi-Ethnic Study of Atherosclerosis and Air Pollution (MESA Air) across six U.S. metropolitan areas. Kaufman et al. [2016] found that higher ambient concentrations of $PM_{2.5}$ and nitrogen oxides (NO_x), but not elemental carbon, were strongly associated with accelerated progression of coronary atherosclerosis as demonstrated by the progression of coronary artery calcium (CAC) scores which is used as a diagnostic marker for CAD risk. The authors also concluded that long-term exposure to air pollution contributes to atherosclerosis progression in the coronary arteries, helping to explain previously observed associations between air pollutants, cardiovascular events, and mortality.

Cohen et al. [2017] estimated global population-weighted mean $PM_{2.5}$ and ozone concentrations. It then explored global spatial and temporal trends from 1990 to 2015 in increased mortality and burden of disease, including increased

20 *See* supra, note 16.

IHD attributable to $PM_{2.5}$. Ambient $PM_{2.5}$ was found to be the fifth-ranked risk factor for global deaths in 2015, with CVD (comprising IHD and cerebrovascular disease)[21] accounting for most of those deaths. The authors described the potential for substantial health benefits from reduction of air pollution exposure.

Thurston et al. [2017] is a joint European Respiratory Society/American Thoracic Society policy statement to answer the question "what constitutes an adverse health effect of air pollution?" It provides an analytical framework on how to interpret scientific evidence on the health effects of air pollution for risk management purposes. The statement provides a non-systematic review, including a review of the adverse CVD effects from exposure to $PM_{2.5}$.

Cascio and Long [2018] provided a non-systematic review on the CVD effects of air pollution. The review reported that $PM_{2.5}$ is associated with increased severity of CAD and a higher likelihood of having an MI in the previous year.

EPA [2019] is a detailed integrated science assessment that examined the impact of PM, including $PM_{2.5}$, on various CVD outcomes. The assessment concluded that there is sufficient evidence to support a causal relationship between both short-term (hours to approximately 1 month) and long-term (1 month to years) exposure to $PM_{2.5}$ and adverse cardiovascular outcomes, including IHD.

Newman et al. [2020] is a Journal of the American College of Cardiology (JACC) state-of-the-art review of the cardiopulmonary impact of PM in high-risk populations. It recognized that air pollution, including $PM_{2.5}$, poses CVD risks. The authors proposed actions to reduce those CVD risks and suggested methods to study the effectiveness of those actions.

Insufficient Medical Basis Studies. Nineteen studies submitted with **Petition 047** did not provide sufficient medical basis [Lioy et al. 2002; Wanahita et al. 2010; Jordan et al. 2011b; Jordan et al. 2013; Brackbill et al. 2014; Devlin et al. 2014; Beristianos et al. 2016; Shanley et al. 2016; Edmondson and von Kanel 2017; Yu et al. 2018; Ghio et al. 2018; McGuinn et al. 2019; Ward-Caviness 2019; Jhun et al. 2019; Scherrer et al. 2020; Serra et al. 2021; O'Donnell et al. 2021; Yu et al. 2021; Hargrave et al. 2022].

Three of the 19 studies that did not provide sufficient medical basis were previously evaluated as part of the 2014 evaluation of **Petition 004** [Jordan et al. 2011b; Jordan et al. 2013; Brackbill et al. 2014] and therefore were not sufficient medical basis. These three studies are discussed in Section VIII.C.1.a. through c. The other 16 studies did not examine the association between 9/11 exposures and CVD within the 9/11-exposed population or did not find a positive association between CVD and 9/11 exposures. Therefore, these 16 studies were not eligible for further review. However, information from these 16 studies was considered in the evaluation and synthesis of biological plausibility, coherence, and analogy. *See* Section IX.B.4.

Five of 19 studies that did not provide sufficient medical basis were supportive of the biological plausibility for a causal relationship between PTSD and IHD [Beristianos et al. 2016; Edmondson and von Kanel 2017; Scherrer et al. 2020; O'Donnell et al. 2021; Hargrave et al. 2022]. Two studies were cross-sectional studies that evaluated the association between particulate matter exposure and

21 The terms" IHD" and "cerebrovascular disease" are explained in Section V.

elevated serum lipids, potentially mediating air pollution-related effects on CVD [Shanley et al. 2016; McGuinn et al. 2019]. Two studies were longitudinal studies[22] that examined the risk of stroke among WTCHR enrollees [Yu et al. 2018; Yu et al. 2021]. One study characterized the dust/smoke that settled in lower Manhattan after the collapse of the WTC on September 11, 2001, but did not examine any health conditions related to 9/11-exposures [Lioy et al. 2002]. One study provided a review of gene-air pollution interaction studies for CVD and suggested possible mechanistic information on the association between particulate matter exposure and CVD [Ward-Caviness 2019]. One study provided a review of environmental pollutant exposures associated with peripheral artery disease [Serra et al. 2021]. Three studies examined the CVD risks from environmental exposures not known to be 9/11 agents, including ultrafine particles (aerodynamic diameter < 0.1 μm), humic-like substances,[23] and black carbon [Devlin et al. 2014; Ghio et al. 2018; Jhun et al. 2019]. A final study, Wanahita et al. [2010], is a cross-sectional study of CAC scores in New York City (NYC) police officers; it did not identify evidence of increased prevalence of premature CAD in the 9/11-exposed population and, therefore, was not found to provide sufficient medical basis for **Petition 047**. However, Wanahita et al. [2010] was identified in the literature review and is discussed in Section VIII.B.2.a.

E. Petition 051

Petition 051 provided four studies as medical basis. Three of these studies were determined to be sufficient medical basis [Remch et al. 2018; Cohen et al. 2019; Sloan et al. 2021].[24] For discussion of these three studies, *see* Section VIII.C.2.d., e., and h.

A fourth study was an editorial commentary on coronary microvascular disease (CMD), also known as small artery disease or small vessel disease, that posited CMD as a potential contributing cause of IHD [Berry and Duncker 2020]. Although providing insights into the diagnosis of CMD and potential mechanisms linking CMD to IHD, Berry and Duncker [2020] did not provide any information explicitly linking environmental exposures, such as 9/11 agents, to CMD; therefore, it did not constitute sufficient medical basis and was not considered further.

F. Petition 056

Petition 056 provided one study, Sloan et al. [2021], which was determined to be sufficient medical basis and is discussed in Section VIII.C.2.h.

G. Petition 058

Petition 058 included four studies as medical basis. Each of the four studies provided sufficient medical basis [Lin et al. 2010; Cohen et al. 2019; Sloan et al.

22 Longitudinal studies follow individuals over prolonged periods of time — often years or decades — using continuous or repeated measures. The longitudinal study type is particularly useful for evaluating the relationship between risk factors and the development of disease. *See* Caruana et al. [2015].

23 Humic substances are derived from degraded plant remains and are an important source of organic matter. *See* Tiwari et al. [2023].

24 As noted in Section II.E. above, the Administrator exercised his discretion to separate the scientific evaluation of IHD (**Petition 051**) from stroke (**Petition 051a**). Two studies submitted with **Petition 051** were found to provide sufficient medical basis for "stroke" [Cohen et al. 2019; Sloan et al. 2021]. The relevant medical basis for stroke will be discussed separately in the scientific evaluation for **Petition 051a**.

2021; Mueller et al. 2024]. Cohen et al. [2019] and Sloan et al. [2021] are described above. Mueller et al. [2024] is a cross-sectional study of CVD prevalence in male FDNY firefighters; it found a positive association between self-reported CVD, including CAD, MI, and angina when comparing firefighters with September 11, 2001, exposures versus firefighters without those exposures. Cohen et al. [2019], Sloan et al. [2021], and Mueller et al. [2024] are discussed further in Section VIII.C.2.e., h., and j.

Lin et al. [2010] is an ecologic study comparing crude cardiovascular hospital admission rates pre- and post-September 11, 2001, in the "affected area" as well as comparing admission rates in the affected area with a "control area." CVDs included chronic rheumatic heart disease, hypertension, acute and chronic CAD, cardiac dysrhythmia, and congestive heart failure. The study found a significant increase in the rate of CVD hospitalizations during the weeks of September 18, 2001, and October 9, 2001, compared to the same weeks during the preceding 10 years. However, no such increases in the rate of CVD hospitalizations were observed in several other weeks in 2001, including the weeks of September 11, September 25, October 2, October 16 and October 30. Lin et al. [2010] contributed to discussion in the section on synthesis of biological plausibility, coherence, and analogy. See Section IX.B.4.

H. Petition 067

Petition 067 provided one study as medical basis, Lin et al. [2010], described above. Lin et al. [2010] contributed to discussion in the section on synthesis of biological plausibility, coherence, and analogy. *See* Section IX.B.4.

V. EVALUATED HEALTH CONDITIONS

As described above in Section II, each of the eight petitions included in this evaluation requested the addition of a type or types of CVD. Causal associations involving aggregate outcomes, such as the large health condition grouping called "cardiovascular disease" cannot always be adequately assessed due to widely varying etiology within a large system of the body like the cardiovascular system. This was the case with the various health conditions requested to be added to the List by **Petitions 024, 042, 046, 047, 051, 056, 058,** and **067**.

CVD encompasses a large heterogeneous group of adverse health conditions of differing etiologies that are loosely defined as diseases of the heart and blood vessels. Given its broad definition, CVD is highly prevalent, with nearly 131 million Americans ≥ 20 years of age (48.9%) presenting with one or more types of CVD [Palaniappan et al. 2026]. CVD definitions vary in the literature and have included outcomes such as rheumatic fever/rheumatic heart disease (International Classification of Diseases [ICD]-10 I00–I09); hypertensive diseases (I10–I15); ischemic (coronary) heart disease (I20–I25); pulmonary heart disease and diseases of pulmonary circulation (I26–I28); other forms of heart disease (I30–I52); cerebrovascular disease (e.g., stroke) (I60–I69); atherosclerosis (I70); other diseases of arteries, arterioles, and capillaries (I71–I79); diseases of veins, lymphatics, and lymph nodes not classified elsewhere (I80–I89); and other and unspecified disorders of the circulatory system (I95–I99) [Palaniappan et al. 2026]. Although many CVD outcomes might share characteristics and risk factors, causes among the various subcategories of CVD can vary widely. Therefore,

causal inference based on evidence of an association between 9/11 exposures and the overarching category of CVD is scientifically infeasible.

The health conditions requested by **Petitions 024, 042, 046, 047, 051, 056, 058,** and **067** are health conditions and treatment interventions related to IHD, also known as coronary heart disease (CHD), according to the ICD-10 classification scheme. IHD is among the most prevalent subgroups of CVD (IHD prevalence = 5.2%; 95% confidence interval (CI): 4.7%, 5.8%, in adults aged ≥ 20 years) and is the leading cause of CVD death, accounting for about 57% of CVD deaths (all ages) globally in 2021 [Palaniappan et al. 2026].

To define the health condition for purposes of this evaluation, the Science Team used the code-mapping scheme developed for the 119-cause rate file used in the NIOSH Life Table Analysis System (LTAS) [Robinson et al. 2006; Schubauer-Berigan et al. 2011].[25] NIOSH LTAS classifies (groups) health conditions for person-year analyses. The NIOSH LTAS classification scheme was intended to improve health-effects research by combining conditions in a balance of statistical power and maintaining within-group homogeneity. ICD-10 codes were grouped into major and minor categories of similar health conditions [WHO 2005]. In applying NIOSH LTAS outcome grouping, the Program reviewed Major category 16, Diseases of the Heart, slightly modifying the scheme for this evaluation to include code I51 (complications and ill-defined descriptions of heart disease) under Minor category 059 (other diseases of the heart). The Program determined that the scope of this evaluation falls within the Minor category 055 of IHD, with associated ICD-10 codes I20-I22 and I24-I25. *See* **Tables 2** and **3**.

In accordance with the *Policy and Procedures* [NIOSH 2026a], the Science Team reviewed the information provided by petitioners, including the medical basis information and other scientific references submitted with each petition, and determined that the health condition of interest for this evaluation is ischemic heart disease. Subgroups of IHD considered in this evaluation include angina pectoris, acute MI or "heart attack," subsequent ST segment elevation MI (STEMI) and non-ST segment elevation MI (NSTEMI), other acute IHD, and chronic IHD (e.g., coronary atherosclerosis and ischemic cardiomyopathy), as shown in **Table 3**. For this evaluation, the Program considered the evidence of an association between IHD and 9/11 exposures, primarily encompassing exposure to 9/11 agents, as described in Section VI. As permitted by WTC Health Program regulations, **Petitions 024, 042, 046, 047, 051, 056, 058,** and **067** are considered together in this evaluation.[26]

VI. RISK FACTORS FOR EVALUATED HEALTH CONDITION

A. General Risk Factors

There are numerous general risk factors for IHD. In the past 30 years, age-standardized rates for the major risk factor of tobacco use decreased substantially. However, during that same period, the prevalence of other risk factors (e.g., obesity, dyslipidemia, diabetes, exposure to air pollution, and sedentary behavior) continued to rise, offsetting the benefits of reduced tobacco use [Zaman et al. 2025; Palaniappan et al. 2026]. Age-adjusted IHD mortality has progressively decreased since the 1990s globally, although prevalence has largely plateaued [Roth et al. 2020].

25 NIOSH LTAS is computer software commonly used to conduct comparisons of cause-specific incidence and mortality rates by age, sex, race, calendar time, and duration or level of exposure. NIOSH LTAS support was discontinued in 2022, but its functionality was retained in software available on another platform. *See* Bertke and Kelly-Reif [2022].

26 *See* 42 C.F.R. § 88.16(a)(4).

Age is a strong risk factor for IHD and is considered to be non-modifiable. The prevalence of IHD progressively increases with advancing age [Shih et al. 2011]. IHD prevalence rates among individuals aged 75 years and older was 19.7% in 2022 [Khalid et al. 2024]. Sex is also a risk factor, although IHD is a leading cause of death in both sexes [Palaniappan et al_2026]. Females tend to live longer and develop IHD later in life. Hormonal changes, particularly those involving sex hormones, influence IHD risk. Estrogen concentrations, which protect the cardiovascular system, decline in postmenopausal females [Vogel et al. 2021]. The prevalence of IHD among men was 6.4% in 2022, and among women was 3.6% [Khalid et al. 2024]. White adults (males and females combined) had the highest IHD prevalence of any racial group (5.4%) in 2022, while Asian adults had the lowest (3.8%) [Khalid et al. 2024].

Family history is also a risk factor for IHD, especially among those with a closely related family member with premature IHD (e.g., premature IHD can be defined as IHD in a first-degree male relative < 55 or female relative < 65 years of age) [Visseren et al. 2021; Sivapalaratnam et al. 2010]. This may reflect an interplay between genetics and the environment. However, family history only marginally improves the prediction of IHD risk beyond other conventional IHD risk factors (e.g., smoking, hypertension, obesity, and dyslipidemia) [Zaman et al. 2025].

Elevated blood pressure is considered the most important risk factor for IHD [Zaman et al. 2025]. Elevated blood pressure places both mechanical and neurohormonal stress on the coronary arterial wall leading to disrupted endothelial homoeostasis, thereby initiating and accelerating coronary atherosclerosis. Reducing blood pressure is an extremely effective method to reduce IHD risk. For every 10 millimeters of mercury (mm Hg) reduction in blood pressure, the risk of IHD events (defined as fatal and non-fatal MI and sudden cardiac death) is reduced by 17%, irrespective of starting blood pressure [Ettehad et al. 2016].

Smoking is a strong risk factor for IHD [Zaman et al. 2025]. Among current tobacco smokers, the excess relative IHD risks attributed to smoking were higher in women compared to men, although such a sex difference does not appear to exist for former smokers [Huxley and Woodward 2011]. Fortunately, the prevalence of this modifiable risk factor is dropping in the United States [Cornelius et al. 2023].

Obesity is characterized by excess adiposity, with causes that are multifactorial and still incompletely understood [Rubino et al. 2025]. Obesity as measured by body mass index (BMI), which is a useful measure of obesity in epidemiological studies, is strongly associated with a higher IHD prevalence and death [Global BMI Mortality Collaboration 2016]. Pathophysiological mechanisms almost ubiquitous with obesity include atherogenic dyslipidemia (such as increased triglycerides and high low-density lipoprotein (LDL) cholesterol), insulin resistance, raised blood pressure, and chronic inflammation (e.g., visceral fat secretes proinflammatory cytokines) [Zaman et al. 2025].

Type 1 diabetes mellitus, type 2 diabetes mellitus, and prediabetes are independent risk factors for IHD [Visseren et al. 2021] and confer a two-fold elevated risk for IHD [Emerging Risk Factors Collaboration 2010]. These conditions lead to IHD through distinct biochemical pathways that directly or

indirectly damage the coronary vasculature and induce coronary inflammation [Bornfeldt and Tabas 2011].

Dyslipidemia is a well-known risk factor for IHD [Prospective Studies Collaboration 2007]. Dyslipidemia is generally characterized by elevated concentrations of LDL cholesterol (i.e., harmful cholesterol) and low concentrations of high-density lipoprotein (HDL) cholesterol (beneficial cholesterol).

Chronic kidney disease is another major and independent risk factor for IHD [Sarnak et al. 2019]. The relationship between chronic kidney disease and IHD is complex and multifaceted, involving a combination of traditional cardiovascular risk factors, which are over-represented in the chronic kidney disease patient population, and non-traditional risk factors unique to chronic kidney disease, including inflammation, oxidative stress, and abnormal calcium-phosphorus metabolism [Sarnak et al. 2019]. This relationship is bidirectional because IHD also contributes to the progression of chronic kidney disease.

Physical inactivity and prolonged sedentary behavior are well recognized risk factors for IHD [Lee et al. 2012]. Minimal physical activity can lead to obesity, insulin resistance, hypertension, and dyslipidemia, all of which contribute to IHD. However, physical inactivity is related to increased IHD risks even after adjustment for these confounders. Regular physical activity has been shown to improve endothelial function, reduce inflammation, and enhance lipid profiles [Winzer et al. 2018]. Adjunctive resistance training is additionally associated with fewer IHD events [Zaman et al. 2025].

Mental health factors, including chronic stress (e.g., PTSD), depression, anxiety, and substance use disorder have been linked to IHD [Zaman et al. 2025]. The precise mechanism by which mental disorders increase IHD remains uncertain [Visseren et al. 2021]. However, chronic stress triggers the release of stress hormones like cortisol and epinephrine, which can lead to increased heart rate, hypertension, and endothelial dysfunction. Additionally, poor mental health can lead to unhealthy behaviors such as smoking, unhealthy diet, and physical inactivity, further exacerbating IHD risk.

Sleep disturbance and abnormal sleep duration (i.e., both short and long sleep durations) are associated with increased IHD risk, with a sleep duration of 7 hours apparently optimal for heart health [Visseren et al. 2021]. There is growing recognition that OSA is a crucial independent risk factor for IHD. OSA produces intermittent hypoxia and sleep fragmentation which contributes to systemic inflammation, oxidative stress, and sympathetic nervous system activation, leading to atherosclerotic lesions in coronary arteries [Zaman et al. 2025].

Air pollution is a growing concern for cardiovascular health due to the magnitude of the exposed population. In 2019, the EPA released the *Integrated Science Assessment (ISA) for Particulate Matter* and concluded that evidence is sufficient to support a causal relationship between both short-term (hours to approximately 1 month) and long-term (1 month to years) exposure to $PM_{2.5}$ and adverse cardiovascular outcomes, including IHD [EPA 2019, 2025]. Proposed biological mechanisms include inflammation of the respiratory tract leading to systemic inflammation and oxidative stress, loss of bioavailable nitric oxide leading to endothelial dysfunction; enhanced sympathetic signaling leading to raised blood

pressure; and increased platelet activation. Evidence supporting exposure to ground-level ozone and increased IHD risk continues to grow [Posadas-Sánchez et al. 2022].

B. 9/11 Risk Factors

When the airplanes struck the World Trade Center towers in NYC, they produced a series of explosions that led to fires consuming both buildings. In less than 2 hours, the 110-story Twin Towers had collapsed, resulting in a massive and dense cloud of suspended toxic dusts, gases, and smoke that engulfed the highly populated areas of southern Manhattan and Brooklyn [Lioy and Georgopoulos 2006]. The bulk (about 80% to 90%) of the aerosolized dust resulted from the cascading impacts of concrete floor slabs that crushed the building materials and contents into a dispersible powder [Lippmann et al. 2015]. The suspended dust entered nearby office, school, and residential buildings resulting in exposures both indoors and outside. The 6-story pile of smoking rubble at Ground Zero burned intermittently for more than 3 months [Landrigan et al. 2004]. Exposures continued in the days and months that followed, initially mostly from burning jet fuel and building fires, and later by the resuspension of dust during the many months of cleanup and recovery. Similar hazards were found at the Pentagon disaster site, although at lower levels [Gaborek et al. 2001]. The hazards at the Shanksville, Pennsylvania disaster site were limited to residual jet fuel and hydraulic fluids, emissions from small-scale fires or smoldering debris from the plane and surrounding groundcover, human remains, and potential hazards created during the response and cleanup (e.g., carbon monoxide, diesel exhaust, and noise) [NIOSH 2012].

In 2018, the WTC Health Program published the *Inventory*, a catalog of chemical, physical, biological, and other hazards that may have been present at the disaster areas [NIOSH 2018]. The over 350 hazards referenced in the *Inventory* are recognized as "9/11 agents,"[27] including five different variants of "WTC dust;" glass shards: PM_{10}; $PM_{2.5}$; particles > 2µm; and particles > 5µm.

Settled WTC dust collected shortly after the attacks indicated that about 1% to 2% of the total mass comprised $PM_{2.5}$ [Lioy et al. 2002; Landrigan et al. 2004]. Airborne measurement data were not available during and immediately following the attacks; however, persons engulfed in the dust cloud were likely exposed for several hours to concentrations of inhalable particles that exceeded 1,000 µg/m³ [Lippmann et al. 2015]. Environmental measurement data on $PM_{2.5}$ available weeks after the attacks showed that among 13 monitoring sites maintained by the EPA, approximately 6% of the representative daily averages of $PM_{2.5}$ through June 2002 exceeded the screening criterion of 40 µg/m³.[28] Most exceedances occurred at sites near Ground Zero; however, concentrations of $PM_{2.5}$ had generally fallen to values below 40 µg/m³ by November 2001 and decreased to background ambient concentrations by February 2002 [Lippmann et al. 2015].

$PM_{2.5}$ collected at Ground Zero and within a half-mile radius has been shown to contain gypsum and calcite as major components originating from construction

27 *See supra*, note 16.

28 The EPA sets national ambient air quality standards (NAAQS) for PM. The primary (health-based) annual average standard for $PM_{2.5}$ is 9.0 µg/m³ and the 24-hour standard is 35 µg/m³. For PM_{10}, the 24-hour primary standard (with one-expected exceedance) is 150 µg/m³.

materials such as cement, concrete aggregate, ceiling tiles, and wallboard and were different from the components found in control dust samples [McGee et al. 2003]. Nonetheless, research on the health effects of non-WTC $PM_{2.5}$ (i.e., general $PM_{2.5}$ not comprised of WTC dust) has examined cardiovascular impacts in relation to particle size, source, dose, and composition, and suggests that these effects likely arise from a combination of mechanisms associated with both the small size and the chemical composition of the particles [Krittanawong et al. 2023]. For example, health effects of small particles may be amplified by compositions including sulfur compounds, metals, and combustion products [Thurston et al. 2016; Weichenthal et al. 2021]. $PM_{2.5}$ exposures may have cardiotoxic effects in general due to the biological mechanistic effects of small particles being inhaled into the lungs irrespective of chemical make-up. Thus, WTC $PM_{2.5}$ may be cardiotoxic both as a function of size and composition. There is no evidence to suggest that $PM_{2.5}$ arising from the WTC disaster site is less toxic than non-WTC $PM_{2.5}$ exposures that were previously shown to have cardiotoxic effects.

Exposures to $PM_{2.5}$ (the 9/11 agent "WTC Dust: $PM_{2.5}$") is of particular interest for this evaluation. Cardiotoxicity (damage to the heart caused by a toxin) has been linked to exposures to $PM_{2.5}$ [Brook et al. 2010; Cohen et al. 2017; Thurston et al. 2017; EPA 2019; Newman et al. 2020; EPA 2025]. $PM_{2.5}$ has a strong capacity to generate reactive oxygen species, which are widely recognized for their role in inflammation, cell death, genotoxicity, and epigenetic alterations. Studies also show that exposure to $PM_{2.5}$ can impair the body's antioxidant defenses, contributing to cellular oxidative stress. Because $PM_{2.5}$ particles can enter the bloodstream and circulate throughout the body, they can cause systemic damage to multiple organs. At the cellular level, cumulative injury associated with prolonged exposure may lead to a range of pathologies, as documented in epidemiologic studies. Exposure to $PM_{2.5}$ has been linked to adverse effects on the cardiopulmonary, nervous, renal, gastrointestinal, and reproductive systems [Garcia et al. 2023].

With respect to occupational exposures, Geyh et al. [2005] examined inhalation exposures among truck drivers (^{n} = 54) who were hauling debris away from the rubble pile during WTC cleanup. Area perimeter monitoring conducted in October 2001 indicated $PM_{2.5}$ concentrations ranging from 21 to 321 µg/m^3, and up to 865 µg/m3 at the pile. Personal monitoring, also conducted during that time, recorded total particulate concentrations ranging from 72 to 790 µg/m^3, with a median personal exposure of 346 µg/m^3 [Geyh et al. 2005].

In addition to $PM_{2.5}$ exposure, other 9/11 agents included in the *Inventory* may have roles in IHD risk. Some 9/11 chemical agents known or suspected to be present in the WTC dust and debris, including polychlorinated biphenyls, arsenic, cadmium, and lead, are also potential cardiovascular toxicants. The *Inventory* also includes among 9/11 agents "other hazards," defined as "experiences that might cause psychological harm … identified in studies that assessed exposure to trauma or stress" based on exposure assessment studies. One such other hazard identified in the *Inventory* is the experience of having "sustained injury on 9/11" (9/11 injury). Sustaining a 9/11 injury was considered by the Science Team as a 9/11 exposure that may also be a potential independent risk factor for IHD.

In summary, the Science Team evaluation considered 9/11 agents, including $PM_{2.5}$ and chemical cardiovascular toxicant exposures in WTC dust, as well as physical

injury sustained on September 11, 2001, as the exposures of primary interest of a causal association between 9/11 exposure and IHD. The Science Team also looked at the confounding, modifying, or mediating effects of PTSD on the causal association between 9/11 exposure and IHD. However, PTSD itself is not considered a 9/11 exposure; therefore, studies that only examined the association between PTSD and IHD in the 9/11 population (e.g., Giesinger et al. [2020]) cannot provide evidence in support of a causal association between 9/11 exposures and IHD.

VII. SCIENTIFIC EVALUATION APPROACH

The Science Team evaluation was carried out in accordance with the *Policy and Procedures* [NIOSH 2026a] and includes the following steps: (1) develop a literature search protocol and conduct a search for peer-reviewed, published, epidemiologic studies of the health condition being evaluated among 9/11-exposed populations;[29] (2) review identified studies to determine which studies are high-quality studies for further evaluation;[30] (3) evaluate and integrate the evidence of a causal association between 9/11 exposures and the health condition being evaluated;[31] and (4) synthesize and interpret all findings to categorize the weight of evidence of a causal association between 9/11 exposures and the health condition evaluated.[32] The Science Team then advises the Administrator of its findings.[33]

VIII. REVIEW OF THE LITERATURE

A. Literature Search

The literature search identifies high-quality peer-reviewed, published, epidemiologic studies that provide evidence on the likelihood of a causal relationship between 9/11 exposures and the health condition under consideration—IHD. To identify potentially relevant studies, the Science Team searched abstracts and titles from peer-reviewed English language literature. In addition to search terms used to identify epidemiologic studies of the 9/11-exposed population, keywords used to uncover potentially informative studies in an initial search included: cardiovascular disease, myocardial infarction (MI, acute MI), acute coronary syndrome, coronary thrombosis, stroke (cerebrovascular accident, transient ischemic attack, intracerebral hemorrhage, cerebral hemorrhage, subarachnoid hemorrhage, brain ischemia, brain infarction, cerebral infarction),[34] angina (unstable angina, stable angina), angina pectoris, coronary occlusion, coronary artery obstruction, ischemia/reperfusion injury, reperfusion injury, myocardial ischemia, acute cardiac disease, coronary artery stenoses, coronary artery disease, ischemic heart disease, arterial stenosis, coronary artery surgery, coronary bypass surgery, coronary artery bypass graft surgery (CABG), percutaneous coronary intervention (PCI), percutaneous intervention, angioplasty, coronary revascularization, myocardial revascularization, coronary artery revascularization, stent (OR stents OR

29 *See Policy and Procedures*, Section III.B. [NIOSH 2026a].
30 *See Policy and Procedures*, Section III.C. [NIOSH 2026a].
31 *See Policy and Procedures*, Section IV. [NIOSH 2026a].
32 *See Policy and Procedures*, Section V. [NIOSH 2026a].
33 *See Policy and Procedures*, Section VI. [NIOSH 2026a].
34 Although this evaluation was restricted to IHD, the list of search terms included both cardiovascular and cerebrovascular outcomes to ensure that no IHD studies were overlooked.

stenting) placement AND (heart or coronary or artery), coronary artery stenting, drug-eluting stent (OR stents OR stenting), carotid artery surgery, surgical revascularization, surgical bypass, aortic aneurysm, arterial aneurysm, arterial dissection, aortic dissection, peripheral arterial vascular intervention, peripheral artery disease, atherosclerotic disease, arteriosclerotic disease, peripheral artery occlusive disease, arterial syndrome, embolism, aortoiliac disease, femoropopliteal disease, and ischemic cardiomyopathy.

A subsequent search included additional terms in recognition of new information obtained from later petitions. The new terms were: brain aneurysm, intracranial aneurysm, cerebral aneurysm, saccular aneurysm, berry aneurysm, intracranial hemorrhage, varicose veins, venous thromboembolism, pulmonary embolism, deep vein thrombosis, VTE, DVT, thrombosis, venous thrombosis, vein thrombosis, venous disease, chronic venous disease, chronic venous insufficiency, venous leg ulcer, venous ulcer, venous ulceration, venous incompetence, venous stasis, varicose disease, coronary artery spasm, coronary spasm, prinzmetal angina, microvascular angina, MVA, vasospastic angina, spastic angina, coronary vasospasm, variant angina, anginal attack, coronary microvascular obstruction, coronary microvascular dysfunction, cardiac syndrome X, syndrome X, INOCA (ischemia with non-obstructive coronary artery disease), MINOCA (myocardial infarction with no obstructive coronary atherosclerosis), ischemic congestive heart failure, heart failure, arrythmias, ventricular, arrhythmia(s), cardiac arrest, ventricular fibrillation, ventricular tachycardia, sudden cardiac death, sudden death, atrial fibrillation, atrial flutter, tachyarrhythmia(s), tachycardia, supraventricular tachycardia, cardiac ectopy, ectopy, atrioventricular block, AV block, bundle branch block, heart block, cardiac conduction disease, and cardiac conduction defect. Searches were conducted among the following databases: APA PsycInfo®, CINAHL (EBSCOhost), Embase Classic+Embase, Health & Safety Science Abstracts (ProQuest), NIOSHTIC-2, Ovid MEDLINE®, Scopus, and Toxicology Abstracts (ProQuest).

Periodic follow-up searches were conducted using the WTC Health Program Bibliographic Database, a database of relevant 9/11-related research maintained by the Program and updated at least weekly using a standing search of the previously mentioned databases. The last follow-up search was conducted in June 2026. This two-pronged approach ensures all relevant and up-to-date literature is available for this evaluation.

The literature search identified a total of 20 studies published between September 2001 and June 2026 that were peer-reviewed, published, epidemiologic studies of IHD in the 9/11-exposed population for full review as potential studies for evaluation [Brackbill et al. 2006; Wanahita et al. 2010; Jordan et al. 2011a; Jordan et al. 2011b; Jordan et al. 2013; Mani et al. 2013; Brackbill et al. 2014; Stein et al. 2016; Alper et al. 2017; Jordan et al. 2018; Remch et al. 2018; Cohen et al. 2019; Colbeth et al. 2020; Alper et al. 2021; Sloan et al. 2021; Li et al. 2023; Singh et al. 2023; Mueller et al. 2024; Krasnov et al. 2025; Parvin et al. 2026].[35]

35 Seven of the 20 studies identified as peer reviewed, published, epidemiological studies of IHD in the 9/11-exposed population were also included as sufficient medical basis information provided by petitioners [Alper et al. 2017; Jordan et al. 2018; Remch et al. 2018; Cohen et al. 2019; Sloan et al. 2021; Li et al. 2023; Mueller et al. 2024]. Another study identified in the literature search, Wanahita et al. [2010], was submitted to support Petition 047 but was not found to provide sufficient medical basis for the Petition because it did not identify evidence of increased prevalence of coronary artery disease in the 9/11-exposed population.

Five of the 20 studies identified in the literature search were included in the evaluations of previous petitions [Jordan et al. 2011a; Jordan et al. 2011b; Jordan et al. 2013; Mani et al. 2013; Brackbill et al. 2014]. Among these five previously reviewed studies, the Science Team determined that two studies did not demonstrate sufficient validity indicators to be considered high-quality studies,[36] thus they were removed from further consideration [Jordan et al. 2011a; Mani et al. 2013]. These two studies are described in Section VIII.B.1. and **Table 4**. Three of the five previously reviewed studies were found to meet the standard for high-quality studies [Jordan et al. 2011b; Jordan et al. 2013; Brackbill et al. 2014]. These three studies are reexamined in Section VIII.C.1. and **Table 4**.

Another four studies identified in the literature search were determined not to demonstrate sufficient validity indicators to be further evaluated as high-quality studies [Wanahita et al. 2010; Stein et al. 2016; Singh et al. 2023; Parvin et al. 2026]. All four studies were removed from further consideration but are discussed in Section VIII.B.2. for completeness.

In addition to the 3 previously evaluated studies [Jordan et al. 2011b; Jordan et al 2013; Brackbill et al 2014], the Science Team determined that another 11 of the 20 identified studies [Brackbill et al. 2006; Alper et al. 2017; Jordan et al. 2018; Remch et al. 2018; Cohen et al. 2019; Colbeth et al. 2020;[37] Alper et al. 2021; Sloan et al. 2021; Li et al. 2023; Mueller et al. 2024; Krasnov et al. 2025] had sufficient validity indicators to meet the standard for high-quality studies.[38] The review and evaluation of these 11 newly identified high-quality studies are included in Section VIII.C.2. *See* **Table 5**.

B. Studies Removed from Further Consideration

1. Previously Reviewed Studies Removed from Further Consideration

Two previously reviewed studies that were identified in the literature search were determined by the Science Team to not demonstrate sufficient validity indicators to be considered high-quality studies and were therefore removed from further consideration [Jordan et al. 2011a; Mani et al. 2013]. One of these studies [Jordan et al. 2011a] was previously reviewed in the 2014 evaluation of **Petition 004**. The other study [Mani et al. 2013] was reviewed in the 2016 evaluation of **Petition 012**. *See* **Table 4**. The findings from these two studies and their notable limitations were discussed in the published decisions on **Petition 004**[39] and **Petition 012**.[40] They are also summarized below for completeness.

a. Jordan et al. [2011a]

Jordan et al. [2011a] examined mortality in a cohort study of WTCHR enrollees followed between 2003 and 2009. The cohort comprised both rescue/recovery workers (*n* = 13,337; 74,967 person-years) and community members (*n* = 28,593; 161,519 person-years), the latter consisting of residents, workers, school students and staff, and

36 *See Policy and Procedures*, Section III.C. [NIOSH 2026a].
37 Colbeth et al. published a correction to their 2020 article in 2023. *See* Colbeth et al. [2023].
38 *See Policy and Procedures*, Section III.C. [NIOSH 2026a].
39 *See supra*, note 1.
40 *See supra*, note 2.

passers-by. Jordan et al. [2011a] was largely superseded by another similar study with a larger population and more extended follow-up [Jordan et al. 2018]. Unlike the subsequent study [Jordan et al. 2018], participants in Jordan et al. [2011a] were restricted to persons residing in NYC at the time of enrollment. Information about WTC exposures was derived from WTCHR Wave 1 (2003–2004) questionnaire data. In general, exposure was classified as high, intermediate, or low using different classification schemes for rescue/recovery workers and community members, as well as for the full cohort (restricted to high vs. low). The underlying causes of death were identified primarily via linkage to NYC vital records. The CDC National Death Index (NDI)[41] was used only to identify deaths among NYC residents that occurred outside of NYC. Deaths were grouped according to the NIOSH LTAS [Robinson et al. 2006; Schubauer-Berigan et al. 2011].

The health condition of interest was heart disease (NIOSH LTAS Major 16). Pre-September 11, 2001, heart disease was defined as self-reported diagnosis of CAD, angina, heart attack, or any other heart disorder occurring before September 11, 2001. External and internal comparisons were reported. Standardized mortality ratios (SMRs) accounting for age, sex, race/ethnicity, and calendar period were calculated for all participants and stratified by enrollment, with U.S. population rates referent. HRs were calculated using proportional hazards regression adjusting for age, sex, race/ethnicity, education, smoking, and diabetes mellitus and heart disease diagnosed prior to September 11, 2001.

There were 187 heart disease deaths among participants in the Jordan et al. [2011a] study. Heart disease mortality was significantly decreased in all participants (SMR = 0.42; 95% CI: 0.36, 0.48), in rescue/recovery workers (SMR = 0.39; 95% CI: 0.27, 0.54; *n* = 34), and in community members (SMR = 0.42; 95% CI: 0.36, 0.50; *n* = 153). In the full cohort, there was no evidence of an association between WTC-dust cloud exposure (high vs. low) and heart disease mortality (HR = 1.04; 95% CI: 0.77, 1.42). In stratified analyses, heart disease risk was significantly increased among community participants in the high exposure category when compared to the low exposure category (HR = 2.06; 95% CI: 1.10, 3.86); however, there were only 14 heart disease deaths in this group. The estimate comparing intermediate with low exposure was also increased (HR = 1.21; 95% CI: 0.80, 1.83), suggesting a positive exposure-response trend; however, a formal statistical test was not reported. *See* **Table 6**. In contrast, the subsequent study extending follow-up to 2014, Jordan et al. [2018], did not replicate increased heart disease risk; it reported a high vs. low HR of 1.14 (95% CI: 0.76, 1.73) and no evidence of heart disease mortality risk increasing with exposure (*p* for trend = 0.21). Neither study found evidence of increased heart disease mortality risk among rescue/recovery workers (data not shown).

41 The NDI is a resource to help researchers find out if participants in their studies have died. NDI also can help researchers learn selected mortality information for study participants' deaths. NDI provides the public health and medical research community a single source for obtaining selected mortality data from death certificates for approved uses. *See* https://www.cdc.gov/nchs/ndi/.

In addition to the limitations inherent to mortality studies and external comparisons (i.e., external comparisons are particularly vulnerable to strong selection bias given large differences between the 9/11-exposed population and the general population reference group, and this selection bias would tend to underestimate IHD risks), there were weaknesses in the exposure-response analysis in the Jordan et al. [2011a] study. For example, the study had limited statistical power due to small numbers of deaths and few years of observation in the exposure categories. These limitations were the main reason for preferring the subsequent study that extended follow--up through 2014 [Jordan et al. 2018]. Furthermore, this study has other limitations that were also found in the Jordan et al. [2018] study. These include objective measures of 9/11 exposure and other risk factors that were lacking. Therefore, the potential for bias from measurement error could not be ruled out. In addition, both papers did not control for important risk factors for CVD mortality, including BMI, alcohol use, family history of heart disease, and PTSD status.

Because Jordan et al. [2018] is an update of Jordan et al. [2011a] and included more years of follow-up and a larger sample size, the Science Team considered Jordan et al. [2018] the more informative of the two studies. Moreover, Jordan et al. [2011a] was previously reviewed in the 2014 evaluation of **Petition 004** and found not to provide sufficient medical basis evidence for a decision on whether to add CVD to the List. Therefore, Jordan et al. [2011a] is not included in the Synthesis of Evidence for Categorization in Section IX. and is not further discussed in this evaluation.

b. Mani et al. [2013]

Mani et al. [2013] described a cross-sectional pilot study exploring the feasibility of using dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) to evaluate differences in atherosclerosis profiles in WTC responders exposed to high levels of WTC dust (arrived at "Ground Zero" during the morning of September 11, 2001, and were present during the collapse of one or both towers and the associated dust cloud) versus low levels (exposed on or after September 13, 2001). The study was a convenience sample of 31 law enforcement personnel (19 with self-reported high exposures; 12 with self-reported low exposures) recruited from the Law Enforcement Cardiovascular Screening Program (LECS) subset of the WTC Medical Monitoring and Treatment Program (MMTP) that preceded the WTC Health Program. The bilateral carotid arteries of all subjects were imaged with both multi-contrast MRI and DCE-MRI.[42] For DCE-MRI, the area under the curve (AUC) was calculated at 2 and 7 minutes after contrast agent

42 Multi-contrast MRI uses multiple different MRI sequences acquired at different time points to characterize plaque components based on inherent tissue properties, typically without contrast administration. DCE-MRI involves rapid, serial imaging over time (typically 5-10 minutes) after injection of a single bolus of contrast to measure signal intensity changes and quantify plaque neovascularization through pharmacokinetic modeling. *See* Saba et al. [2018].

injection. Ankle-brachial index (ABI) measures (left and right) were also obtained.[43]

Participants were primarily male (90%), mean age was 45 years, and those with high WTC dust exposure were more likely to be smokers (Current smokers: high WTC dust exposure = 5%; low WTC dust exposure = 0%. Former smokers: high WTC dust exposure = 16%; low WTC dust exposure = 8%). There were no significant differences in multi-contrast MRI results between exposure groups. None of the persons in either exposure group had complex carotid artery plaques that could be classified. However, compared with those with low WTC dust exposure, those with high WTC dust exposure had significantly higher DCE-MRI AUC uptake (increased neovascularization) (AUC at 7 minutes: 2.65 ± 0.63 for high WTC dust exposure vs. 1.88 ± 0.69 for lower WTC dust exposure, $p = 0.016$). The authors reported that fitting a multivariable regression model indicated that high WTC dust exposure, total cholesterol, and C-reactive protein levels were independent predictors of DCE-MRI AUC uptake (i.e., increased neovascularization); however, parameter estimates were not shown. Higher DCE-MRI AUC uptake may be a marker of increased progression of atherosclerosis. The authors also found that those with high WTC dust exposure had significantly lower mean right-sided ABI (high WTC dust exposure: ABI = 1.18 ± 0.08; low WTC dust exposure: ABI = 1.26 ± 0.08; $p = 0.017$). These measurements mean ABI measures were within the normal range. ABI measures on the left side were not associated with WTC dust exposure.

Mani et al. [2013] has several limitations. The sample size was small and not representative of all 9/11-exposed groups since the study included only law enforcement responders. The authors did not report when the study was conducted and the length of time between 9/11 exposure and the study could not be determined. Detailed ABI methodology was not reported (e.g., whether the highest or lowest low extremity systolic pressures were used). Variables used to adjust findings were not reported. As such, although those with high WTC dust exposure were more likely to be smokers, it was not clear if findings were adjusted for smoking. The Science Team concurred with the study authors that these results are preliminary.

Mani et al. [2013] was found not to have sufficient validity indicators to be considered a high-quality study. In addition, Mani et al. [2013] was previously reviewed in the 2016 evaluation of **Petition 012** and found not to provide sufficient evidence for a decision on whether to add CVD to the List. Therefore, Mani et al. [2013] is not included in the Synthesis of Evidence for Categorization in Section IX; however, it is included

43 The ABI is a ratio of systolic blood pressure in the ankle to systolic pressure in the brachial arteries (i.e., the artery in the upper arm), assessed with Doppler ultrasonography. At the ankle, the dorsalis pedis or posterior tibial systolic pressure is used, generally whichever is higher, because the higher pressure may reflect best leg perfusion. However, using the lower of the dorsalis pedis and posterior tibial artery pressures for ABI calculation is more sensitive for detecting peripheral artery disease. In those without atherosclerotic obstruction, systolic pressures increase with greater distance from the heart, yielding higher systolic pressures at the ankle than at the brachial artery. Therefore, a normal ABI ranges from more than 1.00 to 1.40. Borderline low ABI is 0.91-0.99, and abnormal ABI is defined as < 0.90. ABI is separately measured on the right and left sides of the body. *See* Aboyans et al. [2012].

in the discussion of atherosclerotic profiles under Consideration of Biological Plausibility, Coherence, and Analogy in Section IX.B.4.c.(7).

2. Newly Identified Studies Removed from Further Consideration

Four newly identified studies in the literature search were determined not to demonstrate sufficient validity indicators to be further evaluated as high-quality studies [Wanahita et al. 2010; Stein et al. 2016; Singh et al. 2023; Parvin et al. 2026].

Three of these four studies were excluded because they conducted external comparisons that were particularly vulnerable to strong selection bias given large differences between the 9/11-exposed population and the general population (the general population was the external reference population in all three studies) [Wanahita et al. 2010; Stein et al. 2016; Singh et al. 2023]. Selection bias would tend to cause underestimation of IHD risks. None of these three studies provided any evidence of an association between 9/11-exposures and IHD, likely because the general population was used as the reference population. In contrast, the high-quality studies summarized in Section VIII.C. used more appropriate reference populations (e.g., comparing those who experienced high levels of WTC exposures to those who experienced low levels of WTC exposures).[44]

The Science Team also excluded the study by Parvin et al. [2026] because it did not examine the association between 9/11-exposures and any CVD outcomes. Instead, it compared the mortality experience of responders enrolled in the WTC Health Program to responders who were not enrolled (i.e., WTCHR enrollees). Parvin et al. [2026] found lower mortality among WTC Health Program-enrolled responders. Each of these four excluded studies is briefly described below.

a. Wanahita et al. [2010]

Wanahita et al. [2010] conducted a cross-sectional study examining CAC scores among 2,064 police officers taking part in a voluntary health screening program for the New York Police Department (NYPD). A subset of these officers (n = 75) were 9/11 responders who were examined separately. All subjects underwent screening by electron beam computed tomography (EBCT) for quantification of CAC, which is sometimes used as a noninvasive diagnostic marker for CAD risk. The EBCT testing was conducted over a 2-year period and completion of screening appears to be 5 years post-September 11, 2001. A total CAC score was calculated by summing the scores for all calcified plaques found along the length of the individual coronary arteries. Participants with CAC scores > 100 were considered to be at moderate risk for adverse cardiovascular events. Participants with CAC scores > 400 and those with a score placing them at or above the 75th percentile for their age and sex were considered to be at high risk. Logistic regression analyses were conducted to examine predictors of CAC scores greater than 100. The distributions of CAC scores were compared with an age- and sex-matched general population.

44 *See Policy and Procedures*, Section IV.A.1., footnote 28 [NIOSH 2026a].

In the full cohort, the study found that increasing age, diabetes mellitus, and dyslipidemia were independent risk factors for higher total CAC scores. There was sparse information provided on WTC responders, who were mostly male (88%) and on average were aged 41 years at examination. Approximately 7% of male WTC responders exceeded a CAC score of 100, while 74% had a score of zero. All female responders had a CAC score of zero. Although data were not shown, the authors reported that there was no evidence of increased CAC scores in the WTC subgroup compared with age-matched non-9/11-exposed peers.

Overall, Wanahita et al. [2010] showed no evidence of 9/11 exposure-related excess CAD risk in this small group of relatively young WTC responders. However, given that coronary artery calcification is typically slow progressing, it is not clear whether any positive findings just 5 years after 9/11 exposure would be indicative of 9/11 exposure-related disease or a pre-existing condition. No information on the representativeness of the sample was provided. Additional limitations include the small sample size, lack of information on potential risk factors, and few results pertaining to WTC responders.

b. Stein et al. [2016]

Stein et al. [2016] examined mortality patterns in a longitudinal study of rescue and recovery workers (*n* = 30,947) in the GRC followed between 2002 and 2011 (164,563 person-years). The underlying cause of death was identified via linkage to the CDC NDI. Deaths were grouped according to the NIOSH LTAS [Robinson et al. 2006; Schubauer-Berigan et al. 2011], with Major 16 (heart diseases) indicating the outcome of interest. The SMRs were calculated, controlling for age, sex, race, and calendar period. A proportionate mortality ratio (PMR) was also calculated with similar standardization.

The cohort was mostly male (85.2%), non-Hispanic White (63.3%), with an average age on September 11, 2001, of 39 years. The SMR for Major 16 was significantly below expectation (SMR = 0.35; 95% CI: 0.27, 0.46; *n* = 59 deaths). The PMR also provided no evidence of increased risk for Major 16 (PMR = 0.81; 95% CI: 0.62, 1.05). Stein et al. [2016] had notable limitations, including use of cause of death information from death certificates by linkages to NDI and likely death undercounting, increased potential for selection bias from the use of external referent groups, incomplete information on risk factors, lack of IHD-specific analyses, and lack of internal analyses examining the exposure-response association among cohort members for IHD or CVD mortality. An additional limitation is the use of a PMR as a risk measure, which relies heavily on strong assumptions that may not be valid for this population [Miettinen and Wang 1981]. Furthermore, since the PMR is the proportion of cases classifiable to a particular cause in relation to the overall number of disease cases, it is affected by all other causes of death, which could lead to biased estimates of risk. Without additional information, the magnitude and direction of bias is not clear.

c. Singh et al. [2023]

Singh et al. [2023] conducted a longitudinal study examining mortality among 10,786 male WTC-exposed[45] firefighters from the FDNY and 8,813 male non-WTC-exposed firefighters from other urban fire departments who were employed on September 11, 2001. Follow-up began on September 11, 2001, and continued through 2016, resulting in 163,583 person-years. Death information was obtained from the NDI. The underlying causes of death were grouped according to the NIOSH LTAS [Robinson et al. 2006; Schubauer-Berigan et al. 2011] with Major 16 (heart diseases) the outcome of interest. SMRs stratified by exposure group were estimated using U.S. national mortality rates as referent. Rate ratios (RRs) comparing FDNY firefighters to the non-exposed firefighter referent group were calculated using Poisson regression controlling for age on September 11, 2001, and race/ethnicity. An internal analysis examining the exposure-response association among FDNY firefighters that was limited to all-cause mortality was considered to provide limited information on CVD risk. Internal analyses examining the exposure-response association among FDNY firefighters for IHD or CVD mortality were not reported.

At enrollment, the FDNY cohort was mostly non-Hispanic White (93.8%) and never smokers (66.4%). The average age on September 11, 2001, was 40.4 years. Among FDNY firefighters, nearly all (99.8%) had at least one WTC Health Program visit during the study period, with a median of 10 visits per person. For FDNY firefighters, the SMR for heart disease was 0.27 (95% CI: 0.20, 0.35; n = 52) compared with 0.51 (95% CI: 0.42, 0.60; n = 120) among the non-WTC-exposed firefighters with both groups compared with the general population. There was less heart disease mortality among FDNY firefighters compared with non-WTC-exposed firefighters (RR = 0.61; 95% CI: 0.55, 0.67).

Overall, Singh et al. [2023] provided no evidence of increased heart disease risk among FDNY firefighters compared with the general population or with an external group of Philadelphia, San Francisco, and Chicago career firefighters. Methods used were appropriate for the available data. A unique strength of the study is its use of a similarly employed control group in RR analyses. Important limitations included the use of cause of death information from death certificates by linkages to NDI, increased potential for selection bias from the use of external referent groups, incomplete information on important risk factors (e.g., smoking, diet, alcohol consumption, and healthcare access) that could contribute to differences in mortality rates, and the lack of IHD-specific analyses, including exposure-response modeling. Regarding the latter, Singh et al. [2023] examined the exposure-response association between categories of arrival time and all-cause mortality among FDNY firefighters in a Poisson regression model adjusting for age, race/ethnicity, and smoking status. That model provided no evidence of increasing risk with exposure. Similar analyses restricted to CVD outcomes were not reported.

45 This evaluation adopts the terminology employed by the authors in their manuscripts. Therefore, the terms "9/11-exposure" and "WTC-exposure" are used interchangeably throughout the document.

d. Parvin et al. [2026]

Parvin et al. [2026] conducted a longitudinal study that compared mortality risk between WTC Health Program members and non-members. The study did not assess the association between 9/11 exposure and mortality. The study used a subset (*n* = 28,430) from the established combined cohort of 9/11 responders (*n* = 69,100) that includes responders from FDNY, the GRC, and the WTCHR. The subset consists of only those responders who were submitted by the WTCHR to the combined cohort, since all members of this subset had WTCHR-collected comorbidity data. The use of this subset helped to ensure uniformity of the captured comorbidity data. These WTCHR members were stratified into two groups: FDNY/GRC members who had enrolled in the WTC Health Program by December 31, 2016 (i.e., WTCHR members who were also WTC Health Program members, *n* = 9,467) vs. non-FDNY/non-GRC members (i.e., WTCHR members who never enrolled in the Program or enrolled after December 31, 2016, *n* = 18,963). The studied sample excluded those who were < 18 years on 9/11, those who died or turned 85 years or older within the first year of enrollment, those who had unknown smoking status, unknown race/ethnicity, or were incapacitated and required a proxy to respond to the WTCHR questionnaires. Among the 9,467 FDNY/GRC members, 4,315 (46%) initially enrolled in the WTCHR before joining FDNY or GRC.

Vital status was ascertained through December 31, 2020. Data were collected on several comorbidities in the WTCHR's Waves 1 through 4 (which were conducted between 2003 and 2016). The comorbidities included aerodigestive disorders, mental health conditions, cancer, and cardiovascular diseases based on self-reported diagnosis by a healthcare professional. Smoking status and baseline demographics (e.g., sex, race/ethnicity, and 9/11 exposure) were obtained from the cohort in which the participant first enrolled (FDNY, GRC, or WTCHR). Cox proportional hazards regression was used to estimate HRs for the association between WTC Health Program membership status and all-cause mortality. For analysis of cause-specific mortality, they used cause-specific hazard regression models to account for competing risks.

Compared to non-members, WTC Health Program members were more likely to be male, in the age groups of 30 to 39 and 40 to 49 on September 11, 2001 (they were less likely to be 18 to 29 on September 11, 2001), non-Hispanic White, never smokers, and to have arrived earlier at the WTC site and performed tasks on the pile. In addition, WTC Health Program members had a statistically significantly higher proportion of post-9/11 comorbidities compared to non-WTC Health Program members. However, non-members had significantly higher pre-9/11 diagnoses of certain conditions, including asthma, depression, and cardiovascular conditions. Male WTC Health Program members had a significantly lower risk of all-cause mortality compared to male non-members after adjusting for demographics, smoking status, and

9/11 exposure (Model 2: adjusted hazard ratio (aHR) = 0.85; 95% CI: 0.75, 0.96), but not among women (Model 2: aHR = 1.16; 95% CI: 0.80, 1.68). WTC Health Program members had a lower risk of smoking-related mortality compared to non-members, after adjusting for demographics, smoking status, 9/11 exposure and comorbidities (aHR = 0.83; 95% CI: 0.69, 0.99). Risk was not modified by gender. The findings for heart-related mortality were mixed. WTC Health Program membership was associated with reduced heart-related mortality before adjusting for comorbidities (aHR = 0.76; 95% CI: 0.58, 0.99), but not after adjusting for comorbidities (aHR = 0.87; 95% CI: 0.67, 1.13). WTC Health Program membership was also not associated with cancer-specific mortality.

When determining all-cause and smoking-related mortality risk, it appears the authors did not adjust their HRs by using more recent smoking status. Instead, they obtained smoking status at first enrollment only, which was reported to be 16% among WTC Health Program members and 18% among non-WTC Health Program members. Smoking rates dropped dramatically among WTC Health Program members and on December 31, 2024, were 4.5% at FDNY and 6.3% at GRC (internal data). It is not known if non-WTC Health Program members were similarly encouraged/supported to quit smoking. The sharp smoking reductions among WTC Health Program members may explain the lower risk of smoking-related mortality among WTC Health Program members. The authors also speculated that better healthcare access among WTC Health Program members may have contributed to all-cause and smoking-related mortality risks. Although Program membership was not associated with reduced cancer-specific mortality, this finding may have been observed because reduced smoking rates may not have had time to impact cancer rates, given long cancer latencies.

The study did not assess the association between 9/11 exposure and mortality, instead, it compared mortality risk between WTC Health Program members versus non-members. WTC Health Program membership was not associated with reduced heart-related mortality after adjusting for comorbidities. The authors attributed the lack of an effect on heart disease risk to it not being covered by the WTC Health Program, potentially limiting the Program's ability to influence cardiovascular outcomes. However, more complete ascertainment of comorbidities among WTC Health Program members compared to non-members may have biased the aHR towards the null. It is reasonable to assume that WTC Health Program members have more complete comorbidity ascertainment because all the adjusted comorbidities except CVD are covered by the Program. Furthermore, many CVD diagnostics are covered by the Program to assist in detecting WTC-related lung disease (i.e., many heart and lung diseases share the same symptoms, therefore, to diagnose lung disease, clinicians need to rule out heart disease). Consequently, CVD is likely to have more complete ascertainment among Program members.

C. Studies Considered High-Quality

The Science Team determined that 14 of the 20 identified studies had sufficient validity indicators to be considered high-quality studies for this evaluation [Brackbill et al. 2006; Jordan et al. 2011b; Jordan et al. 2013; Brackbill et al. 2014; Alper et al. 2017; Jordan et al. 2018; Remch et al. 2018; Cohen et al. 2019; Colbeth et al. 2020; Alper et al. 2021; Sloan et al. 2021; Li et al. 2023; Mueller et al. 2024; Krasnov et al. 2025]. Eleven of the 14 high-quality studies are newly identified studies published between April 2006 and May 2026; three were previously reviewed in the evaluation of **Petition 004** [Jordan et al. 2011b; Jordan et al. 2013; Brackbill et al. 2014]. These three studies were reexamined for this evaluation and found by the Science Team to meet the standard for high-quality studies under the current version of the *Policy and Procedures* [NIOSH 2026a].[46]

1. Previously Reviewed High-Quality Studies

Three previously reviewed studies were found by the Science Team to have sufficient validity indicators to be high-quality studies [Jordan et al. 2011b; Jordan et al. 2013; Brackbill et al. 2014]. These three studies were previously evaluated as part of **Petition 004** and although that evaluation ultimately determined that the evidence available in those studies alone did not have the potential to provide a basis for a decision on whether to add CVD to the List, the studies were nevertheless considered high-quality for this evaluation. Each of these three studies are summarized below.

a. Jordan et al. [2011b]

Jordan et al. [2011b] conducted a longitudinal study of heart disease risk using information from the Wave 2 survey of WTCHR enrollees conducted between November 2006 and January 2008. Follow-up averaged 2.9 years. Eligible participants included 39,324 WTCHR enrollees who were aged ≥ 18 years on 9/11 and completed the Wave 2 survey. "Heart disease" was defined as self-reported angina, heart attack, or any other heart condition first diagnosed by a physician between WTCHR enrollment and the Wave 2 survey. Probable PTSD was determined using the 9/11-specific PTSD checklist (PCL-S), which is a validated event-scaled instrument inquiring information on 17 self-reported symptoms of PTSD [Blanchard et al. 1996; Ventureyra et al. 2002]. Probable PTSD was defined as a PCL-S score ≥ 44 out of a possible 85. PCL-S scores were stratified into six mutually exclusive categories: 17 to 19 (20.9% of participants); 20 to 25 (28.6%); 26 to 34 (23.7%); 35 to 43 (13.3%); 44 to 49 (5.1%); and ≥ 50 (8.4%) years of age.

Injury was defined as reporting any of the following on September 11, 2001: cut, abrasion, or puncture wound; eye injury or irritation; sprain or strain; burn; broken or dislocated bone; and concussion or head injury. Data on sociodemographic factors, smoking, and physician-

46 The original version of the *Policy and Procedures* was in effect at the time the evaluation of **Petition 004** was published [NIOSH 2014]. The 2014 version of the *Policy and Procedures* did not make mention of high-quality studies. However, under the current *Policy and Procedures* [NIOSH 2026a], these three studies have sufficient validity indicators to be considered high-quality studies eligible for further evaluation.

diagnosed hypertension and diabetes mellitus were obtained from the Wave 1 (2003–2004) survey questionnaire. Exposure to the 9/11 dust cloud was categorized as either intense, some, or none based on questionnaire responses. Exposure potential for rescue/recovery workers was also assessed in ordinal categories of arrival time on the pile. For lower Manhattan residents and area workers, exposure potential was assessed as three ordinal categories based on the extent of damage to the home or workplace. HRs and associated 95% CIs were estimated using proportional hazards regression adjusting for age, race/ethnicity, education, marital status, smoking, history of hypertension, and history of diabetes mellitus. Multivariable analyses were stratified by sex and by enrollee type (i.e., all enrollees, rescue/recovery workers, or area residents).

Participants were primarily White persons, aged 25 to 44 years on September 11, 2001, and highly educated. Nearly one-third reported being heavily exposed to the 9/11 dust cloud. There were 1,162 enrollees (2.9%) who reported heart disease. Among reports of a single outcome (n = 1,101), 26% comprised either angina or MI and 64.2% reported other heart disease (exact nature was unknown). Compared with those with no dust cloud exposure, women with intense dust cloud exposure had a significantly increased risk of heart disease; this increased risk was not observed in men with intense dust cloud exposure. The increased risk in women persisted but was attenuated (and no longer statistically significant) when including probable PTSD in the model, which appeared to be the stronger risk factor. *See* **Table 7**.

There was also evidence of an association between self-reported injury on September 11, 2001, and heart disease in both men and women. As with dust cloud exposure, risk from 9/11 injury persisted but was attenuated when modeled jointly with probable PTSD (women: HR = 1.35; 95% CI: 1.09, 1.68; men: HR = 1.29; 95% CI: 1.12, 1.50). Again, probable PTSD appeared to be the stronger risk factor. When the six strata of PCL-S scores were assessed, there was a monotonic increase in heart disease risk with increasing PCL-S score category; however, the results of a formal statistical trend test were not reported.

In analysis by enrollee type, men who worked on the pile on September 11, 2001, had higher heart disease risk compared with those who arrived on September 18, 2001, or later. Women who worked on the pile on September 11, 2001, also had increased risk, although the confidence interval was wide. *See* **Table 7**. Among lower Manhattan area residents, the association between heavy dust in the home and self-reported heart disease was significant among males but not females. Similarly, encountering a heavy layer of dust upon return to a lower Manhattan area workplace was associated with an elevated heart disease risk among men but not women.

Overall, the study provided evidence of modest associations between self-reported heart disease (including IHD) and 9/11 exposures (i.e.,

9/11 injury and dust cloud exposure). The associations appeared in both sexes and among residents and workers, although inconsistencies were observed. A strength of the study was control for probable PTSD at enrollment in multivariable models examining the exposure-response association between 9/11 exposures and heart disease. These models showed that probable PTSD had a marked effect on the association between WTC dust and heart disease that should be accounted for in risk estimates.

The study by Jordan et al. [2011b] has several limitations. First, the health condition of interest comprised a large group of conditions and symptoms grouped as heart disease. Although included in the outcome definition, analyses were not specific to IHD; therefore, causal inference for IHD is uncertain. Still, the authors reported that they found similar associations between heart disease and both 9/11-related exposures and probable PTSD when the outcome was restricted to incident angina and/or heart attack (data not shown). This claim was later confirmed based on review of the unpublished data provided to the Science Team upon request; therefore, the potential for strong bias from the composite outcome in this study appears small.[47] Second, objective measures of the outcome and 9/11 exposures were not available; therefore, the potential for bias from ascertainment errors and exposure misclassification cannot be ruled out. The authors acknowledged the need to replicate findings using objectively measured outcomes; however, an assessment of the potential effects on risk estimates from ascertainment error and exposure misclassification was not conducted. Third, although the authors adjusted for several known risk factors, information on other risk factors (e.g., dyslipidemia, family history, and depression) was not available; therefore, the potential for residual confounding cannot be ruled out. Lastly, the observation period began between 2003 and 2004 and averaged only 3 years, which substantially limited study power.

b. Jordan et al. [2013]

Jordan et al. [2013] conducted a longitudinal study of CVD hospitalizations in a cohort of 46,346 adult WTCHR enrollees residing in New York State to address questions raised in the previous study by Jordan et al. [2011b]. Follow-up began at WTCHR enrollment (2003–2004) and ended at the earliest date of heart disease hospitalization, death, or December 31, 2010. Ascertainment of CVD hospitalization data was made by linking participants to the New York State hospital discharge reporting system that is managed by the Statewide Planning and Research Cooperative System (SPARCS). Hospitalizations were categorized based on codes from ICD, 9th Revision (ICD-9) for the principal discharge diagnosis. Heart disease comprised hypertension (ICD-9 401–405), acute (ICD-9 410, 411) and chronic CAD (ICD-9 412–414), dysrhythmia (ICD-9 427), and congestive

47 Data provided in personal communication from study co-author, James Cone, MD, MPH, on August 31, 2021.

heart failure (ICD-9 428). The authors also studied a subset of heart disease hospitalization restricted to CAD. Probable PTSD status (yes/no) was determined at enrollment using the 17-item 9/11-specific PTSD checklist (PCL-S) with score ≥ 44 [Ventureyra et al. 2002; Blanchard et al. 2006].

Exposures were defined based on combinations of responses in WTCHR Wave questionnaires. Injury was defined as self-report of eye injury or irritation; cut, abrasion, or puncture wound; sprain or strain; burn; broken or dislocated bone; or concussion or head injury. Dust cloud exposure was defined as being in the dust cloud on September 11, 2001 (yes/no). For those with 9/11 dust cloud exposure, intensity was defined by ordinal categories (high, intermediate, low) derived from rescue/recovery workers' responses on arrival time, location, type, and duration of work. For community members, the exposure categories were based on the number of injuries experienced on September 11, 2001, and whether home evacuation occurred. Analyses were conducted using proportional hazards regression, adjusting for age, race/ethnicity, smoking, education, marital status, and self-reported physician-diagnosed hypertension and diabetes mellitus. Analyses were stratified by sex and by enrollee type. Primary predictors (i.e., PTSD, injury on September 11, 2001, and WTC dust exposure) were examined separately.

The cohort comprised slightly more males (59.7%) than females and more non-Hispanic White persons (59.7%) compared to other races; nearly half were college educated (48.1%). There were 1,151 heart disease hospitalizations during 302,742 person-years of observation. Of these events, about 60% were CAD hospitalizations. Among males with complete information (n = 27,511), rescue/recovery workers assigned high exposure had significantly increased heart disease risk compared with those with low exposure (HR = 1.82; 95% CI: 1.06, 3.13); there was evidence of an exposure-response trend across exposure categories, although the trend was not statistically significant. *See* **Table 8**.

Elevated risks were also observed among women (*n* = 18,551), but estimates were less precise given smaller numbers. Heart disease risk was modestly increased in women with probable PTSD (HR = 1.32; 95% CI: 1.01, 1.71) compared with those without probable PTSD. In contrast, heart disease in men with probable PTSD was not significantly increased (HR = 1.16; 95% CI: 0.97, 1.40). There was no evidence of an association between 9/11 dust cloud exposure or injury, and hospitalizations for either CAD or heart disease. Compared with main analyses, the magnitude of the association was similar in comparable analyses restricted to CAD in males; however, estimates were not statistically significant.

An important strength of the study is the use of an objective measure for outcome ascertainment. Jordan et al. [2013] noted that the lack of an association between heart disease and 9/11 injury was inconsistent

with the previous study of this cohort that used self-reported outcomes [Jordan et al. 2011b]. The authors suggested that differences in outcome ascertainment methods between the previous study using a subjective measure derived from self-report and the current study using an objective measure derived from hospital discharge records may explain the inconsistency. For example, the inconsistency between studies may be due to a lack of statistical power from fewer cases using discharge records, a stronger association between 9/11 injuries and milder self-reported cases compared with hospitalization cases, or an upward bias from overreporting by self-report.

There are notable limitations in Jordan et al. [2013]. First, as in all selected studies, objective measures of exposure were not available. The data obtained from WTCHR enrollees were self-reported. Second, under ascertainment of hospitalizations is likely because the discharge reporting system did not include federal or psychiatric hospitals, nor hospitalizations that occurred outside of New York State. The directionality of potential bias from under ascertainment has not been investigated, i.e., it is not known whether ascertainment is differential with respect to exposure status. Third, the authors did not adjust for all important risk factors, such as family history and dyslipidemia; therefore, residual confounding cannot be ruled out. Fourth, hypertension was included in heart disease hospitalizations and is a major contributor to total CVD, as described by the AHA [Palaniappan et al. 2026]. In 2026, the AHA estimated that 125.9 million adults ≥ 20 years of age have hypertension [Palaniappan et al. 2026]. Hypertension is also described as a major risk factor for other CVD outcomes, such as MI; therefore, there is uncertainty in the representation of the causal pathway. Although the number of hypertension events was not reported, hospitalization for hypertension is presumed unlikely; therefore, strong bias in risk estimates from including hypertension in the outcome appears unlikely. Lastly, models examining the effects of 9/11 dust and injuries did not consider the effects from PTSD. Probable PTSD was associated with heart disease in this study, suggesting its importance as a contributing factor; however, PTSD was not accounted for in models examining the relationship between 9/11 exposure and CVD outcomes. Based on this limitation, the authors acknowledged that the study could not determine whether "… PTSD was part of the causal pathway between 9/11-related environmental exposures and CVD hospitalizations or whether PTSD and rescue/recovery-related exposures were independent risk factors."

c. Brackbill et al. [2014]

Brackbill et al. [2014] examined the associations between injuries sustained on September 11, 2001, probable PTSD, dust/debris cloud exposure on 9/11, and self-reported heart disease in WTCHR enrollees (*n* = 14,087). Eligibility was restricted to enrollees completing the WTCHR Wave 1 (2003–2004) and Wave 2 (2006–2008) surveys who were aged < 64 years on 9/11 and present south of Chambers Street

that morning. Using the Wave 2 questionnaire on an array of health conditions, persons reporting a physical or mental health condition diagnosis before 2002 were excluded. Survey data obtained during Waves 1 and 2 were used to define exposure and outcome. Heart disease was defined as self-reported diagnosis of angina, heart attack, or other heart condition. Self-reported exposure to the dust/debris cloud was dichotomously classified as being intense or some/none. Intense exposure was defined as being caught in the dust/debris cloud on September 11, 2001, and having at least one the following experiences: "being unable to see more than a couple of feet; having trouble walking or finding the way; finding shelter, such as under a car; being covered head to toe with dust; or not being able to hear." Probable PTSD was assessed at Wave 1 as a score ≥ 44 on the "17-item 9/11-specific PTSD checklist," which is presumed to be identical to that previously described for WTCHR enrollees (i.e., PCL-S). Logistic regression was used to calculate odds ratios (ORs) and associated 95% CIs adjusted for age, enrollee type, race/ethnicity, sex, education level, history of hypertension, and smoking status.

There were 1,980 (14%) participants reporting at least one type of injury on September 11, 2001. Those reporting any injury were more likely to be male (69% vs. 59%), a rescue or recovery worker (49% vs. 21%), experienced intense dust cloud exposure (69% vs. 38%), and positive for probable PTSD at Wave 1 (22% vs. 10%) when compared with those without injury. Among persons without probable PTSD, the odds of self-reported heart disease were significantly increased among those with one injury compared with those with no injuries (OR = 1.6; 95% CI: 1.2, 2.3). Similar increases in odds were evident for persons with two or more injuries. The effect of injury was stronger in the group with probable PTSD, suggesting that PTSD has important influence on the association between injury and heart disease. The odds of self-reported heart disease were modestly increased among WTCHR enrollees with intense dust cloud exposure compared with those without intense exposure (OR = 1.3; 95% CI: 1.05, 1.6). *See* **Table 9**. However, it is not clear whether the effects of PTSD and injury, either separately or in combination, were considered in the estimate.

There are notable limitations in Brackbill et al. [2014]. First, the cross-sectional design provided limited information on the temporality of the associations examined. Second, objective measures of the outcome and exposure were not available; therefore, the potential for bias from errors in ascertainment and exposure misclassification cannot be ruled out. Third, information on potential risk factors was incomplete; therefore, the potential for residual confounding cannot be ruled out. Fourth, the findings suggested a potentially complex interaction between heart disease, PTSD, dust cloud exposure, and injury; however, data were inadequate to fully elucidate this relationship. The methods on model specification were not clear; therefore, it could not be determined whether the estimate for the association between dust cloud exposure and self-reported heart disease controlled for

the effects of either PTSD or injury. Fifth, risk estimates stratified by sex or type of enrollee (e.g., rescue/recovery worker vs. not) were not available. Sixth, information on "other heart conditions" included in the analysis was not available. Finally, information on injury severity was not available.

2. Newly Identified High-Quality Studies

The Science Team determined that 11 of the 20 studies newly identified in the literature search [Brackbill et al. 2006; Alper et al. 2017; Jordan et al. 2018; Remch et al. 2018; Cohen et al. 2019; Colbeth et al. 2020; Alper et al. 2021; Sloan et al. 2021; Li et al. 2023; Mueller et al. 2024; Krasnov et al. 2025] had sufficient validity indicators to meet the standard for high-quality studies.[48] These 11 studies were not included in the evaluations of **Petition 004** or **Petition 012**. *See* **Table 5**. Each of these newly identified high-quality studies is summarized below.

a. Brackbill et al. [2006]

Brackbill et al. [2006] conducted cross-sectional surveillance of self-reported cardiovascular health conditions among WTCHR enrollees (n = 8,418) aged ≥ 18 years at the time of the Wave 1 survey (2003 to 2004). These WTCHR participants were office workers and visitors present in any one of 38 collapsed or damaged buildings during the time between the first tower (WTC-2) impact and noon on 9/11, excluding those who were involved in rescue and recovery. Three proxy[49] exposure metrics were used separately to characterize 9/11 exposures: (1) being caught in the dust and debris cloud (yes/no); (2) the time of evacuation (before/after first tower collapsed); and (3) type of occupied building (collapsed/damaged). Cardiovascular health conditions were determined by self-report of a healthcare professional-diagnosed coronary heart disease, angina, heart attack, or stroke (among other conditions). The Science Team considered self-reported "coronary heart disease" to represent CAD, and "heart attack" to represent MI. Findings on stroke were not considered in this evaluation. Multiple logistic regression was used to calculate ORs and associated 95% CIs. Models for self-reported angina adjusted for age, race/ethnicity, sex, level of serious psychological distress, and smoking status, except for the model examining time of evacuation as the dependent variable. That model adjusted for recruitment mode (i.e., from a list or self-identified) and sex only because the sample size was too small for stratification by all adjustment variables. Similarly, all models for self-reported CAD and heart attack adjusted for recruitment mode and sex.

Of an estimated 62,092 building occupants, 8,418 adult WTCHR enrollees were recruited for study. Of these, 56% resided in NYC on September 11, 2001, 27% were from New Jersey, and 14% were from

48 *See Policy and Procedures*, Section III.C. [NIOSH 2026a].
49 A proxy variable (measurement) is one that is used in place of a variable that cannot be directly measured. *See* Nilsson et al. [2023].

New York State outside of NYC. About 61% of study participants occupied collapsed buildings before evacuation. The study group was mostly male (54%), and most participants (56%) were aged 25 to 44 years on September 11, 2001. Most participants (59.0%) were never-smokers. About 62% of participants were caught in the dust and debris cloud, and about 64% experienced three or more events that could potentially cause psychological trauma. The odds of reporting a heart attack (OR = 1.7; 95% CI: 0.8, 3.9) or CAD (OR = 1.6; 95% CI: 0.8, 3.3) increased among persons in the dust cloud compared with those without dust cloud exposure; however, confidence intervals were wide. *See* **Table 10**. There was no evidence of association for angina analyses. Likewise, analyses of all outcomes using alternative exposure indices provided little evidence of association.

The study by Brackbill et al. [2006] has notable weaknesses. First, most participants were self-identified and represent a small fraction (16.7%) of the exposed population. Biases from limitations in recruitment were not examined. Second, exposure and outcome data were self-reported without follow-up confirmation. Exposure was based on a single yes/no question regarding presence in the dust and debris cloud, but with no information on how the respondent interpreted being in the dust cloud. The survey was conducted 2 to 3 years after September 11, 2001, which may have affected recall. Reports on the validity of self-reported information on exposure and outcome within the 9/11-exposed population were not available. Third, the study is cross-sectional. Other than the self-reported condition and whether the diagnosis was pre- or post-September 11, 2001, there was no information on severity onset, or persistence of conditions. Fourth, information on other exposures (before and after 9/11), risk factors (e.g., smoking, diet, exercise, family history), or comorbid conditions (e.g., obesity, hypertension) that may have contributed to CVD risk was not available or was not considered. For example, models examining CAD and MI did not control for age, race/ethnicity, and level of serious psychological distress (among other potential risk factors) due to small numbers. Fifth, inclusion of model covariates were limited because of the small sample size for most separate IHD-related health conditions. Lastly, the observed effect sizes related to IHD were modest, and measures were largely imprecise given relatively few observed cases. Estimates indicating small effects are most vulnerable to random and systematic errors.

b. Alper et al. [2017]

Alper et al. [2017] conducted a longitudinal study of select health outcomes, including CVD outcomes, among WTCHR enrollees aged ≤ 64 years who were healthy before 2002 and who were believed to be acutely, but not chronically exposed. Acute exposure was determined by self-report of presence in the “acute exposure zone” near the disaster site (i.e., Manhattan, south of Chambers Street) on September 11, 2001, but not afterwards. Rescue/recovery workers who

worked at the WTC site after the first day of the disaster (*n* = 2,917) and residents who did not evacuate or evacuated but returned to their homes before December 31, 2001 (*n* = 1,508) were excluded. Eligible participants were further restricted to persons completing WTCHR Waves 1 to 3 surveys. The study group also excluded persons reporting a diagnosis of heart attack, angina, other heart conditions, asthma, chronic bronchitis, emphysema, reactive airway disease, other lung conditions, stroke, diabetes mellitus, sarcoidosis, or cancer prior to 2002 (*n* = 10,796). The resulting study group included 8,701 persons (7,503 area workers, 249 rescue/recovery workers, 131 residents, and 818 passersby) considered healthy at the beginning of the study. Exposure indices included number of injuries (in four ordinal categories) and dust/debris cloud exposure (yes/no). The CVD outcome was self-reported angina or MI (angina/MI) that was diagnosed by a health professional and reported by the enrollee in Waves 2 or 3. As in previous WTCHR studies, probable PTSD was determined from a 17-item 9/11-specific PTSD checklist (PCL-S) score ≥ 44 assessed at Wave 1. Analyses were conducted using proportional hazards regression adjusting for sex, age, race/ethnicity, education, BMI, smoking (current, former, never), rescue/recovery worker status (yes/no), having probable PTSD at Wave 1 (yes/no), hypertension (yes/no), and study recruitment source.

Participants comprised slightly more males (51%) than females, were aged 25–44 on September 11, 2001, (56%), non-Hispanic White (69%), and college-educated (67%). About 14% of participants reported probable PTSD. There were 92 incident cases of angina/MI reported during the follow-up period. The authors found that angina/MI was significantly associated with the number of 9/11 injuries with a monotonic exposure-response across exposure categories (p for trend < 0.0001). *See* **Table 11**.

These results were consistent with findings in a previous report of cardiovascular outcomes 5 to 6 years after September 11, 2001 [Brackbill et al. 2014]. The angina/MI risks from 9/11 injury appeared greatest in area workers who returned to workplaces south of Chambers Street between September 12 and December 31, 2001, exhibiting a significant exposure-response association ($p = 0.0003$). There was no association between self-reported angina/MI and intense dust cloud exposure or probable PTSD among all participants.

Notable strengths of Alper et al. [2017] included control for probable PTSD in exposure-response analyses and exclusion of preexisting chronic health conditions. Interestingly, analyses suggested an independent association between injury and angina/MI, with no evidence of association with probable PTSD. The lack of evidence of an association between PTSD and angina/MI is contrary to the positive association reported in a previous WTCHR study [Jordan et al. 2011b]. Alper et al. [2017] posited this difference was attributable to excluding persons reporting a chronic physical health condition prior to 2002; therefore, suggesting that the previously observed positive association

may reflect the effects of chronic health conditions existing prior to 9/11 exposure. This explanation was supported, in part, by findings from *post hoc* analyses conducted by Alper et al. [2017].

Alper et al. [2017] also had notable limitations. First, the study used a highly restricted sample of the WTCHR population who completed Waves 1, 2, and 3. The study population comprised only 12.8% of all adult enrollees; therefore, questions on representativeness remain. Loss to follow-up between WTCHR Wave surveys was large, resulting in 63% retention of original sample; therefore, bias through attrition is an important concern. Second, there was a lack of information on injury severity, body location, whether the injury was treated in an emergency department or hospital, or the circumstances of the injury. As in other analyses, objective measures of the outcome and exposure were not available; therefore, the potential for biases from errors in ascertainment and exposure assignments cannot be ruled out. Third, complete information on risk factors was not available; therefore, the potential for residual confounding cannot be ruled out. Finally, it is not clear whether the model, as specified, adequately controlled for the joint effects of PTSD and WTC dust exposure on IHD. Thus, without a clear understanding of the causal pathway a potential bias in risk estimates from model misspecification cannot be ruled out [Schisterman et al. 2009; NIOSH 2020].

c. Jordan et al. [2018]

Jordan et al. [2018] expanded and extended follow-up of a previous longitudinal mortality study, Jordan et al. 2011a, adding 5 years through 2014. The study population comprised WTCHR enrollees (*n* = 69,923) categorized as rescue/recovery workers and lower Manhattan area community members. Information on the underlying cause of death was obtained by linkage with the NDI. CVD deaths were classified according to the NIOSH LTAS Major 16 [Robinson et al. 2006; Schubauer-Berigan et al. 2011].

IHD deaths were similarly classified according to Minor 55. As with the previous mortality study [Jordan et al. 2011a], exposure to 9/11 agents was categorized as high, intermediate, or low. Separate definitions of the levels were made for rescue/recovery workers and community members. Internal analyses were conducted using proportional hazards regression adjusting for age, sex, race/ethnicity, education, and smoking. Analyses also adjusted for self-reported clinical diagnosis of diabetes mellitus and/or heart disease prior to September 11, 2001. Rescue/recovery participants were analyzed separately from community members.

There were 29,280 rescue/recovery workers and 39,643 community members in the full study group (*n* = 68,923), which was majority male (60%) and non-Hispanic White (63%). There were 596 CVD deaths, of which 450 were classified as IHD deaths. The main results are shown in **Table 12**.

Of the full study group, there were 28,303 rescue/recovery workers (3.3% excluded) and 36,533 community members (7.8% excluded) with sufficient data available for internal analysis. Risk estimates for both high and intermediate exposure groups were modestly increased compared with the low exposure group, although estimates were not statistically significant. Risk appeared greater among rescue/recovery workers than among community members, although exposure definitions differed by enrollee type. Compared with 9/11 exposures, estimates of excess heart disease mortality were much greater among persons with diabetes mellitus (HR = 2.67; 95% CI: 1.74, 4.09) and heart disease diagnosed prior to September 11, 2001 (HR = 2.68; 95% CI: 1.81, 3.97), indicating a strong potential for confounding (without control). Including these variables as covariate control is a notable study strength. However, information from investigating the potential confounding effect on exposure-response estimates was not provided. Comparing estimates with and without covariate control could help elucidate reasons for differences between these findings in Jordan et al. [2018] and those reported earlier by Jordan et al. [2011a].

There were notable limitations in Jordan et al. [2018]. Heart disease comprises a large group of heterogenous conditions and symptoms that may not reflect IHD risk. Objective measures of 9/11 exposure and other risk factors were not available; therefore, the potential for bias from exposure misclassification cannot be ruled out. The authors did not control for PTSD and other risk factors for CVD mortality, including BMI, alcohol use, and family history of heart disease; therefore, residual confounding cannot be ruled out. Lastly, it is noted that mortality as an endpoint for examining CVD risk may be affected by survival, which has varied over time due to differences in available treatment and healthcare access [Mensah et al. 2017].

d. Remch et al. [2018]

Remch et al. [2018] conducted a prospective longitudinal study examining 5,971 (83% male) responders who were recruited from two WTC Health Program Clinical Centers of Excellence between January 2012 and June 2013 and followed at least once per year through 2016 to determine whether probable PTSD and exposure to 9/11 agents are risk factors for a composite outcome of MI and stroke. Outcomes included “recurrent” events, which were defined as an event occurring in persons with a previous event prior to observation but after 2001. Findings restricted to MI were limited to examining its association with probable PTSD. The main analyses used outcomes obtained from self-report; however, medical chart review was conducted for about 60% of the study group. Additional analyses restricted to New York State residents (*n* = 5,454) were conducted using outcome information from linkage to SPARCS. Multiple indices of 9/11 exposure were derived from information in self-administered questionnaires. Analyses were conducted using proportional hazards regression adjusting for sex, age, hypertension, total cholesterol, BMI, tobacco use, and respirator

use. Models examining the association between 9/11 exposure and MI/stroke also adjusted for probable PTSD as an independent risk factor. PTSD was assessed using the PTSD checklist for civilians (PCL-C) [Ruggiero et al. 2003], that included a preamble for relating answers to participation in the WTC cleanup. PTSD was defined either dichotomously (PCL-C score ≥ 44) or by treating PCL-C scores as a continuous variable.

Participants were mostly male (82.7%), non-Hispanic White (54.1%), and college-educated (74.6%). The prevalence of probable PTSD was 19.9% in men and 25.9% in women. There were 70 MIs during the observation period, of which 20 were recurrent. There were 53 strokes (15 recurrent). There was evidence of differential misclassification of MI by PTSD status. The confirmation fraction of self-reported (interview-based) MI diagnosis by medical chart review was smaller for the probable PTSD group (47%) than for non-PTSD cases (74%). When restricted to persons linked to SPARCS, all incident MI and strokes were present in the hospital discharge system; however, 49 hospital discharge events were not found in active follow-up (i.e., not self-reported). The distribution of missing discharge events by WTC dust exposure was not reported. The main results regarding 9/11 exposures are shown in **Table 13**.

Findings restricted to MI were not available for analyses of WTC dust exposure indices; therefore, results are reported for MI and stroke combined. Overall, there was little evidence supporting an association between MI/stroke and indices of exposure to WTC dust. In contrast, the authors reported evidence of PTSD as a strong risk factor for both self-reported MI (HR = 2.22; 95% CI: 1.30, 3.82) and stroke (HR = 2.51; 95% CI: 1.39, 4.57). The association between PCL-C score and MI/stroke persisted in analyses treating PCL-C score as a continuous variable. Interestingly, associations between MI and many known risk factors were not observed, including blood pressure, BMI, and total cholesterol, although MI risk in current smokers was significantly increased compared with never smokers (HR = 2.82; 95% CI: 1.35, 5.91).

Remch et al. [2018] has multiple strengths, including the prospective cohort design, partial validation of outcomes by medical chart review, and additional validation via linkage to hospital discharge records. There are also important limitations. First, the observation period was limited to 4 years beginning more than a decade after September 11, 2001; therefore, MI risks between 2001–2012 are not clear and power to estimate risks afterwards is limited. Second, few results excluding persons with recurrent cases were reported. The effect on risk estimates from including persons with MI events prior to observation is unclear. Moreover, the ascertainment of recurrent cases is not clear; therefore, completeness of information on CVD prior to observation is uncertain. Fourth, findings from analyses using a composite outcome of MI and stroke are difficult to interpret with respect to IHD given that stroke contributed nearly half of the events. Fifth, the medical

chart review revealed evidence of MI ascertainment that differed by PTSD status and linkage to discharge records showed discordance with self-report; therefore, errors in ascertainment may have biased risk estimates. Finally, a strength of the study was control for PTSD as an independent risk factor; however, residual effects from incomplete control resulting from model misspecification cannot be ruled out [Schisterman et al. 2009].

e. Cohen et al. [2019]

Cohen et al. [2019] conducted a longitudinal cohort study of FDNY male firefighters (*n* = 9,796) to assess whether exposure to 9/11 agents was associated with elevated CVD risk. The study population included male firefighters who were active duty on September 11, 2001, and arrived at the WTC site within the first two weeks. The primary outcome was any diagnosis in the FDNY electronic medical record of MI, stroke, unstable angina, coronary artery surgery or angioplasty, congestive heart failure, or CVD death. Deaths were identified through linkage to the NDI. Outcome data was collected through December 31, 2017. Two exposure indices were derived from self-report of arrival time and duration of work on the WTC site. Two separate instruments were used to determine PTSD status over the course of study. Status was determined from the earliest of either the PTSD checklist as modified by FDNY (PCL-m) administered during 2001–2005 [Berninger et al. 2010], or the 17-item 9/11-specific PTSD checklist (PCL-S) [Ruggiero et al. 2003] administered thereafter.[50] For the latter (comprising only 6% of participants), a score ≥ 44 was considered probable PTSD as in other studies. In contrast to the PCL-S, the PCL-m included 14 binary choice questions modified for 9/11 context. Probable PTSD for PCL-m was determined by indication of symptoms within each of three PTSD symptom groups identified in the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition [APA 1994]. The authors reported that the PCL-S and the PCL-m provided similar results, although results were not shown. Statistical analyses were conducted using proportional hazards regression models adjusted for age, race/ethnicity, and baseline values of BMI, hypertension, hypercholesterolemia, diabetes mellitus, smoking, and probable PTSD.

The study population was mostly non-Hispanic White (94.2%), with a mean age of 40.3 years. Probable PTSD prevalence was 10.4%. There were 489 primary CVD events during the observation period (147,680 person-years), of which nearly all (87.3%) were attributable to IHD, followed by stroke (12.5%). The main results are shown in **Table 14**.

Modest significant associations were observed between CVD and both exposure indices. The linear trend for HRs across three arrival group categories was also significant (p for trend = 0.009). Well-established

50 Email correspondence conducted on September 4, 2025, with Rachel Zeig-Owens, the corresponding author of Cohen et al. [2019], indicated that from 2005 through 2007, the specific traumatic event used in PCL-S was the September 11, 2001, terrorist attack. However, starting in 2008, the FDNY member could select their own worst traumatic event and that event was populated into the PCL-S questions. Singh et al. [2020] observed that despite having this choice, 78% selected September 11, 2001, as their most traumatic event.

CVD risk factors, including hypertension, hypercholesterolemia, diabetes mellitus, smoking, and obesity were associated with CVD in multivariable analysis. There was no evidence of an association between CVD and PTSD in either multivariable model.

Cohen et al. [2019] has several important strengths. First, the FDNY's firefighter cohort is large and longstanding, having been established prior to September 11, 2001, and followed through 2017. This cohort included only firefighters who were active duty and arrived at the WTC within 2 weeks of September 11, 2001; therefore, they may be more likely to be healthy and free of clinical CVD at that time. Second, FDNY firefighters, on average, are likely to have higher 9/11 exposure levels compared to other 9/11-exposed population subgroups; therefore, the cohort offers greater statistical power to observe an exposure-response association. Third, CVD outcomes were confirmed using FDNY medical records rather than relying on patient self-report. Fourth, although a composite CVD outcome was defined, the primary outcome comprised mainly IHD, thereby reducing uncertainty in the outcome definition. Fifth, models attempted to control for the effects of probable PTSD. Lastly, information was available on a large set of known CVD risk factors, which were used to derive covariates for multivariable analysis. Results from these analyses appeared consistent with current knowledge of these risk factors.

Cohen et al. [2019] also has limitations. First, only male firefighters were examined; therefore, generalization is limited. Second, objective measures of exposure were not available; therefore, exposure misclassification from recall errors cannot be ruled out. Efforts to examine potential bias from exposure misclassification are lacking. Third, the study lacked exact dates of some CVD events, which the authors suggest may have biased risk estimates toward the null. Fourth, occupational exposure from firefighting that occurred after September 11, 2001, was not considered and investigations into whether these exposures are differentially distributed across exposure groups have not been conducted. Therefore, confounding by other occupational (or environmental) exposure cannot be ruled out. Fifth, the relationship between PTSD, WTC dust exposure, and IHD is not clear; therefore, model misspecification cannot be ruled out. There was no evidence of an association between PTSD and CVD; therefore, the potential for bias from PTSD was suggested to be small. However, the Science Team noted that dissimilar methods were used to ascertain probable PTSD status over the course of the study, with most participants assessed using the earlier PCL-m method. Although efforts to examine the potential effects on risk estimates from mixing PTSD screening methods were briefly described, the effect (if any) was not sufficiently elucidated by study authors. Finally, estimates did not control for important risk factors, such as alcohol consumption and family history of heart disease, which might confound an association between 9/11 exposures and CVD.

f. Colbeth et al. [2020]

Colbeth et al. [2020] conducted a longitudinal study to examine mortality patterns among FDNY firefighters and emergency medical service providers (EMS). The study population comprised 15,431 persons who worked at the WTC site between the morning of the terrorist attacks and July 25, 2002, and who were actively employed by FDNY for at least 18 months. The cohort was followed through 2017. The underlying cause of death was identified via linkage to the NDI. CVD mortality was defined according to NIOSH LTAS Major 16 [Robinson et al. 2006; Schubauer-Berigan et al. 2011]. Self-reported exposure intensity was described by ordinal categories (high, arrived on the morning of September 11, 2001; moderate, arrived afternoon of September 11, 2001, or on September 12, 2001; low, arrived between September 13, 2001, and July 25, 2002). The authors conducted both external and internal analyses. The latter was used in this evaluation. Internal (exposure-response) analyses were conducted using proportional hazards regression accounting for age, sex, race/ethnicity, smoking history, and other relevant confounders. 373 people were excluded (2.4%) because of missing covariate data. These analyses examined associations between 9/11 exposure intensity (high vs. moderate/low) and mortality. A test for trend was conducted using the high, moderate, and low exposure categories.

Participants were largely male (96.8%), firefighters (86.0%), non-Hispanic White (87.2%), and never-smokers (60.9%). There were 120 CVD deaths (85 IHD deaths) for 248,665 person-years of observation. In contrast with Cohen et al. [2019], the authors found no association between 9/11 exposure and CVD in this population; the risk of CVD mortality among persons with high exposure did not differ from those with moderate/low exposures (HR = 0.93; 95% CI: 0.52, 1.68). The test for trend across exposure categories was not significant (*p* for trend = 0.48).

Among the strengths of Colbeth et al. [2020], the study cohort is relatively large and was followed over a long period. The study methods used are well-established and appropriate for the available data. However, there are notable limitations. First, internal analyses restricted to IHD were not conducted. Second, the cohort comprised mostly White males; therefore, generalizability to other 9/11 populations is limited. Third, 9/11 exposure was self-reported which could lead to bias in risk estimates from recall errors. The potential for exposure misclassification bias has not been investigated. Fourth, the authors did not control for several important risk factors that might mediate the association between 9/11 exposures and CVD, such as PTSD, dyslipidemia, hypertension, alcohol consumption, and family history of heart disease. Finally, markedly improved survival among cardiovascular patients due to medical advancements and increased access to medical care means fewer deaths available for study and a potential underestimation of CVD risk when using mortality as the

endpoint. For example, there continues to be lower than expected IHD mortality among FDNY members (SMR = 0.33; 95% CI: 0.27, 0.41; *n* = 85 deaths),[51] which is likely because of improved health due to physical requirements for employment (i.e., a healthy worker effect), improved lifestyle, and access to physical and mental health annual monitoring examinations, screening tests, diagnostic procedures and treatments, and disease management counseling as part of the WTC Health Program.

g. Alper et al. [2021]

Alper et al. [2021] conducted a longitudinal study that investigated the agreement between survey and hospitalization data with respect to estimates of disease prevalence and exposure-chronic disease associations. The investigation of exposure-chronic disease associations included an assessment of four measures of 9/11 exposure and select health outcomes, including "heart attack." To be eligible for inclusion in this study of WTCHR enrollees, the enrollee had to have completed all of the first four survey Waves[52] and resided in New York State at Waves 2 and 3. The resulting study group included 18,206 persons (the authors did not report how many were area workers, rescue/recovery workers, residents, or passersby).

The four measures of 9/11 exposure self-reported at Wave 1 included: (1) probable PTSD defined as a 17-item 9/11-specific PTSD checklist (PCL-S) score ≥ 44 (yes/no); (2) caught in the dust cloud on 9/11 (yes/no); (3) having experienced one or more injuries on 9/11 (yes/no); and (4) witnessed three or more traumatic events on September 11, 2001 (e.g., seeing planes hit buildings, witnessing people jumping from buildings) (yes/no). Two binary CVD outcomes were created: (1) self-reported "heart attack" that was diagnosed by a health professional between 2002 and 2015 and was reported by the enrollee in any of Waves 1 through 4; and (2) a hospitalization or emergency department visit that was assigned an ICD-9 code of 410.XX (acute MI)[53] or 428.XX (heart failure) found by linking participants to SPARCS data for the period 2002-2015. Analyses of the exposure-heart attack association were conducted using logistic regression adjusting for sex, age on 9/11, race/ethnicity, and education. They also investigated the difference between the ORs based on the self-report versus SPARCS outcomes on the log scale (i.e., the difference between the β) for all four exposure-disease pairs and assessed the statistical significance of those differences.

Participants included more males (60.5%) than females, were aged 25 to 44 on September 11, 2001 (51%), non-Hispanic White (70%), and college-educated (52%). About 15% of participants had probable

51 This result was reported in the erratum by Colbeth et al. [2023].
52 The initial WTCHR survey was conducted in 2003–2004 (Wave 1), and subsequently in 2006–2007 (Wave 2), 2011–2012 (Wave 3), and 2015–2016 (Wave 4).
53 The "XX" represent two placeholder digits used to specify additional details about the diagnosis. This notation is commonly used in research documents to refer to the entire range of codes under a category rather than a specific one. The "XX" denotes all subcodes within those myocardial infarction and heart failure categories without enumerating each one.

PTSD. The prevalence of "heart attack" between 2002–2015 was 3.8% based on self-report and 1.6% based on SPARCS (the counts of these outcomes were not reported) (*kappa* = 0.31, which is considered to represent a fair amount of agreement). For the self-reported "heart attack" outcome, the ORs for three exposure measures were significantly elevated: PTSD (OR = 2.3; 95% CI = 1.9, 2.8), injury on September 11, 2001 (OR = 1.3; 95% CI = 1.1, 1.6), and witnessing traumatic events on September 11, 2001 (OR = 1.3; 95% CI = 1.1, 1.5). For the SPARCS "heart attack" outcome, the only exposure measure with a significantly elevated OR was PTSD (OR = 1.7; 95% CI = 1.2, 2.2). *See* **Table 15**.

When considering the exposure "injury on 9/11," the findings for the two "heart attack" outcomes were inconsistent. This was the only exposure where there was a significant difference in risk between the two "heart attack" outcomes (an association was observed for self-report, but not for SPARCS-based data), suggesting measurement bias. Other WTCHR studies also reported significant associations between injury on 9/11 and CVD outcomes, but study sizes in those earlier studies were smaller compared to Alper et al. [2021]. One such study of cardiovascular outcomes captured in Waves 1 and 2 only [Brackbill et al. 2014] found that among 14,087 subjects, self-reported angina/MI/other heart disease (heart disease) risks from 9/11 injury were significantly elevated among those present south of Chambers Street on September 11, 2001. The heart disease risks were higher among those with both PTSD and higher numbers of injuries, but the risks were also significantly elevated among those with no PTSD and one injury (heart disease risk was non-significantly elevated among those with no PTSD and more than one injury, and the lack of significance was attributed by the authors to the low number of heart disease cases in those groups). That study also reported significantly elevated heart disease risks among those with intense dust exposure. Another study, Alper et al. [2017], which examined an even more highly restricted sample of WTCHR enrollees (i.e., those who were exposed only acutely, and not chronically, to the 9/11 terrorist attacks, *n* = 8,701), found that self-reported angina/MI risks were significantly associated with 9/11 injury, and there was a significant exposure-response association with increasing number of 9/11 injuries ($p < 0.0001$). However, Alper et al. [2017] found no association between self-reported angina/MI and intense dust cloud exposure nor with probable PTSD at Wave 1. Neither Brackbill et al. [2014] nor Alper et al. [2017] used objective outcome data (i.e., SPARCS data).

A notable strength of Alper et al. [2021] was that it used a large prospective cohort and objective outcome data (i.e., SPARCS). Another strength was the comparison of self-reported and hospitalization data sources for the heart attack outcome. Heart attack prevalence was 26% higher using self-reported data. In addition, there was agreement in the association between those outcomes and two measures of 9/11 exposures: dust cloud exposure (neither outcome source was

associated) and PTSD (both outcome sources were associated). This suggests that strong bias in exposure-response estimates from misreport of MI was unlikely, although ascertainment error cannot be ruled out as possible explanations of study findings.

The study by Alper et al. [2021] also had notable limitations. First, the study used a restricted sample of the WTCHR population who completed Waves 1, 2, 3, and 4. The study population comprised only 25.5% of all enrollees; therefore, representativeness is a concern, as well as bias through attrition across the Waves. Second, there was a lack of information or control for injury severity, number of injuries, body location, and whether the injury required treatment. There was also a lack of objective measures for the other exposures; therefore, the potential for biases from errors in ascertainment and exposure assignments cannot be ruled out. Third, several risk factors were not controlled for, including BMI, smoking, hyperlipemia, diabetes, and hypertension; therefore, the potential for residual confounding cannot be ruled out. Fourth, the single source of hospitalization data (i.e., SPARCS) used does not capture out-of-state hospitalizations, which could lead to reduced hospitalized heart attack prevalence estimates. Finally, another limitation was that the SPARCS outcome included both MI and heart failure, whereas the self-report outcome included only MI (i.e., heart attack). This likely contributed to biases from errors in ascertainment.

h. Sloan et al. [2021]

Sloan et al. [2021] conducted a longitudinal study of CVD among rescue/recovery workers in the GRC (*n* = 37,723) of the MMTP who were recruited under open enrollment beginning July 16, 2002, and followed through March 31, 2019. CVD was defined as self‐reported physician diagnosis of, or current treatment for, CAD, MI, stroke, or congestive heart failure. Self-reported information on arrival was used to define ordinal exposure categories as either "very high," including responders with first arrival at the WTC site on September 11, 2001, and reporting exposure to the dust cloud; "high," first arrival on September 11, 2001, but not reporting dust cloud exposure; or "low/intermediate," first arrival on or after September 12, 2001. The effects of very high and high exposure were compared with low/intermediate exposure using proportional hazards regression stratified by sex and adjusted for race/ethnicity, smoking, cholesterol, hypertension, diabetes mellitus, and BMI. Analyses also adjusted for occupation in "protective services," recognizing that high stress occupations may be a risk factor for CVD. Over half of the WTC Health Program GRC were classified as employed in protective services, such as police or the military; however, details on the composition of occupations within the category were not reported. Participants were mostly male (86.3%), non-Hispanic White (54.7%), and never-smokers (57.7%). About 6.3% (*n* = 2,385) of the study group reported having been diagnosed with or treated for first–time CVD. IHD was most prevalent, with CAD and MI

comprising 67% of CVD events. The results from exposure-response analysis stratified by sex are shown in **Table 16**. The authors reported significantly increased CVD risk in males and females within the very high and high exposure groups compared with those in the low/intermediate exposure group. In a fully adjusted model combining sexes, the HR was 1.12 (95% CI: 1.03, 1.22). Risk estimates were markedly attenuated after adjustment for employment in protective services.

Although attenuated, significantly increased risk remained in two of four comparisons shown after adjustment for protective services. This finding suggested that employment in protective services may confound the association between 9/11 exposures and CVD in this cohort, which may, in part, explain the observed response.

Protective services employment on September 11, 2001,[54] was a significant CVD risk factor in multivariable models for both men (HR = 2.16; 95% CI: 1.97, 2.37) and women (HR = 2.94; 95% CI: 2.10, 4.11), with a strength of association that was greater than that for 9/11 exposure and CVD. Given the indication of confounding by protective services and its strong effect size relative to that observed for 9/11 exposure, it is not clear why the potential effects from employment in other sectors (e.g., construction, transportation) were not also investigated. The authors reported that a previous cancer diagnosis was "highly associated" with CVD, although results were not shown.

Study strengths of Sloan et al. [2021] include large cohort size, inclusion of many female responders, and observation up to 17 years post-September 11, 2001. The methods were appropriate for the available data. This is the first study adjusting for confounding by occupation in protective services on September 11, 2001, which showed a marked effect on risk estimates. However, this study also has several limitations. First, the study did not conduct analyses restricted to IHD outcomes; therefore, interpretation of IHD risk is uncertain. Second, objective measures of exposure and outcome were not available; therefore, bias in risk estimates from errors in recall cannot be ruled out. Third, study participants were only followed until their most recent monitoring exam, and over time there was a decreasing number of members who returned to the clinic for their annual reexamination. As such, cases of CVD are likely under-reported. Fourth, employment in protective services confounded the association between 9/11 exposure and CVD, although evidence of increased risk remained after adjustment. Nevertheless, residual confounding cannot be ruled out. Furthermore, the true relationship between multiple explanatory variables and the dependent variable may not be accurately depicted by a simple covariate model. For example, the authors cautioned against overinterpretation given observed violations of the proportional hazards assumption (i.e., the effect measure for any predictor is constant over time) for some covariates, including smoking, cholesterol, and BMI status. Violation

54 The authors did not report if these workers continued protective services employment after September 11, 2001.

of proportional hazards assumption may indicate that the model specification used poorly describes the true association. The authors also acknowledged comorbidities and potential risk factors may lie on the causal pathway (a causal pathway refers to the sequence of events and mechanisms through which a cause leads to an effect, particularly in understanding how certain exposures influence health outcomes) between 9/11 exposures and CVD; therefore, standard covariate adjustment might have distorted risk estimates. Fifth, the authors did not control for important risk factors that might bias estimates of the association between 9/11 exposures and CVD, including PTSD status, alcohol consumption, and family history of heart disease. Lastly, as recognized by Sloan et al. [2021], entry into the GRC is voluntary and membership is more diverse compared with the FDNY cohort. The GRC has observed diminishing numbers of members attending monitoring visits over time. These factors suggest a potential for bias from self-selection. The extent to which findings in this cohort are representative of the population of all 9/11-exposed general responders is unclear.

i. Li et al. [2023]

Li et al. [2023] examined mortality patterns in a longitudinal study of 60,631 rescue/recovery workers from FDNY (n = 15,887), GRC (n = 25,657), and WTCHR (n = 19,087). The pooled cohort was restricted to workers who were 18 years or older on September 11, 2001, and had complete information on race and ethnicity. To reduce the potential for selection bias, the study also excluded persons who enrolled after 2010 or had died or reached their 85th birthday during the first year of enrollment. To avoid overlap (i.e., duplication of subjects), pooling followed a hierarchy that included FDNY members first, followed by GRC, then WTCHR enrollees. Follow-up was through 2016 (697,943 person-years). Vital status and the underlying cause of death were ascertained via linkage with the NDI. Heart disease mortality was defined according to the NIOSH LTAS Major 16 [Robinson et al. 2006; Schubauer-Berigan et al. 2011]. Self-reported exposure to 9/11 agents was described separately using two metrics consisting of categories of the date of arrival or whether individuals had worked on the pile. External comparisons examined mortality using U.S. and state referent rates. Exposure-response associations were examined for each subgroup by proportional hazards regression using attained age as the timescale and adjusting for sex, race/ethnicity, and smoking status at baseline. Models included a cross-product term between exposure and cohort group to examine between-group heterogeneity; however, the overall exposure-response for the pooled cohort was not reported. Models were also adjusted for competing risks using Fine and Gray methods [Fine and Gray 1999], although there was no indication that competing risks were significant in subsequent sensitivity analyses.

The cohort was mostly male (84.2%), non-Hispanic White (71.3%), and never smokers at enrollment (59.5%). FDNY members had the highest proportion arriving on September 11, 2001 (58.4% vs. 35.8%

and 18.2% for GRC and WTCHR enrollees, respectively) and working on the pile (81.9% vs. 25.9% and 21.0% for GRC and WTCHR enrollees, respectively). There were 378 heart disease deaths observed during the study period. Heart disease mortality was significantly less than expected using U.S. (SMR = 0.39; 95% CI: 0.35, 0.43) or state rates (SMR = 0.41; 95% CI: 0.37, 0.46), suggesting a strong healthy worker effect. Among FDNY members, there was no evidence of a positive exposure-response association between heart disease mortality and either WTC exposure metric. *See* **Table 17**.

In contrast, there was evidence of a modest exposure-response association among subgroups of GRC and WTCHR enrollees; however, estimates were largely imprecise and there was no evidence of monotonicity. Of 12 internal comparisons reported, one estimate was statistically significant, which indicated increased risk among WTCHR enrollees who responded between September 13 and 17, 2001, compared with those responding from September 18, 2001, to June 30, 2002 (HR = 1.50; 95% CI: 1.01, 2.23). Between-group heterogeneity was reported, although p-values were not shown. Overall, heart disease risk appeared to be slightly greater among WTCHR workers compared with first responders enrolled in the FDNY and GRC cohorts, suggesting the potential for selection bias from potential differences in lifestyle, employment, and access to healthcare.

Strengths of Li et al. [2023] included the large sample size and lengthy follow-up. Methods used were appropriate for the available data. Limitations include the use of cause of death information from death certificates by linkages to NDI and the lack of IHD-specific analyses. Information on comorbidities and potentially important risk factors such as PTSD was lacking. Findings among subgroups were inconsistent, suggesting the importance of other unmeasured factors that may have influenced estimates. Completeness of exposure information varied by subgroup and metric. For example, information on first arrival was missing for about 7% of the cohort, ranging from 0.85% among the WTCHR enrollees to nearly 12% among the GRC. The authors did not specify how missing exposure information was treated in the analyses.

j. Mueller et al. [2024]

Mueller et al. [2024] conducted a cross-sectional study examining CVD prevalence in male FDNY firefighters who experienced WTC exposures. Main analyses were external comparisons using two separate referent groups: (1) career firefighters actively employed by fire departments in Chicago, Philadelphia, or San Francisco on September 11, 2001; or (2) respondents of the 2019 National Health Interview Survey (NHIS) conducted by CDC's National Center for Health Statistics [NCHS 2024]. The non-exposed firefighter referent group comprised male firefighters who completed a self-administered health questionnaire between 2019–2021, did not report 9/11 exposure, and consented to research (*n* = 2,729). The WTC-exposed

group comprised FDNY firefighters who were alive at the start of administration of the non-WTC-exposed questionnaire, first arrived at the WTC site before September 24, 2001, and answered CVD-related questions on separately administered health questionnaires completed during periodic physical examinations beginning immediately following the attacks (*n* = 9,789). The health conditions were defined as stroke, CAD, or stroke/CAD combined. CAD was ascertained as a self-reported diagnosis "coronary artery disease, MI [myocardial infarction], angina (ischemia), or blockage." Ascertainment for non-WTC-exposed firefighters was from a single baseline response of ever being diagnosed. FDNY ascertainment used information from all post-September 11, 2001, questionnaires available through May 26, 2021. WTC exposure was classified as high, moderate, or low based on self-reported arrival time to the WTC site. Multivariable logistic regression was used to calculate ORs. Model 1 adjusted for age, race, and BMI. Model 2 included Model 1 covariates and additionally controlled for self-reported high cholesterol, diabetes mellitus, hypertension, and smoking status (ever/never). Internal comparisons (within the FDNY group) were made in supplemental analyses, with the low exposure group as referent. In these analyses, Models 1 and 2 were used for covariate control; case ascertainment was established by either self-report alone or confirmed by medical chart review.

As reported in Mueller, FDNY firefighters on September 11, 2001, when compared with non-FDNY firefighters, were slightly younger on September 11, 2001 (40 vs. 44 years of age), less likely to report ever smoking (33% vs. 44%), and more likely to be White (94% vs. 75%). In comparisons using non-exposed firefighters as the referent group, the odds of self-reported CAD among FDNY firefighters were significantly increased in a partially-adjusted model (Model 1), with a monotonically increasing trend in risk across exposure categories. *See* **Table 18**. However, in fully-adjusted models (Model 2), these associations were strongly attenuated. Still, there was a significantly increasing linear trend in risk across increasing categories of 9/11 exposure for self-reported CAD ($p = 0.03$). The ORs for CAD were nearly the same as those for CAD/stroke combined.

Internal comparisons revealed modest but significantly increased ORs for self-reported CAD in moderate and high exposure categories compared with the low exposure category, with a monotonic positive trend across categories. *See* **Table 19**. However, when restricted to chart-confirmed cases, the strength of the association decreased and the ORs and trend were no longer statistically significant. The positive predicted value (PPV) and sensitivity for CAD were 56% and 79%, respectively.

All ORs from comparisons with the NHIS cohort were significantly less than 1.0, indicating large differences between FDNY and NHIS cohorts. Based on this observation, NHIS comparisons were largely vulnerable to selection bias; therefore, comparisons between FDNY and the NHIS group were not considered informative.

In summary, Mueller et al. [2024] reported estimates of increased CAD risk in male FDNY responding firefighters that appeared largely dependent on the model specification and ascertainment method used. A strength of the study was using other career firefighters as controls; therefore, reducing the potential for bias from healthy worker effects commonly found when comparing a working population with the general population. However, differences remain between FDNY and non-FDNY firefighters that may still lead to selection bias. For example, FDNY firefighters undergo annual physical exams and are likely to be enrolled in the WTC Health Program; therefore, access to healthcare and health awareness are likely improved in FDNY firefighters compared with other firefighters. There were other notable limitations. First, there were group differences in methods of collecting study information, such as the instrument used and the frequency of collection. These differences can potentially lead to biased estimates in group comparisons. Second, internal analyses of FDNY firefighters using self-reported case status with and without medical confirmation showed substantial attenuation of exposure-related effects following case confirmation; therefore, ascertainment bias cannot be ruled out. Third, bias from residual confounding is likely given that significant associations observed in partially adjusted models were largely absent after controlling for additional CVD risk factors and other risk factors (e.g., PTSD) were not considered. Fourth, the strength of association was relatively small for all outcomes tested; therefore, risk estimates are particularly vulnerable to potential biases. Fifth, the cross-sectional design used by this study is generally considered to be minimally informative on causal association. Steps taken to address certain biases or limitations inherent to cross-sectional studies were not described; therefore, interpretation of study findings merits additional caution.

k. Krasnov et al. [2025]

Krasnov et al. [2025] conducted a longitudinal study of CAD among GRC members (*n* = 47,795) using outcome data that were collected from 2003 to 2021. CAD and date of diagnosis were self-reported and were collected using a medical questionnaire that was administered at each monitoring visit. Other information collected at the monitoring visit included 9/11 exposures (collected only at the initial monitoring visit), sociodemographic variables, smoking and alcohol consumption history, and measured BMI. Responders who were diagnosed with CAD within 2 years of the September 11, 2001, terrorist attacks were excluded. Those 9/11 exposures that were assessed included: (1) total number of hours on-site on September 11, 2001; (2) presence in lower Manhattan on September 11, 2001; (3) total number of days on-site at the WTC site between October 2001 and June 2002; (4) sustained a 9/11 injury or witnessed horror; (5) lost someone; and (6) the WTC

exposure index described by Wisnivesky et al. [2011].[55] Separate single-exposure Cox proportional hazard regressions were used to examine the association between each WTC exposure and CAD. Models were adjusted for sociodemographic characteristics (i.e., age, sex, race, education, and marital status), BMI, and census tract-level socioeconomic variables based on residence at the initial visit.

The average age of the study population at cohort entry was 41 years; most were White (52%) and male (87%). A total of 3.2% (*n* = 1,520) had CAD. The associations between CAD and 9/11 exposure measures are provided in **Table 20**. Almost all the associations were positive, but none were statistically significant.

The study by Krasnov et al. [2025] has several strengths. First, the GRC is large and longstanding and was followed from 2003 until 2021. Second, several types of 9/11 exposure were assessed, including a composite exposure variable that considered overall time working at the WTC site, dust cloud exposure, and direct work on the debris pile. Finally, information was available for several known CVD risk factors.

The study by Krasnov et al. [2025] also has limitations. First, the outcome variable and 9/11 exposure variables were self-reported and not independently confirmed with objective data. Efforts to examine potential bias from exposure misclassification are lacking. Second, outcome data were obtained from monitoring exams, and over time there has been a decreasing number of members who returned to the clinic for their annual monitoring exam. As such, CAD cases are likely under-reported. Third, estimates did not control for important risk factors, such as PTSD status and family history of heart disease, which might confound any association between 9/11 exposures and CVD. Finally, whether findings in this cohort are representative of the entire population of 9/11-exposed general responders is unclear.

IX. SYNTHESIS OF EVIDENCE FOR CATEGORIZATION

In accordance with the *Policy and Procedures* [NIOSH 2026a], the Science Team evaluates and synthesizes evidence from the high-quality studies identified following the literature review and from the medical basis provided in the current and previous petitions. Synthesis refers to the process by which the Science Team evaluates the evidence presented in scientific studies, individually and together, to characterize the evidence of a causal association between 9/11 exposures and the health condition of interest and to assign findings regarding causal association to one of five categories as described in Section IX.A.4.[56] This evaluation includes a consideration of a weight-of-the-evidence framework commonly referred to as the "Bradford Hill criteria," limitations, and representativeness of the findings.

55 Per the Krasnov et al. [2025] study, "the WTC exposure index is a derived exposure variable that incorporates data on the overall time working at the WTC site, exposure to the dust cloud, and direct work on the debris pile. The 'low' category included responders who worked less than 40 days, were not exposed to the dust, and did not work directly on the pile. The 'intermediate' category included responders who were not exposed to the cloud but worked 40 to 90 days or directly on the pile. The 'high' category included responders who were directly exposed to the cloud or worked for more than 90 days."

56 *See Policy and Procedures*, Section IV.A. [NIOSH 2026a].

A. Introduction

1. Bradford Hill Framework for Weight-of-the-Evidence Determinations

The Policy and Procedures [NIOSH 2026a] utilizes the Bradford Hill criteria to determine the degree to which the weight of evidence presented by high-quality peer-reviewed, published, epidemiologic studies supports a causal association between 9/11 exposures and the health condition.

The Bradford Hill criteria include: (1) **strength of the association** between 9/11 exposures and the health condition under consideration and precision of the risk estimate; (2) **consistency of associations** across multiple studies; (3) **specificity** that an association is more likely to be causal if one cause (9/11 exposures) and one effect (IHD) is observed; (4) **temporality** of the cause and effect, that is 9/11 exposure precedes the health condition (IHD); (5) **biological gradient** or dose-response relationship where changes in 9/11 exposures are associated with corresponding changes in the magnitude of the outcome (IHD); (6) **biological plausibility** — the extent to which 9/11 studies align with known facts about the biology of the health condition being evaluated (IHD); (7) **coherence** between a causal association and known disease etiology; and (8) **analogy** with an established similar causal relationship [Hill 1965].

Four Bradford Hill criteria — strength of the association, consistency of associations, temporality, and biological gradient — are directly applicable to the evaluation of evidence from high-quality studies identified in the scientific literature review. Each of these four criteria is given significant weight in synthesizing evidence from high-quality studies found after a review of the scientific literature. In contrast, the Bradford Hill criterion of specificity is given no weight due to the multiple causes that can lead to IHD.

Biological plausibility, coherence, and analogy are related criteria that require reasonable knowledge of the biology of the health condition of interest, including facts about disease etiology and any established direct or analogous causal relationships. Although previous biological evidence may have motivated the high-quality epidemiologic studies identified for evaluation, these studies themselves may not provide sufficient information to evaluate the criteria of biological plausibility, coherence, and analogy. To address any concerns regarding incomplete information in the identified studies, the Science Team exercises scientific and medical judgment to refer to additional information from biological, toxicologic, and epidemiologic research, usually from references cited in the identified studies or medical basis studies, or from an additional, limited review of the literature to assess biological plausibility, coherence, and analogy. This approach permits a more complete analysis of these criteria, offsetting the likelihood of reaching a default decision that there is inadequate information to evaluate the likelihood of a causal association.

2. Study Limitations

In synthesizing evidence from high-quality studies, the Science Team considers limitations that may affect the validity of study findings. Limitations include the potential for residual confounding of effect measures from

incomplete information on risk factors and major sources of selection or information biases, such as healthy worker effects, adequacy of the control group, ascertainment errors, exposure misclassification, and conflicts of interest, among others. Study limitations are integral to assessing aspects of association, such as strength of the association, consistency of associations, temporality, and biological gradient. For example, large effects (i.e., strength of the association) are generally less vulnerable to study biases. Likewise, cross-sectional studies, by design, generally offer little information on temporality compared with longitudinal studies.

3. Study Representativeness

In synthesizing evidence from high-quality studies, the Science Team considers the representativeness of the evidence to assess whether the high-quality studies, taken together, represent both WTC responder and survivor populations or, if only a subgroup of 9/11-exposed responder or survivor populations is represented. If the 9/11-exposed population is only partially represented, then the Science Team considers whether the results can reasonably be extrapolated to the full 9/11-exposed population. Representativeness is linked to consistency of associations such that similar findings observed in multiple populations are generally weighted more heavily than findings observed in a single population.

Due to the interrelatedness of certain Bradford Hill criteria (e.g., strength of the association, consistency of associations, temporality, and biological gradient) and consideration of study limitations and representativeness, those respective criteria may be grouped together for the purpose of synthesizing evidence from the totality of high-quality studies. The evaluation and synthesis of the evidence from high-quality studies is provided in two parts: (1) consideration of the strength of the association, consistency of associations, temporality, and biological gradient in the identified high-quality studies, including an assessment of study limitations and representativeness of study populations; and (2) consideration of biological plausibility, coherence, and analogy that combines information from the identified high-quality studies with additional information. A summary of the evaluation and synthesis of high-quality studies is provided in Section IX.B. *See* **Table 21**.

4. Categorization of Evidence

After evaluation of the totality of the evidence from high-quality studies, the Science Team categorizes the totality of the evidence into one of the following five categories: (1) Category I — the evidence supports the *substantial likelihood* of a causal association; (2) Category II — the evidence supports the *high likelihood* of a causal association; (3) Category III — the evidence supports a *limited likelihood* of a causal association; (4) Category IV — the *evidence does not support* a causal association; or (5) Category V — the evidence is *inadequate* to determine the likelihood of a causal association [NIOSH 2026a].

This evaluation and categorization of the evidence is used by the Administrator to determine if there is sufficient evidence of a causal

association to conclude that 9/11 exposures are *substantially likely* to be causally associated with the health condition. If the evaluation and categorization of the evidence demonstrate a high, but not substantial, likelihood of causal association between 9/11 exposures and the health condition (Category II), the Administrator may direct the Science Team to evaluate additional highly-relevant scientific information regarding exposures to known 9/11 agents in *non-9/11 exposure scenarios*. Based on such information, coupled with evidence from the evaluation of high-quality studies of the health condition in 9/11-exposed populations, the Science Team will determine whether the totality of the evidence supports a causal association as either Category I (*substantial likelihood*) or Category II (*high likelihood*).

B. Evaluation and Synthesis of High-Quality Studies

1. Consideration of Strength of the Association, Consistency of Associations, Temporality, and Biological Gradient

a. Specific Ischemic Heart Disease Outcomes

Four high-quality studies reported risk estimates from analyses of specific IHD outcomes [Brackbill et al. 2006; Alper et al. 2017; Alper et al. 2021; Mueller et al. 2024], as did one previously reviewed study [Jordan et al. 2013]. Overall, results from these studies were inconsistent. Among longitudinal studies, Jordan et al. [2013] examined associations between CAD hospitalizations and 9/11 exposure among WTCHR enrollees and found evidence of excess CAD risk with exposure in male and female rescue/recovery workers with HR between 1.7 and 5.3, but estimates were not statistically significant. Trends across increasing exposure categories were also not significant (p = 0.11–0.14); thus, providing little evidence of a biological gradient. Still, these estimates were comparable to statistically significant estimates from main analyses using the broader definition of heart disease, suggesting that the reduction in cases from restricting the outcome definition had little effect on the magnitude of the estimate. *See* **Table 8**.

In contrast, Alper et al. [2017] examined angina and MI (n = 92 combined cases) in a limited sample of WTCHR enrollees (n = 8,701) who were primarily acutely exposed through injury or intense dust on 9/11. That study found that IHD exhibited an exposure-response association with sustaining injury on 9/11 but there was no evidence of an association between IHD and acute dust cloud exposure. *See* **Table 11**.

Alper et al. [2021] evaluated the associations between heart attack and four types of exposures: dust cloud exposure, injuries, traumatic events, and PTSD. The study examined associations among a sample of WTCHR enrollees (n = 18,206), comparing self-report of heart attack to hospitalization for heart attack. The authors reported no association between dust cloud exposure and heart attack, using either one of the outcome data sources. Conversely, they found an association between

witnessing three or more traumatic events and heart attack for both self-reported and hospital discharge heart attack. Inconsistent findings were reported for the association between sustaining an injury and heart attack, as the relationship was observed only for self-reported heart attack. For both heart attack outcomes, significant elevated risks were found among those with PTSD. *See* **Table 15**.

Mueller et al. [2024] conducted a cross-sectional study of self-reported CAD in male FDNY firefighters that found significantly increased self-reported CAD risk compared with external referent groups in logistic regression models adjusting for age, race/ethnicity, and BMI. That study reported modest but statistically significant elevated ORs when comparing exposed and unexposed groups (OR = 1.25) and comparing high- (OR = 1.48) and moderate-exposure groups (OR = 1.32) with the unexposed external group as referent. However, risk estimates were attenuated and no longer statistically significant in models controlling for other CVD risk factors (i.e., high cholesterol, hypertension, diabetes, and smoking), although the monotonic trend in risk with increasing categories of exposure persisted (p = 0.03). Effects from these risk factors treated separately were not reported. In internal comparisons, the risk was similarly attenuated and the trend no longer significant when restricting analysis to CAD cases that were confirmed by chart review. Overall, the findings from Mueller et al. [2024] pointed to the potential for residual confounding by unmeasured risk factors and ascertainment bias from self-reported case status. In contrast, the early cross-sectional study of WTCHR community members by Brackbill et al. [2006] found no evidence of increased risk of CAD, angina, or MI among persons reporting dust and debris cloud exposure compared with those without dust exposure.

b. Studies with Composite Cardiovascular Disease Endpoints

The largest group of studies examined the association between 9/11 exposures and composite CVD endpoints that included IHD [Jordan et al. 2011b, Jordan et al. 2013, Brackbill et al. 2014, Jordan et al. 2018, Remch et al. 2018, Colbeth et al. 2020, Cohen et al. 2019, Sloan et al. 2021, Li et al. 2023, Krasnov et al. 2025]. Case definitions varied among studies. Results were also mixed but were generally supportive of a positive association between the 9/11 exposure and a composite health condition. Statistically significant positive associations were reported in two high-quality studies of general responders [Sloan et al. 2021] and FDNY firefighters [Cohen et al. 2019]. These associations were observed in both men and women. Overall, associations appeared modest, with relative risk estimates in the range of 1.16–1.61. There was evidence of a biological gradient, with exposure-response monotonicity across increasing categories of exposure [Cohen et al. 2019]. Two earlier studies reported mixed results that varied by sex and between exposure indices [Jordan et al. 2011b; Jordan et al. 2013].

A large study of FDNY, GRC, and WTCHR rescue/recovery workers also reported inconsistent results on the association between self-reported

exposure and heart disease mortality [Li et al. 2023]. A cross-sectional study of WTCHR adult enrollees reported significantly increased self-reported heart disease risk from 9/11 injury and dust cloud exposure [Brackbill et al. 2014]. That study also provided evidence suggesting an interaction between self-reported heart disease, PTSD, dust cloud exposure, and injury, although data were insufficient to clarify this relationship. Other studies did not report significant associations between composite CVD endpoints and proxies of WTC dust exposure [Jordan et al. 2018; Remch et al. 2018; Colbeth et al. 2020; Krasnov et al. 2025].

c. Injury Studies

The body of evidence on the association between 9/11 injury and CVD was limited to six high-quality studies, three of which are newly identified [Alper et al. 2017; Alper et al 2021; Krasnov et al. 2025] and three of which were previously reviewed [Jordan et al. 2011b; Jordan et al. 2013; Brackbill et al. 2014]. Four of these studies reported statistically significant positive associations between 9/11-related injuries and self-reported CVD [Jordan et al. 2011b; Brackbill et al. 2014; Alper et al. 2017; Alper et al. 2021]. However, in the Alper et al. [2021] study, the association was no longer observed when an objective measure of the CVD outcome (i.e., using hospital-discharge data to identify heart attacks) was used. Overall, these associations appeared stronger than those observed for particulate exposures, with relative risks in men and women ranging between 1.0–6.8. There was monotonically increasing CVD risk with an increasing number of injuries, with the highest risk reported among those with three or more injuries (HR = 6.8; 95% CI: 2.0, 22.6) in a multivariable model examining angina and MI, adjusted for age, race/ethnicity, education, study recruitment source, hypertension, smoking, and obesity [Alper et al. 2017]. In contrast, the remaining two studies provided little evidence of associations between 9/11 injuries and IHD [Jordan et al. 2013; Krasnov et al. 2025].

Studies of WTC-related illnesses (e.g., asthma) have examined injury as a proxy for exposures to high levels of the dust cloud and psychological stress [Brackbill et al. 2009; Jordan et al. 2011b]. However, compared with PM exposures, there is less evidence supporting a causal association between acute injury and CVD. Injury has been described as both physical and psychological traumatic experiences. It is plausible that sustaining injuries during the 9/11 attacks induces psychological trauma, which in turn initiates stress-related psychological and biological mechanisms that might lead to increased CVD risk. This pathway suggests mental health conditions, such as PTSD and depression, act as intermediaries. It is also possible that injury could act more directly by altering physical function that causes changes in physiology (e.g., blood cholesterol, BMI, hypertension, blood glucose levels) or lifestyle behaviors (e.g., diet, physical activity, smoking) that adversely affect cardiovascular

health and increase the risk of a cardiovascular event [Rozanski et al. 1999; D'Andrea et al. 2011]. For example, there is emerging evidence linking spinal cord and brain injuries to increased CVD risk [Cragg et al. 2013; Izzy et al. 2023]. Physical inactivity is a major risk factor for CVD [Palaniappan et al. 2026] and may result from disability sustained by injury. However, biological mechanisms of injury-related CVD in the absence of physical disability and chronic stress are not currently known. Given that conditions currently on the List (e.g., PTSD; depression) may also be conditions that have a role in the causal pathway between 9/11 exposure and IHD, a firm understanding of the underlying mechanisms involved in a causal relationship between specific injuries sustained on 9/11 and IHD is needed to inform decisions on the likelihood of causation.

2. Study Limitations

Study limitations were considered in the evaluation of strength of the association, consistency of associations, temporality, and biological gradient, per the *Policy and Procedures* [NIOSH 2026a]. In addition to information on strength of the association, consistency of associations, temporality, and biological gradient described in this section, other important limitations in the design and available information of each identified high-quality study are found in **Tables 4** and **5**. Important sources of estimated uncertainty common to the selected studies are described below. This list is not exhaustive but illustrates major areas of concern regarding the internal validity of study findings.

a. Outcome Measures

Most, but not all, studies defined cardiovascular outcomes as broad categories (e.g., heart disease, CVD incidence, CVD death) comprising an array of heterogeneous circulatory system conditions, including conditions not grouped as IHD (e.g., stroke, dysrhythmia, rheumatic heart disease, and congestive heart failure). Only two longitudinal studies estimated IHD risk that was associated with injury or dust exposure [Jordan et al. 2013; Alper et al. 2017]. Alper et al. [2017] reported significant increased risk of self-reported angina/MI with 9/11 injuries. Jordan et al. [2013] broadly defined heart disease as hypertension (ICD-9 401–405), acute (ICD-9 410, 411) and chronic CAD (ICD-9 412–414), dysrhythmia (ICD-9 427), and congestive heart failure (ICD-9 428), but replicated analyses after restriction to CAD only. Restricted analyses findings were similar in magnitude to results using a broader outcome definition, albeit none reached statistical significance for increased CAD risk. The plausibility of separate and distinctly different cardiovascular outcomes within the composite outcome analyzed having similar exposure-related risks is suspect. Rather, it is more likely for the findings of these analyses to be indicative of the most common outcome or a less frequent outcome with much greater exposure-related risk. In either event, findings from analyses using grouped outcomes are largely uncertain and merit cautious interpretation in causal inference.

Ascertainment methods and definitions also varied by study, which increases the uncertainty in between-study comparisons (i.e., assessing consistency). Health outcomes were mostly derived from self-reported information. Exceptions were three mortality studies using cause of death information from death certificates by linkages to NDI [Stein et al. 2016; Singh et al. 2023; Li et al. 2023], two studies using physician diagnoses in medical records [Cohen et al. 2019; Mueller et al. 2024], and three studies using hospital discharge records [Jordan et al. 2013; Remch et al. 2018; Alper et al. 2021]. Correct case ascertainment from self-report is known to vary by outcome and population, although overreporting is more common. For example, one cross-sectional study found relatively poor agreement comparing self-reported CAD to cases confirmed by chart review [Mueller et al. 2024]. In exposure-response analyses, that study suggested the potential for case misclassification that was differential with respect to exposure, as evidenced by attenuation of the exposure effect when using "validated" cases compared with self-reported cases.

Other efforts to validate classifications or to determine the extent of potential bias from misclassification were sparse. One study attempted using hospital records to confirm physician-diagnosed outcomes in employer medical records, although hospital records were not available for complete confirmation [Cohen et al. 2019]. Another study examining the association between PTSD and CVD also attempted validation of self-reported outcomes by medical record review and linkage to hospital discharge records. The study found that confirmation of MI was lower for those with PTSD (47%) than those without PTSD (74%), indicating differential misclassification by PTSD [Remch et al. 2018].

As another example, the exposure-response relationship observed between heart disease (defined as self-reported angina, heart attack, or any other heart condition first diagnosed by a physician) and probable PTSD (HR = 1.62; 95% CI: 1.34, 1.96) reported in an earlier study of male WTCHR enrollees followed between 2003 and2008 [Jordan et al. 2011b] was markedly attenuated (HR = 1.16; 95% CI: 0.97, 1.40) in a later study following male enrollees between 2003–2010 [Jordan et al. 2013]. That later study used hospital discharge records for ascertainment, with heart disease comprising hypertension (ICD-9 401–405), acute CAD (ICD-9 410, 411), chronic CAD (ICD-9 412–414), dysrhythmia (ICD-9 427), and congestive heart failure (ICD-9 428). This contrast provided evidence affirming a potential for bias from self-reported outcome data.

A study of WTCHR enrollees who completed surveys for Waves 1 to 4 and resided in New York State at Waves 2 and 3 (n = 18,206) compared heart attack prevalence and exposure-disease associations using self-report and hospitalization data [Alper et al. 2021]. That study reported 3.8% heart attack prevalence (2002–2015) using self-reported information compared to 1.6% using hospital discharge records (*kappa*

= 0.31). However, analyses of the measures of association between exposure and heart attack suggested that misreporting of heart attack status was nondifferential for all exposure measures examined, including dichotomous (yes/no) self-reported injury and dust cloud exposure. Therefore, a strong bias in exposure-response estimates from misreport of MI appeared unlikely, although ascertainment error cannot be ruled out as possible explanations of study findings. Future research that examines IHD risk separately and specifically in the 9/11 population using objective outcome measures is needed to elucidate a causal association between 9/11 exposure and IHD.

b. Explanatory Variables (9/11 Exposures)

As noted above, WTC dust is listed among 9/11 agents in the *Inventory* [NIOSH 2018]. All studies used exposure indices for WTC dust that were derived from self-reported information. Data that are obtained directly from study participants are subject to potential bias from inaccurate recall. Differential self-reporting of exposure status has not been ruled out as a potential explanation of an observed exposure-response association. Dust-related exposure indices varied by study, using combinations of sparse information on time (e.g., dates worked) and location to classify persons in either dichotomous or ordinal dust exposure categories, increasing uncertainty in comparisons. Exposure misclassification (i.e., errors in the exposure assignment) is likely. There were no efforts to validate classifications or to assess the potential bias from exposure misclassification in any study assessed in this evaluation. Overall, systematic bias assessment is lacking from the research even though adverse effects from exposure typically appear modest and therefore most vulnerable to bias. Future research that examines the potential for bias in risk estimates from exposure measurement errors is needed to elucidate a causal association between 9/11 exposure and IHD.

Information on injuries was limited to self-reported information on the number and, in some cases, the type of injury (e.g., laceration, burn). Information on the severity, body area, extent of treatment required, and length of disability was not available. Exposure misclassification is likely and differential self-reporting of injury status cannot be ruled out as a possible explanation of an observed exposure-response association. There were no efforts to validate classifications or to assess the extent of potential bias from exposure misclassification. Mechanisms of injury-related CVD in the absence of physical disability and chronic stress are not clear. Finally, the interrelationship between particulate exposures, injury, and PTSD is not clear. For example, those who experienced higher injury counts may also have had higher exposure to other 9/11 agents.

c. Other Risk Factors

Most studies used stratified analyses to address potential effect modification (e.g., sex, age) and all studies controlled for confounding from several known CVD risk factors; however, such risk factors varied by study. Except for studies relying exclusively on self-reported WTCHR information, information on risk factors relied on both self-reports (e.g., smoking) and medical records assessment. Self-reported information is subject to potential bias from inaccurate recall. Misclassification is likely and differential misclassification cannot be ruled out. Most studies controlled for smoking, obesity, and hypertension. Although study authors made extensive efforts to control for confounding, the potential for residual confounding from unmeasured risk factors (e.g., family history, hypercholesterolemia, and dyslipidemia) remains. Interestingly, one study of general responders [Sloan et al. 2021] found that controlling for employment in protective services on September 11, 2001, substantively attenuated estimates of the excess cardiovascular risk observed from environmental exposure. *See* **Table 16**. This finding is supported by a high prevalence of CVD risk factors commonly observed among firefighters, which when coupled with other factors associated with firefighting, help to explain why CVD is a leading cause of line of duty death [Soteriades et al. 2011]. Furthermore, analyses that include covariate control may still suffer from residual confounding because of limited data and model misspecification. For example, the same study of general responders noted assumptions necessary for the regression methods used may have been invalid, suggesting cautious interpretation of cardiovascular risk estimates [Sloan et al. 2021]. Given the relatively small effect sizes reported for primary exposures, bias might fully explain existing findings.

3. Study Representativeness

As explained in Section IX.A.3., the Science Team assessed whether the 14 high-quality studies, taken together, represent both WTC responder and survivor populations. Among the 14 high-quality studies, three included only FDNY responders [Cohen et al. 2019; Colbeth et al. 2020; Mueller et al. 2024]. Three other studies included only GRC responders [Remch et al. 2018; Sloan et al. 2021; Krasnov et al. 2025]. Six studies included both responders and survivors enrolled in the WTCHR [Jordan et al. 2011b; Jordan et al. 2013; Brackbill et al. 2014; Alper et al. 2017; Jordan et al. 2018; Alper et al. 2021]. One study included only survivors enrolled in the WTCHR [Brackbill et al. 2006]. Finally, one study included FDNY responders, GRC responders and responders enrolled in the WTCHR [Li et al. 2023].

All 14 high quality studies included only those who were exposed in the New York City disaster area (as defined in 42 C.F.R. § 88.1). Although the Science Team is unaware of any IHD studies involving responders at the Pentagon site, or Shanksville, Pennsylvania site, the Science Team has no reason to assume that their 9/11-related IHD risks would differ from responders in the New York City disaster area. As such, the Science Team concluded that there was representation of all groups of 9/11-exposed populations.

4. Consideration of Biological Plausibility, Coherence, and Analogy

The evaluation assesses studies primarily examining associations between 9/11 CVD outcomes (mostly IHD) and 9/11 exposures to hazards listed in the *Inventory* [NIOSH 2018]. Among listed 9/11 agents, $PM_{2.5}$ in WTC dust and "sustained injury on September 11, 2001," were considered most relevant; however, it is noted that other hazards may have an important role in IHD risk. Therefore, the Science Team also considered biological plausibility of other 9/11 agents, such as chemical cardiovascular toxicants, which are briefly discussed in this section. The selected literature for each cause and effect was examined to determine significant deterrents (if any) to biological plausibility.

a. Particulate Matter

There is a large body of evidence linking short-term (i.e., hours up to approximately 1 month) and long-term (i.e., 1 month to years) exposures to PM from ambient air pollution with increased CVD, including IHD [Brook et al. 2004; Brook et al. 2010; Cohen et al. 2017; Thurston et al. 2017; EPA 2019; Newman et al. 2020; EPA 2025]. The *ISA* published by the EPA in 2019 provided the scientific foundation for the National Ambient Air Quality Standard (NAAQS) [EPA 2019]. It documents a comprehensive evaluation and synthesis of the epidemiologic and toxicologic literature published from January 1, 2009, through March 31, 2017, that supports the conclusion that there is a causal relationship between short- and long-term $PM_{2.5}$ exposure and adverse cardiovascular effects, including IHD [EPA 2019, 2025]. Suggested causal pathways include respiratory tract inflammation leading to systemic inflammation and oxidative stress or modulation of the autonomic nervous system.

Although a causal relationship between environmental exposures to $PM_{2.5}$ and CVD was recognized in the *ISA*, few studies have examined the temporality of the exposure and response, which is an important area of uncertainty. Most short-term exposure studies have examined the association between air pollution events and hospital admissions or emergency room visits to treat relatively immediate cardiovascular effects (i.e., appearing within 0–5 days of exposure) [EPA 2019]. There is no information on the relevant biologic period for potential delayed effects, which are of greater interest in the 9/11 population. Moreover, exposures to low levels of $PM_{2.5}$ found in environmental air pollution markedly differ both chemically and physically from 9/11 exposures. Persons exposed to the dust and debris cloud on September 11, 2001, were acutely exposed to a unique mixture of chemicals and PM consisting mostly of pulverized cement, glass, and building materials as coarse particles in an alkaline (pH 9.0–11.0) matrix [Landrigan et al. 2004]. In samples of settled WTC dust, 0.88% to 1.98% of the total mass was from particles < 2.5 µm in aerodynamic diameter and more than 95% of the mass was > 10 µm in diameter [Lioy et al. 2002; Landrigan et al. 2004]. The coherence between observations in

populations exposed to air pollution and the 9/11-exposed population is largely uncertain given substantial differences in exposure composition, duration, and intensity.

b. Chemical Cardiovascular Toxicants

In addition to PM, WTC dust may contain other cardiotoxic agents. There is sparse information on chemical agents that may be linked to cardiotoxic effects. For example, there is emerging evidence suggesting that exposure to environmental toxicants such as polychlorinated biphenyls, polycyclic aromatic hydrocarbons (PAHs), and metals (primarily arsenic, cadmium, and lead) may be causally associated with adverse cardiovascular outcomes [Lind et al. 2021; Habeeb et al. 2022]. To facilitate a systematic assessment of cardiovascular hazards, Lind et al. [2021] defined a set of key characteristics (KCs) of chemical and nonchemical agents known to cause cardiovascular toxicity. The KCs were grouped by those primarily a□ecting cardiac tissues (1 through 4 below), affecting the vascular system (5 through 7), or affecting both (8 through 12), as follows: (1) impairs regulation of cardiac excitability; (2) impairs cardiac contractility and relaxation; (3) induces cardiomyocyte injury and death; (4) induces proliferation of valve stroma; (5) impacts endothelial and vascular function; (6) alters hemostasis; (7) causes dyslipidemia; (8) impairs mitochondrial function; (9) modifies autonomic nervous system activity; (10) induces oxidative stress; (11) causes inflammation; and (12) alters hormone signaling. In reviewing the literature and applying the KCs, Lind et al. [2021] concluded there is evidence of KCs 7, 10, 11, and 12 for dioxin-like polychlorinated biphenyls; KCs 5, 6, 7, 10, and 11 for environmental arsenic exposures; and lead exhibits KCs 1, 2, 5, 7, 8, 10, 11, and 12. While these chemical agents are 9/11 agents, causal relationships have not been definitively established.

c. Other Related Research

The Science Team also evaluated pertinent information from other 9/11-related peer-reviewed, published research. This information stemmed primarily from epidemiologic and toxicologic studies on CVD-related conditions, mechanisms, or risk factors included in information submitted by petitioners (as explained earlier in Section IV.B.). The information provided by these studies contributed mostly to the assessment of biological plausibility, coherence, and analogy.

(1) Post-Traumatic Stress Disorder (PTSD)

PTSD is a mental health disorder that can arise in persons exposed to traumatic events, such as the September 11, 2001, terrorist attacks. PTSD is consistently among the most prevalent health conditions for which the WTC Health Program members are certified. Being caught in the dust cloud (an exposure proxy that was used in several exposure-response analyses) has been

identified as an independent predictor of PTSD [DiGrande et al. 2011]. Studies have also linked PTSD to CVD [Boscarino 2012], as well as to several biological, psychosocial, and behavioral factors (e.g., hypertension, depression, smoking, alcohol use) related to CVD [Scherrer et al. 2019].

Although the relationship between PTSD and IHD in the 9/11-exposed population remains uncertain, there is a growing body of evidence supporting PTSD and other stress disorders as potential cardiovascular risk factors and mediators. However, questions remain whether associations are causal or confounded [Dedert et al. 2010; O'Donnell et al. 2021]. In the reviewed studies, the Science Team examined the confounding, modifying, or mediating effects of PTSD on the causal association between 9/11 exposure and IHD. Papers that assessed only the association between PTSD and IHD in the 9/11 population and did not also assess 9/11 exposures were not reviewed because such studies cannot provide evidence in support of a causal association between 9/11 exposures and IHD. Among the seven high-quality studies that assessed CVD outcomes among 9/11-exposed populations with possible PTSD [Jordan et al. 2011b; Jordan et al. 2013; Brackbill et al. 2014; Alper et al. 2017; Remch et al. 2018; Cohen et al. 2019; Alper et al. 2021], the findings provided some evidence of a causal association between PTSD and CVD but were inconsistent. Five studies found statistically significant positive associations between probable PTSD and CVD outcomes [Jordan et al. 2011b; Jordan et al. 2013; Brackbill et al. 2014; Remch et al. 2018; Alper et al. 2021], whereas the two other studies found little evidence of such an association [Alper et al. 2017; Cohen et al. 2019].

Another study, Adams and Allwood [2024], used parallel process latent growth modeling, a statistical method used to estimate simultaneous growth trajectories of two or more variables and examine their relationships over time, to evaluate the evolution of PTSD and cardiometabolic conditions (MetC) among 35,788 enrollees in the WTCHR. MetC included the self-report of doctor-diagnosed conditions or the use of prescription medications for heart disease, hypertension, angina, high cholesterol, heart attack, stroke, or diabetes, while PTSD symptoms were measured using the 9/11-specific PTSD Checklist (PCL-S) [Wilkins et al. 2011]. The authors reported a unidirectional relationship in which PTSD symptoms partially predict early presentations and growth of MetC, after controlling for age, sex, race/ethnicity, preexisting traumas, physical health problems, general psychological distress, smoking, and alcohol use. Hyperarousal ($\beta = 0.172$) and emotional numbing ($\beta = 0.171$), symptoms of PTSD, showed the most significant association with changes in MetC, even after accounting

for control variables and potential confounding factors. *Post hoc* analyses revealed that the use of PTSD-related psychotherapy was linked to a reduction in early presentations of MetC following trauma. This study, however, failed to account for the effect of 9/11 exposures, which could affect MetC and could vary by population in the WTCHR (e.g., rescue and recovery workers vs. passersby). In addition, the MetC composite variable includes health conditions other than IHD.

Even if PTSD were found to cause IHD, PTSD is not a 9/11 exposure. However, when PTSD was assessed in included studies, it informed the potential for PTSD to confound, modify, or mediate an association between 9/11 exposures and IHD.

There are many limitations with how PTSD was assessed in the seven reviewed studies that examined CVD among 9/11-exposed populations with possible PTSD. For example, the presence of PTSD was based on unverified self-report rather than clinical confirmation of diagnosis. Furthermore, these seven studies assessed PTSD measured at baseline only. None took account of variations in PTSD symptoms over time, i.e., PTSD symptoms are generally not permanently fixed and instead can wax and wane over time [Maslow et al. 2015; Welch et al. 2016]. Those with higher baseline PTSD checklist (PCL) scores that wane over time may have reduced CVD risk. For example, mounting evidence suggests that CVD may be prevented through PTSD treatment [Boscarino 2012; Adams and Allwood 2024]; such treatment effects would not be detected when considering only PTSD measured at baseline. Finally, CVD events themselves can lead to the development of PTSD, such that those who experience an MI may develop subsequent PTSD [Edmondson et al. 2012]. As such, studies examining the association between PTSD and IHD need to account for temporality (i.e., whether PTSD preceded or followed the IHD event).

The Science Team's review found that the causal pathways between injury, PTSD, particulate exposures, and CVD, are not clear; therefore, model-form misspecification cannot be ruled out as a potentially important source of estimate error. This occurs when the mathematical structure of the assumed causal model substantively differs from the true biologic exposure-response relationship. This error can result in bias in either direction and will likely cause an overvaluing of estimate precision [NIOSH 2020]. More research is needed to understand and account for the effects of PTSD on the proposed association between 9/11 exposure and IHD.

(2) Psychological Stress

PTSD is not the only psychosocial factor that may impact CVD. A wide range of psychosocial factors have been investigated in relation to CVD and several negative emotional states, such as depression, anger and hostility, and anxiety, as well as chronic and acute stressors, have been found to be associated with increased risk of cardiovascular morbidity and mortality in multiple studies [Everson-Rose and Lewis 2005]. There is accumulating information indicating several psychosocial factors have direct pathophysiological effects. Stress can result in hypothalamic–pituitary–adrenal axis dysfunction, increased inflammation, and abnormal cortisol regulation, which increases the risk of CVD [Brotman et al. 2007; Steptoe and Kivimaki 2012]. Psychosocial stressors arising from 9/11 experiences may be direct acting or act through behavioral changes that mediate other factors (e.g., smoking, alcohol use, and obesity) that can increase CVD risk.

Moreover, the potential effect from stress connected to Septembers 11, 2001, is not limited to the 9/11-exposed population. For example, a national longitudinal study of mental and physical health following the September 11, 2001, terrorist attacks found that high levels of acute stress, primarily through indirect exposure through the media, was positively related to increased healthcare utilization and increases in reports of physician-diagnosed CVD and other health conditions post-September 11, 2001 [Holman et al. 2008; Holman and Silver 2011].

Acute cardiac events following the September 11, 2001, terrorist attacks that were experienced by persons located in New York City, New Jersey, the New York metropolitan area, or in upstate New York were assessed in eight studies, and the evidence of an increased risk for such acute cardiac events is equivocal [Ho et al. 2002; Chi et al. 2003a; Chi et al. 2003b; Steinberg et al. 2004; Allegra et al. 2005; Feng et al. 2006; Lin et al. 2010; Lall et al. 2011].[57] One study reported a statistically significant increase in the number of patients within a 50-mile radius of the WTC site presenting with acute MI within 60 days after the September 11, 2001, terrorist attacks compared with patients 60 days before the attacks [Allegra et al. 2005]. Another study reported increased MI and tachyarrhythmia post-September 11, 2001, in patients admitted to a coronary care unit in Brooklyn, approximately 4 miles from the WTC site [Feng et al. 2006]. However, that study also reported a decrease in post-September 11, 2001, admissions for unstable angina and other cardiac conditions.

57 Participants in these studies were not reported to be directly exposed to the September 11, 2001, terrorist attacks. It is not known if any participants in these studies were exposed to 9/11 agents identified in the Program's *Inventory* within the geographic areas identified in the WTC Health Program's eligibility criteria, therefore, they are not considered 9/11-exposed.

Another study reported increased ventricular arrythmias in patients fitted with an implantable cardioverter-defibrillator when comparing events 30 days post-September 11, 2001, with those pre-September 11, 2001 [Steinberg et al. 2004]. Another study reported evidence of immediate adverse behavioral changes (e.g., changes in sleep, alcohol, smoking, exercise, and socializing) that might have altered cardiovascular risks in persons who were present during the attacks [Ho et al. 2002]. These behaviors persisted for months after the event in nearly 40% of those experiencing changes, which suggested the potential for long-term effects on CVD risk. However, that study did not investigate correlations between changed behaviors and CVD risk. In contrast, other studies have found little evidence of increased cardiac mortality or coronary care hospital admissions in NYC for the period around September 11, 2001 [Chi et al. 2003a; Chi et al. 2003b; Lin et al. 2010; Lall et al. 2011].

Overall, the studies described in the previous two paragraphs comparing pre- and post-September 11, 2001, CVD hospital admissions, mortality, and behaviors are suggestive of a modestly increased frequency in acute CVD events that may stem from the psychological impact of exposure to acts of terrorism. This points to a plausible causal relationship between 9/11-related traumas, including those that may be identified as 9/11 agents, and IHD. However, these studies generally lacked information regarding whether study subjects were directly or indirectly exposed to the event, the patient's stress level, IHD (or specific CVD outcomes), and important risk factors that may have influenced estimates. Other sources of uncertainty include typical seasonal and diurnal variations in hospital admissions, as well as differences in baseline rates when an external referent population is used.

In summary, the evidence suggesting increased IHD risk from acute stress caused by the terrorist attacks is inconclusive. Although acute effects of psychological harm are well-documented, the effects on long-term IHD risk remain unclear. More research is needed to elucidate biological and behavioral mechanisms underlying associations between 9/11 agents that are experiences that might cause psychological harm and IHD.

(3) Obstructive Sleep Apnea

Like PTSD, OSA is included on the List of WTC-Related Health Conditions. OSA may also be linked to increased cardiometabolic risk [Wang et al. 2013; Wang et al. 2015; St-Onge et al. 2016].

Iyengar-Kapuganti et al. [2022] conducted a cross-sectional study of the association between OSA and left ventricular diastolic dysfunction (LVDD) in a convenience sample of responders.

LVDD may be among the early cardiac alterations occurring in patients with OSA, even before development of CVD. Subjects were treated at the Mount Sinai WTC Health Program Clinical Center of Excellence and had to be aged 39+ years at study enrollment which occurred between 2011 and 2014. Study participants (*n* = 1,007) were aged 51 years on average and were mostly non-Hispanic, White men. Participants with OSA were those self-reporting a physician diagnosis of OSA. Participants underwent a comprehensive cardiovascular evaluation including detailed medical history questionnaires and echocardiography with pulse-wave Doppler study; those with no reported physician-diagnosed prior OSA were screened for OSA risk using the Berlin Questionnaire (BQ), taking obesity and history of hypertension into account (*n* = 725). There were 282 patients who reported a physician-diagnosed OSA diagnosis. Among those without physician-diagnosed OSA, 274 patients were classified as having high OSA risk (i.e., two or more positive categories on the BQ), and 451 were considered as having low OSA risk as defined by the BQ. In logistic regression adjusting for waist–hip ratio, diabetes, and CAC score percentile, the odds of having LVDD were greater among those with a self-reported, physician diagnosis of OSA compared to those who screened as having low risk of OSA (OR = 1.45; 95% CI: 1.03, 2.04). Overall, the study provided evidence implicating OSA in CVD risk in the 9/11-exposed population. Still, given the cross-sectional study design and many shared risk factors for CVD, there is great uncertainty in whether the observed association is causal.

(4) Metabolic Syndrome

Metabolic syndrome (MetSyn) comprises a cluster of interrelated risk factors for CVD and type 2 diabetes mellitus, such as hypertension, dyslipidemia, hyperglycemia, and central obesity [Eckel et al. 2005; Alberti et al. 2009]. There is evidence suggesting that work-related psychological stress in law enforcement is a risk factor for MetSyn [Hartley et al. 2012; Garbarino and Magnavita 2015; Janczura et al. 2015].

Moline et al. [2016] estimated the prevalence of MetSyn in a cross-sectional study of law enforcement officers who responded to the September 11, 2001, terrorist attacks. Subjects (*n* = 2,497) were enrolled in the WTC Health Program, were aged 40 years and older, worked or volunteered at the WTC site, and were asymptomatic for CVD at the time of enrollment. Subjects underwent a one-time comprehensive evaluation of CVD risk factors for MetSyn classification. MetSyn was defined using the National Cholesterol Education Program's Adult Treatment Panel III [Grundy et al. 2005].

Prevalences were compared with an age standardized sample of national data from NHANES 2003 to 2006. Other than this external comparison, there was no attempt to relate MetSyn to gradients of WTC exposure. Participants analyzed by Moline et al. [2016] were mostly male (85%), White (69%), with an average age of 47 years. The prevalence of MetSyn in the overall study population was 27%, which was significantly lower than that observed in the national sample (45%). The observed MetSyn prevalence for this WTC-responder group appeared reasonably comparable to, but slightly lower than, most estimates from other studies of similar law enforcement officers [Hartley et al. 2012; Yoo and Franke 2013; Strauss et al. 2021]. Moline et al. [2016] provided information on the prevalence of MetSyn in a group of 9/11 responding law enforcement officers, which was less than expected when compared to the general population but within a range observed in other studies of law enforcement officers. The study did not provide evidence supporting a relationship between exposures to 9/11 agents and MetSyn or establish whether MetSyn is an intermediary between exposure and MI risk in the 9/11-exposed population.

(5) Perfluoroalkyl Substances (PFAS)

PFAS are a large group of widely used human-made chemicals that are ubiquitous in the environment (air, soil, and water) [ATSDR 2021]. PFAS are persistent in the human body, with uptake primarily through consumption of PFAS-contaminated food and water. Although the evidence on cardiovascular toxicity is equivocal, there are reports suggesting an association between PFAS exposure and alterations in serum lipid levels [ATSDR 2021]. There is also evidence of persistent increased serum PFAS levels linked to 9/11-exposures in both WTC responders and area-resident children[58] [Tao et al. 2008; Trasande et al. 2017].

Koshy et al. [2017] examined associations between PFAS serum levels and cardiometabolic markers in a cross-sectional study comparing children enrolled in the WTCHR (n = 123) with controls (n = 185) who were not eligible for WTCHR enrollment. Persons in either group who presented with a serious lung or heart condition, had heart or lung surgery, were pregnant, or were unable to undergo measurements of arterial stiffness were excluded. Eleven serum PFAS levels were measured. Koshy et al. [2017] found positive associations between perfluorooctanoic acid (PFOA) and triglycerides, total cholesterol, and LDL cholesterol, in multivariable analyses adjusting for sex, race, caloric intake, physical activity, cotinine concentration, and BMI. In addition,

58 "Children" means children who participated in the WTCHR and were born between September 11, 1993, and September 10, 2001. *See* Trasande et al. [2017].

PFOA and perfluorononanoic acid (PFNA) serum levels were associated with increased brachial artery distensibility. Overall, Koshy et al. [2017] show that PFAS serum levels were associated with increased blood lipid levels (triglycerides and cholesterol) in WTCHR children. It has been posited that abnormal lipid levels at younger ages might be early markers for increased CVD risk later in life [Pletcher et al. 2016]. Mechanisms underlying the observed associations remain unclear. The study also reported an association between higher PFOA and PFNA serum levels and increased brachial artery distensibility. The mechanisms for this association also remain unclear; however, Koshy et al. [2017] posited that PFAS exposure-induced alterations in sex hormone levels may be an influencing factor.

There were several notable study limitations of Koshy et al. [2017]. First, there were no significant differences in cardiometabolic markers between WTCHR enrollees and controls, and there was no information on the extent that any marker exceeded its normal range in either group. It remains unclear whether the small effects observed in this study are predictive of CVD later in life. Second, although there was evidence of correlations between PFAS and select markers, the lack of exposure-response information is a significant limitation in interpreting findings. Another important study limitation is the cross-sectional design, with data collection completed 15 years after 9/11 exposure. Given this design, there is a strong potential for unmeasured modifiable factors (e.g., other sources of PFAS exposure, diet, lifestyle) and temporal changes in measured factors (e.g., BMI, tobacco use, physical activity, caloric intake) that may have affected the observed PFAS serum levels and cardiometabolic markers. Residual confounding cannot be ruled out.

(6) Cardiovascular Disease Biomarkers and Lung Injury

Weiden et al. [2013] conducted a nested case-control study of FDNY firefighters (n = 227) examining the relationship between select CVD biomarkers and lung injury. Participants were drawn from a cohort of never-smokers who were symptomatic at a subspecialty pulmonary examination between October 1, 2001, and March 10, 2008. Susceptible and resistant lung injury cases were defined by the distribution of the forced expiratory volume in 1 second (FEV_1) percent predicted. The study reported higher levels of apolipoprotein-AII, C-reactive protein, and macrophage inflammatory protein-4 among susceptible lung injury cases. In general, the study found CVD biomarkers in serum 6 months post-September 11, 2001, that were predictors of susceptibility and resistance to lung injury, suggesting the potential sharing

of pathways that might lead to vascular injury and impaired lung function. Although models controlled for categories of arrival time, the study did not examine the association between CVD biomarkers and 9/11 exposure or examine trends in CVD risk. The small sample size was another important limitation.

(7) Atherosclerotic Profiles

The small cross-sectional pilot study conducted by Mani et al. [2013] found no significant differences in multi-contrast MRI results between high and low WTC dust exposure groups. Furthermore, none of the persons in either exposure group had complex carotid artery plaques that could be classified. However, DCE-MRI results suggested that persons exposed to high levels of WTC dust may have increased plaque neovascularization when compared to those with lower exposure, which might point to a potential progression of atherosclerosis. In addition to its small size, analyses did not adjust for other group differences that may potentially bias the results. The Science Team concurred with study authors that these results are preliminary.

Knobel et al. [2024] examined the association between 9/11 exposure and select circulating cardiometabolic biomarkers among GRC participants (*n* = 22,447). The study used repeated measurements of blood glucose (*n* = 81,599) and total cholesterol (*n* = 96,155) collected from GRC members during routine monitoring visits between 2004 and 2019. Ordinal categories of 9/11 exposure (low, medium, and high) were determined from self-reported information. Concomitant $PM_{2.5}$ air pollution exposure during the observation period was estimated for each patient using a previously developed spatiotemporal prediction model. The model related estimates of pollution concentrations between 2000 and 2015, at 1 km^2 resolution, to the patient's address at the time of the monitoring visit for visits during or after 2012, and the first reported address for visits prior to 2012. Knobel et al. [2024] estimated changes in glucose and total cholesterol comparing categories of WTC exposure (low category referent) in a generalized linear mixed model (GLMM) that adjusted for sex, age, year of visit, race, education level, diabetes, hypertension, testing season, and $PM_{2.5}$ exposure averaged 6 months before the study visit, with covariate information obtained from routinely administered questionnaires. The model accounted for clustering of repeated measures among subjects as a random effect. Among blood samples, there was a slight monotonic increase in glucose levels with increase in WTC exposure, with an increase of 0.82 (95% CI: 0.22, 1.43) mg/dL when comparing high with low exposure. The exposure-response for total cholesterol was nonmonotonic,

with an increase in the intermediate category (0.99 mg/dL; 95% CI: 0.30, 1.67), but not in the high category (0.06 mg/dL; 95% CI: -0.74, 0.86). Additional analyses dichotomizing the outcome to indicate abnormally high levels of glucose (> 100 mg/dL) and total cholesterol (> 200 mg/dL) resulted in similar results. Compared with the low-exposed group, the odds of abnormal glucose (OR = 1.08; 95% CI: 1.02, 1.14) were slightly greater in the high-exposed group and slightly greater for abnormal total cholesterol (OR = 1.04; 95% CI: 1.01, 1.08) in the intermediate group.

Overall, Knobel et al. [2024] provided preliminary data showing increases in blood glucose and total cholesterol with increasing 9/11 exposure, which in turn supported the plausibility of a causal relationship between 9/11 exposure and IHD. An important study strength is the statistical power obtained from the relatively large number of blood samples taken over the follow-up period. However, there are notable limitations. First, it is not clear whether blood glucose levels were determined while fasting; therefore, interpretation of these results is considerably uncertain. Similarly, analyses did not control for the use of statins or other lipid-lowering drugs; therefore, total cholesterol results may be distorted. Third, the description of the "generalized additive linear models" used in all analyses was lacking and given its indicated complexity, the robustness of model results is uncertain. Other model forms were not tested. Fourth, information on important risk factors, such as diet, exercise, and obesity, were not considered in analyses and the observed effects from 9/11 exposure appeared very small (i.e., well within the range of laboratory precision of each marker); therefore, the potential for bias and residual confounding cannot be ruled out as alternative explanations of study findings. Finally, although the study points to a plausible biological pathway, it did not explicitly establish a link between the increases in these glucose- and lipid-related biomarkers and increased IHD risk in the 9/11-exposed population.

(8) Toxicologic Studies

Toxicologic studies provided emerging information on the potential cardiovascular toxicity of WTC dust [Tanwar et al. 2019; Hernandez et al. 2020; Veerappan et al. 2020; Park et al. 2022]. For example, a study exposing rats to WTC dust found that acute exposures to WTC dust impacted gene expression in cardiovascular tissues [Park et al. 2022]. The authors posited that the affected genes could influence several cardiovascular functions, including CAD, heart development, cardiac fibrosis, myocardial hypertrophy, myocardial infarction, and heart failure. Interestingly, the dysregulated expression manifested a year after exposure,

suggesting a potential for long-term effects from the progression of cardiac pathologies or a reflection of heart damage from earlier induction from exposure. However, the authors acknowledged several study limitations and that additional research is needed to clarify the potential for exposure-related cardiac disorders.

Another study using a mouse model found evidence of nitritive stress and inflammation in cardiovascular tissues that was related to WTC dust exposure [Hernandez et al. 2020]. Decreased nitric oxide bioavailability is an established indicator of endothelial dysfunction preceding atherosclerotic events [Naseem 2005]. Similar findings were reported in another murine model that showed exposure-induced oxidative stress and elevated soluble receptor for advanced glycation end-products (sRAGE) expression, as well as vascular dysfunction and tissue remodeling [Veerappan et al. 2020]. Levels of sRAGE in plasma have been linked to several late age diseases, including CVD [Falcone et al. 2005; Sharifi-Zahabi et al. 2021]. Veerappan et al. [2020] found that mice exposed to WTC dust presented with changes of the pulmonary artery, aortic, and ventricular hemodynamics. In a non-peer-reviewed meeting abstract, Tanwar et al. [2019] reported an association between WTC dust exposure and altered gene expression profiles related to cardiac health. These preliminary findings showed a potential for exposure-related cardiac dysfunction. However, study limitations were not discussed, and a full-text peer-reviewed article was not published by the authors.

Collectively, these toxicologic studies offered information on potential biological pathways for 9/11 exposure-induced CVD; however, more research is needed to unequivocally establish and clarify cardiovascular pathologies from exposure to WTC dust. A significant limitation shared by these studies is the considerably large uncertainty in extrapolating observations in experimental animals to risk in humans.

C. Summary of Evaluation and Evidence Synthesis

1. General Discussion

The Science Team identified 14 high-quality studies published between September 2001 and May 2026 for evaluation [Brackbill et al. 2006; Jordan et al. 2011b; Jordan et al. 2013; Brackbill et al. 2014; Alper et al. 2017; Jordan et al. 2018; Remch et al. 2018; Cohen et al. 2019; Colbeth et al. 2020; Alper et al. 2021; Sloan et al. 2021; Li et al. 2023; Mueller et al. 2024; Krasnov et al. 2025].

The evidence from longitudinal studies that examined IHD specifically were preferred for causal inference. This group comprised three studies of WTCHR enrollees [Jordan et al. 2013; Alper et al. 2017; Alper et al. 2021]. Jordan et al. [2013] examined objectively-measured CAD incidence among WTCHR rescue/recovery workers and reported positive associations between the overall

level of exposure and CAD hospitalizations in both men and women; however, only small numbers of hospitalizations were available and point estimates and trends across exposure categories were not statistically significant. In contrast, Jordan et al. [2013] found no evidence of association in similar analyses restricted to WTCHR members not classified as rescue/recovery workers. Jordan et al. [2013] also replicated analyses for all heart disease hospitalizations combined, providing risk estimates that were attenuated, but similar to those from CAD-only analyses. When using heart disease hospitalizations as the outcome, the risk estimate comparing high- and low-exposed groups of male rescue/recovery workers was statistically significant and indicated a relative risk in the high-exposed group of nearly two-fold.

Alper et al. [2017] examined the association between acute exposure to WTC dust/debris and self-reported angina and MI combined and found no evidence of an association. However, that study found a statistically significant strong exposure-response association between the number of injury types reported on the Wave 1 survey and self-reported angina and MI combined among WTCHR enrollees. Information on injury cause, body location, and treatment was not available.

Alper et al. [2021] evaluated the agreement between self-report and hospitalization data sources for heart attack among WTCHR enrollees, reporting no association between dust cloud exposure and heart attack, using either one of these outcomes' sources. Conversely, the study found an association between witnessing three or more traumatic events and elevated heart attack risk, but the risk was significantly elevated only for self-reported heart attack. The authors reported inconsistent findings regarding the association between sustaining an injury and heart attack, as an elevated risk was observed only for self-reported heart attack (there was no elevated risk for heart attacks identified using hospital discharge data).

The remaining 11 high-quality studies examined risk using only composite outcomes that included IHD. Six of these 11 studies reported at least one statistically significant positive association between a measure of WTC dust exposure and the composite outcome [Jordan et al. 2011b; Brackbill et al. 2014; Cohen et al. 2019; Sloan et al. 2021; Li et al. 2023; Mueller et al. 2024] compared with five studies that did not find statistically significant increased risk [Brackbill et al. 2006; Jordan et al. 2018; Remch et al. 2018; Colbeth et al. 2020; Krasnow et al. 2025]. Modest positive associations between proxies for WTC dust exposure and CVD outcomes were observed in responders, rescue/recovery workers, or rescue/recovery workers and residents combined. Among these studies reporting at least one positive association, the most persuasive evidence of a causal association between PM exposure and IHD in the 9/11-exposed population stemmed from studies of rescue/recovery workers [Jordan et al. 2011b], general responders [Sloan et al. 2021], and FDNY firefighters [Cohen et al. 2019]. These longitudinal studies were well-designed and examined large populations over long periods. Collectively, they reported comparable estimates of statistically significant modest excess exposure-related CVD risk in mostly male responders despite different study designs, populations, and definitions of CVD.

There were fewer studies examining the association between 9/11 injury and CVD outcomes, including IHD. Overall, results were inconsistent. Four studies of WTCHR enrollees reported at least one positive association [Jordan et al. 2011b; Brackbill et al. 2014; Alper et al. 2017; Alper et al. 2021], while two studies did not [Jordan et al. 2013; Krasnov et al. 2025]. Of note, there was no evidence of an association between injury and heart disease in a study using hospital discharge records as an objective outcome measure [Jordan et al. 2013], while a significant association was observed in the previous study using self-reported information [Jordan et al. 2011b]. Moreover, Alper et al. [2021] reported inconsistent findings, observing a significant association between injury and self-reported heart attack, but no association when heart attack was identified using hospital discharge data. An important limitation shared by all studies is a lack of information on injury severity, body location, the circumstances of the injury, and any subsequent treatment, hospitalization, or disability. Thus, the circumstances and mechanisms for injury-related IHD risk cannot be fully elucidated. Questions remain regarding whether injury sustained on September 11, 2001, is an independent risk factor for IHD, or acts through other potential cardiovascular risk factors, such as PTSD.

Collectively, the 14 high-quality studies reviewed in this section contributed evidence supporting a conclusion that a causal association between 9/11 exposures (including exposures to 9/11 agents that are chemical hazards and experiences that may cause psychological harm) and IHD is plausible. Among 9/11 exposures, the observed effect appeared stronger for injury (positive RR estimates ranging between 1.28 and 6.8) than for WTC dust exposures (positive RR estimates ranging between 1.1 and 1.61). Still, there were many inconsistencies among findings within and between studies that support a conclusion that alternative explanations of findings, such as confounding and bias, are also plausible.

2. Sources of Uncertainty

Identified sources of uncertainty based on the Science Team's review are discussed below. Additional sources of uncertainty may exist.

a. The assessed health conditions differed across studies.

Most studies examined a heterogenous composite outcome comprising several CVD endpoints (e.g., MI, stroke, arrhythmia, and heart valve complications). The etiology and pathophysiology of individual health conditions within the composite can vary, which introduces uncertainty in interpreting observed associations and comparing findings across studies regarding a causal association between 9/11 exposure and IHD.

b. Objective measures of the exposure and outcome in risk models were sparse.

All exposure-response analyses relied on crude proxies for exposure to 9/11 agents based on self-reported information. Many studies also used self-reported information for the outcome definition. Although

errors from recall might be differential with respect to exposure or the outcome, there were few attempts to validate data or assess the potential bias that may ensue from misclassification of the exposure or the outcome [Alper et al. 2021]. Without an assessment of potential bias, ascertainment error and exposure misclassification cannot be ruled out as alternative explanations of study findings [NIOSH 2020].

c. **There is evidence linking other WTC-related health conditions to CVD, including IHD.**

Studies have reported evidence suggesting associations between 9/11 exposure and OSA in responder and survivor populations [Webber et al. 2011; Glaser et al. 2014; Ahuja et al. 2018] and between OSA and cardiometabolic risk [Wang et al. 2013; Wang et al. 2015; St-Onge et al. 2016]. Similarly, associations have been observed between 9/11 exposure and gastroesophageal reflux disease (GERD) [Li et al. 2011; Lin et al. 2017], between GERD and other WTC-related health conditions, such as asthma, psychological disorders (e.g., PTSD, depression and alcohol use disorder), lower respiratory disease [Havermann et al. 2007; de la Hoz et al. 2008; Mizyed et al. 2009; Li et al. 2011; Li et al. 2017], and between GERD and IHD outcomes [Chen et al. 2016; Song et al. 2022; Brackbill et al. 2025]. This is not surprising given that several WTC-related health conditions, as well as other health conditions, share many important risk factors with IHD. However, data are insufficient to determine whether these health conditions are independent risk factors for IHD or reside on the causal pathway. Therefore, without a firm understanding of causal mechanisms and complete information on important comorbidities and the roles they play, the presence of a causal association between 9/11 exposure and CVD outcomes, including IHD, remains unclear.

d. **Estimates of the relative risk of CVD (including IHD) from 9/11 inhalation exposures were generally modest.**

The relative risk of CVD from 9/11 inhalation exposures were smaller than those for common modifiable CVD risks factors (e.g., tobacco smoking, dyslipidemia, diabetes mellitus, and obesity). Small effects are more prone to confounding, bias, and random error that may fully explain study findings.

e. **Causal mechanisms between 9/11 exposures and CVD (including IHD) remain unclear.**

Evidence supportive of an association between $PM_{2.5}$ and CVD stems primarily from studies indicating cardiotoxic effects within days of exposure to fine $PM_{2.5}$ in ambient air pollution [EPA 2019, 2022]. In contrast, persons exposed to the dust and debris cloud on September 11, 2001, were acutely exposed to mostly large (coarse) PM [Lioy et al. 2002; Lioy and Georgopoulos 2006] and the subsequent high-quality studies examining CVD risk in the 9/11-exposed population are focused

on later effects occurring years after exposure. Given widely differing exposure and outcome scenarios, extrapolation of risk is uncertain.

Similarly, there is little known about causal mechanisms in 9/11 injury-related CVD. Information on 9/11 injuries was not sufficient to examine whether the observed association was independent of other causes or was attributable to induced psychological trauma (e.g., PTSD), disability resulting in changes in behaviors linked to CVD (e.g., smoking, alcohol consumption, sedentary lifestyle, or diet), or other related causes occurring after injury that might have increased CVD disease risk.

f. **The ability to examine risk of exposure-related CVD (including IHD) using mortality as an endpoint is limited.**

The potential for selection bias in studies using an external control group is strong given differences in survival. The 9/11-exposed population has a relatively low mortality rate due to the relatively young age at the time of the September 11, 2001, terrorist attacks and improved access to treatment and care from the WTC Health Program. Moreover, fewer deaths available for study means decreased power to observe an effect and may lead to an under-estimate of CVD risk.

g. **The relationship between PTSD and CVD (including IHD) in the 9/11-exposed population remains uncertain.**

The Science Team's review indicated that PTSD may confound, moderate, or mediate the causal relationship between 9/11 exposure and IHD. The underlying causal pathways — reflecting complex interconnections among injury, PTSD, particulate exposures, and CVD — remain uncertain. As a result, the possibility of model-form misspecification cannot be dismissed. This type of error occurs when the mathematical structure of the assumed causal model does not accurately represent the true biological exposure and response relationship and will likely cause an overvaluing of estimate precision [NIOSH 2020]. Additional research is needed to clarify and account for the role of PTSD in the proposed association between 9/11 exposure and IHD.

A summary of the factors used in the Science Team's evaluation and synthesis of the 14 high-quality studies is provided in **Table 21**.

X. CONCLUSION

Based on its evaluation, the Science Team concludes that the proposed causal relationship between 9/11 exposures and IHD (ICD-10 codes I20–I22, and I24–I25) is consistent with existing biological and medical knowledge; therefore, the causal association is considered biologically plausible. However, the current evidence is not sufficient to support a reasonable conclusion that there is a *substantial* or *high likelihood* of a causal association. This review has found inconsistences between studies, small effects that are vulnerable to bias, and weak evidence of temporality and biological gradient. The Science Team finds that

the observed association between 9/11 exposure and IHD is at least as likely to be explained by chance, bias, or confounding. Therefore, the Science Team concludes there is *limited evidence* of a causal association between 9/11 exposures and IHD (Category III).[59]

59 *See* Policy and Procedures, Section V.C. [NIOSH 2026b].

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Trasande L, Koshy TT, Gilbert J, et al. [2017]. Serum perfluoroalkyl substances in children exposed to the World Trade Center disaster. Environ Res *154*:212–221, https://doi.org/10.1016/j.envres.2017.01.008.

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Veerappan A, Oskuei A, Crowley G, et al. [2020]. World Trade Center-cardiorespiratory and vascular dysfunction: Assessing the phenotype and metabolome of a murine particulate matter exposure model. Sci Rep *10*(1):3130, https://doi.org/10.1038/s41598-020-58717-w.

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Visseren FLJ, Mach F, Smulders YM, et al. [2021]. 2021 ESC Guidelines on cardiovascular disease prevention in clinical practice. Eur Heart J *42*(34):3227–3337, https://doi.org/10.1093/eurheartj/ehab484.

Vogel B, Acevedo M, Appelman Y, et al. [2021]. The Lancet women and cardiovascular disease Commission: Reducing the global burden by 2030. Lancet *397*(10292):2385–2438, https://doi.org/10.1016/S0140-6736(21)00684-X.

Wanahita N, See JL, Giedd KN, et al. [2010]. No evidence of increased prevalence of premature coronary artery disease in New York City police officers as predicted by coronary artery calcium scoring. J Occup Environ Med *52*(6):661–665, https://doi.org/10.1097/JOM.0b013e3181e36457.

Wang X, Ouyang Y, Wang Z, et al. [2013]. Obstructive sleep apnea and risk of cardiovascular disease and all-cause mortality: A meta-analysis of prospective cohort studies. Int J Cardiol *169*(3):207–214, https://doi.org/10.1016/j.ijcard.2013.08.088.

Wang J, Yu W, Gao M, et al. [2015]. Impact of obstructive sleep apnea syndrome on endothelial function, arterial stiffening, and serum inflammatory markers: An updated meta-analysis and metaregression of 18 studies. J Am Heart Assoc *4*(11):e002454, https://doi.org/10.1161/JAHA.115.002454.

Ward-Caviness C [2019]. A review of gene-by-air pollution interactions for cardiovascular disease, risk factors, and biomarkers. Hum Genet *138*(6):547–561, https://doi.org/10.1007/s00439-019-02004-w.

Webber MP, Lee R, Soo J, et al. [2011]. Prevalence and incidence of high risk for obstructive sleep apnea in World Trade Center-exposed rescue/recovery workers. Sleep Breath *15*(3):283–294, https://doi.org/10.1007/s11325-010-0379-7.

Weichenthal S, Lavigne E, Traub A, et al [2021]. Association of sulfur, transition metals, and the oxidative potential of outdoor $PM_{2.5}$ with acute cardiovascular events: A case-crossover study of Canadian adults. Environ Health Perspect *129*(10):107005, https://pmc.ncbi.nlm.nih.gov/articles/PMC8513754/pdf/ehp9449.pdf.

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Welch AE, Caramanica K, Maslow CB, et al. [2016]. Trajectories of PTSD among Lower Manhattan residents and area workers following the 2001 World Trade Center disaster, 2003-2012. J Trauma Stress *29*(2):158–166, https://doi.org/10.1002/jts.22090.

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Yu S, Alper HE, Nguyen AM, Brackbill RM [2018]. Risk of stroke among survivors of the September 11, 2001, World Trade Center disaster. J Occup Environ Med *60*(8):e371–e376, https://doi.org/10.1097/JOM.0000000000001361.

Yu S, Alper HE, Nguyen AM, et al. [2021]. Stroke hospitalizations, posttraumatic stress disorder, and 9/11-related dust exposure: Results from the World Trade Center Health Registry. Am J Ind Med *64*(10):827–836, https://doi.org/10.1002/ajim.23271.

Zaman S, Wasfy JH, Kapil V, Ziaeian B, et al. [2025]. The Lancet Commission on rethinking coronary artery disease: Moving from ischaemia to atheroma. Lancet *405*(10486):1264–1312, https://doi.org/10.1016/S0140-6736(25)00055-8.

APPENDIX — TABLES

Table 1a. Information Provided by the Petitioners and Medical Basis Determination.

Petition Number	Information Provided in Each Petition	Medical Basis[1] (Yes/No)
Petition 024	1. Cohen HW, Zeig-Owens R, Joe C, et al. [2019]. Long-term cardiovascular disease risk among firefighters after the World Trade Center disaster. JAMA Network Open *2*(9):e199775, https://doi.org/10.1001/jamanetworkopen.2019.9775	Yes
Petition 042	1. Alper HE, Yu S, Stellman SD, Brackbill RM [2017]. Injury, intense dust exposure, and chronic disease among survivors of the World Trade Center terrorist attacks of September 11, 2001. Inj Epidemiol *4*(1):17, https://doi.org/10.1186/s40621-017-0115-x	Yes
	2. Cohen HW, Zeig-Owens R, Joe C, et al. [2019]. Long-term cardiovascular disease risk among firefighters after the World Trade Center disaster. JAMA Network Open *2*(9):e199775, https://doi.org/10.1001/jamanetworkopen.2019.9775	Yes
	3. Sloan NL, Shapiro MZ, Sabra A, et al. [2021]. Cardiovascular disease in the World Trade Center Health Program General Responder Cohort. Am J Ind Med *64*(2):97–107, https://doi.org/10.1002/ajim.23207	Yes
	4. Park SH, Lu Y, Shao Y, et al. [2022]. Longitudinal impact of WTC dust inhalation on rat cardiac tissue transcriptomic profiles. Int J Environ Res Public Health *19*(2):919, https://pmc.ncbi.nlm.nih.gov/articles/PMC8776213/	No
	5. Iyengar-Kapuganti RL, Maceda CS, Croft LB, et al. [2022]. Obstructive sleep apnoea and left ventricular diastolic dysfunction among first responders to the 9/11 World Trade Center terrorist attack: a cross-sectional study. BMJ Open *12*:e058366. https://doi.org/10.1136/bmjopen-2021-058366	No
	6. Iyengar R, Maceda C, McLaughlin M [2017]. Exposure to particulate matter in World Trade Center law enforcement and its relationship to cardiovascular risk. J Am Coll Cardiol *69*(Suppl 11):1781, https://doi.org/10.1016/S0735-1097(17)35170-7	No

Petition Number	Information Provided in Each Petition	Medical Basis[1] (Yes/No)
Petition 042 (cont.)	7. Koshy TT, Attina TM, Ghassabian A, et al. [2017]. Serum perfluoroalkyl substances and cardiometabolic consequences in adolescents exposed to the World Trade Center disaster and a matched comparison group. Environ Int *109*:128–135, https://doi.org/10.1016/j.envint.2017.08.003	No
	8. Mears MJ, Aslaner DM, Barson CT, et al. [2022]. Health effects following exposure to dust from the World Trade Center disaster: An update. Life Sci *289*:120147, https://doi.org/10.1016/j.lfs.2021.120147	Yes
	9. Moline JM, McLaughlin MA, Sawit ST, et al. [2016]. The prevalence of metabolic syndrome among law enforcement officers who responded to the 9/11 World Trade Center attacks. Am J Ind Med *59*(9):752–760, http://doi.org/10.1002/ajim.22649	No
	10. Remch M, Laskaris Z, Flory J, et al. [2018]. Post-traumatic stress disorder and cardiovascular diseases: A cohort study of men and women involved in cleaning the debris of the World Trade Center complex. Circ Cardiovasc Qual Outcomes *11*(7):e004572, https://doi.org/10.1161/CIRCOUTCOMES.117.004572	Yes
	11. Tanwar V, Bhattacharya S, Rustagi S, et al. [2019]. Exposure to WTC dust alters rat cardiac gap junctional proteins. FASEB J *33*(S1):531.515, https://doi.org/10.1096/fasebj.2019.33.1_supplement.531.15	No
	12. Veerappan A, Oskuei A, Crowley G, et al. [2020]. World Trade Center-cardiorespiratory and vascular dysfunction: Assessing the phenotype and metabolome of a murine particulate matter exposure model. Sci Rep *10*(1):3130, https://doi.org/10.1038/s41598-020-58717-w	No
Petition 046	1. Cohen HW, Zeig-Owens R, Joe C, et al. [2019]. Long-term cardiovascular disease risk among firefighters after the World Trade Center disaster. JAMA Network Open *2*(9):e199775, https://doi.org/10.1001/jamanetworkopen.2019.9775	Yes
Petition 047	1. Jordan HT, Miller-Archie SA, Cone JE, et al. [2011b]. Heart disease among adults exposed to the September 11, 2001 World Trade Center disaster: results from the World Trade Center Health Registry. Prev Med *53*(6):370–376, https://doi.org/10.1016/j.ypmed.2011.10.014	No

Petition Number	Information Provided in Each Petition	Medical Basis[1] (Yes/No)
Petition 047 (cont.)	2. Jordan HT, Stellman SD, Morabia A, et al. [2013]. Cardiovascular disease hospitalizations in relation to exposure to the September 11, 2001 World Trade Center disaster and posttraumatic stress disorder. J Am Heart Assoc *2*(5):e000431, https://doi.org/10.1161/JAHA.113.000431	No
	3. Brackbill RM, Cone JE, Farfel MR, Stellman SD [2014]. Chronic physical health consequences of being injured during the terrorist attacks on World Trade Center on September 11, 2001. Am J Epidemiol *179*(9):1076–1085, https://doi.org/10.1093/aje/kwu022	No
	4. Jordan HT, Stein CR, Li J, et al. [2018]. Mortality among rescue and recovery workers and community members exposed to the September 11, 2001 World Trade Center terrorist attacks, 2003-2014. Environ Res *163*:270–279, https://doi.org/10.1016/j.envres.2018.01.004	Yes
	5. Alper HE, Yu S, Stellman SD, Brackbill RM [2017]. Injury, intense dust exposure, and chronic disease among survivors of the World Trade Center terrorist attacks of September 11, 2001. Inj Epidemiol *4*(1):17, https://doi.org/10.1186/s40621-017-0115-x	Yes
	6. Cohen HW, Zeig-Owens R, Joe C, et al. [2019]. Long-term cardiovascular disease risk among firefighters after the World Trade Center disaster. JAMA Network Open *2*(9):e199775, https://doi.org/10.1001/jamanetworkopen.2019.9775	Yes
	7. Sloan NL, Shapiro MZ, Sabra A, et al. [2021]. Cardiovascular disease in the World Trade Center Health Program General Responder Cohort. Am J Ind Med *64*(2):97–107, https://doi.org/10.1002/ajim.23207	Yes
	8. Li J, Hall CB, Yung J, et al. [2023]. A 15-year follow-up study of mortality in a pooled cohort of World Trade Center rescue and recovery workers. Environ Res *219*:115116, https://pmc.ncbi.nlm.nih.gov/articles/PMC12703491/	Yes
	9. Brook RD, Rajagopalan S, Pope CA 3rd, et al. [2010]. Particulate matter air pollution and cardiovascular disease: An update to the scientific statement from the American Heart Association. Circulation *121*(21):2331–2378, https://doi.org/10.1161/CIR.0b013e3181dbece1	Yes

Petition Number	Information Provided in Each Petition	Medical Basis[1] (Yes/No)
Petition 047 (cont.)	10. Newby DE, Mannucci PM, Tell GS, et al. [2015]. Expert position paper on air pollution and cardiovascular disease. Eur Heart J *36*(2):83–93, https://doi.org/10.1093/eurheartj/ehu458	Yes
	11. Kaufman JD, Adar SD, Barr RG, et al. [2016]. Association between air pollution and coronary artery calcification within six metropolitan areas in the USA (the Multi-Ethnic Study of Atherosclerosis and Air Pollution): A longitudinal cohort study. Lancet *388*(10045):696–704, https://doi.org/10.1016/S0140-6736(16)00378-0	Yes
	12. Yu S, Alper HE, Nguyen AM, et al. [2021]. Stroke hospitalizations, posttraumatic stress disorder, and 9/11-related dust exposure: Results from the World Trade Center Health Registry. Am J Ind Med *64*(10):827–836, https://doi.org/10.1002/ajim.23271	No
	13. Yu S, Alper HE, Nguyen AM, Brackbill RM [2018]. Risk of stroke among survivors of the September 11, 2001, World Trade Center disaster. J Occup Environ Med *60*(8):e371–e376, https://doi.org/10.1097/JOM.0000000000001361	No
	14. Remch M, Laskaris Z, Flory J, et al. [2018]. Post-traumatic stress disorder and cardiovascular diseases: A cohort study of men and women involved in cleaning the debris of the World Trade Center complex. Circ Cardiovasc Qual Outcomes *11*(7):e004572, https://doi.org/10.1161/CIRCOUTCOMES.117.004572	Yes
	15. Wanahita N, See JL, Giedd KN, et al. [2010]. No evidence of increased prevalence of premature coronary artery disease in New York City police officers as predicted by coronary artery calcium scoring. J Occup Environ Med *52*(6):661–665, https://doi.org/10.1097/JOM.0b013e3181e36457	No
	16. Lioy PJ, Weisel CP, Millette JR, et al. [2002]. Characterization of the dust/smoke aerosol that settled east of the World Trade Center (WTC) in lower Manhattan after the collapse of the WTC 11 September 2001. Environ Health Perspect *110*(7):703–714, https://pmc.ncbi.nlm.nih.gov/articles/PMC1240917/	No

Petition Number	Information Provided in Each Petition	Medical Basis[1] (Yes/No)
Petition 047 (cont.)	17. Newman JD, Bhatt DL, Rajagopalan S, et al. [2020]. Cardiopulmonary impact of particulate air pollution in high-risk populations: JACC state-of-the-art review. J Am Coll Cardiol *76*(24):2878–2894, https://doi.org/10.1016/j.jacc.2020.10.020	Yes
	18. McGuinn L, Schneider A, McGarrah R, et al. [2019]. Association of long-term $PM_{2.5}$ exposure with traditional and novel lipid biomarkers related to cardiovascular disease risk. Environ Int *122*:193–200, https://doi.org/10.1016/j.envint.2018.11.001	No
	19. Ghio A, Soukup J, Madden M [2018]. The toxicology of air pollution predicts its epidemiology. Inhal Toxicol *30*(9–10):327–334, https://doi.org/10.1080/08958378.2018.1530316	No
	20. Ward-Caviness C [2019]. A review of gene-by-air pollution interactions for cardiovascular disease, risk factors, and biomarkers. Hum Genet *138*(6):547–561, https://doi.org/10.1007/s00439-019-02004-w	No
	21. Cascio W, Long T [2018]. Ambient air quality and cardiovascular health: Translation of environmental research for public health and clinical care. N C Med J *79*(5):306–312, https://doi.org/10.18043/ncm.79.5.306	Yes
	22. Devlin RB, Smith CB, Schmitt MT, et al. [2014]. Controlled exposure of humans with metabolic syndrome to concentrated ultrafine ambient particulate matter causes cardiovascular effects. Toxicol Sci *140*(1):61–72, https://doi.org/10.1093/toxsci/kfu063	No
	23. Jhun I, Kim J, Cho B, et al. [2019]. Synthesis of Harvard Environmental Protection Agency (EPA) Center studies on traffic-related particulate pollution and cardiovascular outcomes in the Greater Boston Area. J Air Waste Manag Assoc *69*(8):900–917, https://doi.org/10.1080/10962247.2019.1596994	No
	24. Cohen AJ, Brauer M, Burnett R, et al. [2017]. Estimates and 25-year trends of the global burden of disease attributable to ambient air pollution: An analysis of data from the Global Burden of Diseases Study 2015. Lancet *389*(10082):1907–1918, https://doi.org/10.1016/S0140-6736(17)30505-6	Yes

Petition Number	Information Provided in Each Petition	Medical Basis[1] (Yes/No)
Petition 047 (cont.)	25. Thurston GD, Kipen H, Annesi-Maesano I, et al. [2017]. A joint ERS/ATS policy statement: What constitutes an adverse health effect of air pollution? An analytical framework. Eur Respir J *49*:1600419, https://doi.org/10.1183/13993003.00419-2016	Yes
	26. EPA [2019]. Integrated Science Assessment (ISA) for Particulate Matter (Final Report, Dec 2019). Washington, DC: Environmental Protection Agency, EPA/600/R-19/188, https://hero.epa.gov/reference/6591812/	Yes
	27. Shanley RP, Hayes RB, Cromar KR, et al. [2016]. Particulate air pollution and clinical cardiovascular disease risk factors. Epidemiology *27*(2):291–298, https://pubmed.ncbi.nlm.nih.gov/26605815/	No
	28. Serra R, Abramo A, Ielapi N, et al. [2021]. Environmental pollution and peripheral artery disease. Risk Manag Healthc Policy *14*:2181–2190, https://doi.org/10.2147/RMHP.S307150	No
	29. O'Donnell CJ, Schwartz Longacre L, Cohen BE, et al. [2021]. Posttraumatic stress disorder and cardiovascular disease: State of the science, knowledge gaps, and research opportunities. JAMA Cardiol *6*(10):1207–1216, https://doi.org/10.1001/jamacardio.2021.2530	No
	30. Edmondson D, von Känel R [2017]. Post-traumatic stress disorder and cardiovascular disease. Lancet Psychiatry *4*(4):320–329, https://doi.org/10.1016/S2215-0366(16)30377-7	No
	31. Hargrave AS, Sumner JA, Ebrahimi R, Cohen BE [2022]. Posttraumatic stress disorder (PTSD) as a risk factor for cardiovascular disease: Implications for future research and clinical care. Curr Cardiol Rep *24*(12):2067–2079, https://doi.org/10.1007/s11886-022-01809-y	No
	32. Scherrer JF, Salas J, Schneider FD, et al. [2020]. PTSD improvement and incident cardiovascular disease in more than 1000 veterans. J Psychosom Res *134*:110128, https://doi.org/10.1016/j.jpsychores.2020.110128	No
	33. Beristianos MH, Yaffe K, Cohen B, Byers AL [2016]. PTSD and risk of incident cardiovascular disease in aging veterans. Am J Geriatr Psychiatry *24*(3):192–200, https://doi.org/10.1016/j.jagp.2014.12.003	No

Petition Number	Information Provided in Each Petition	Medical Basis[1] (Yes/No)
Petition 051	1. Cohen HW, Zeig-Owens R, Joe C, et al. [2019]. Long-term cardiovascular disease risk among firefighters after the World Trade Center disaster. JAMA Network Open *2*(9):e199775, https://doi.org/10.1001/jamanetworkopen.2019.9775	Yes
	2. Sloan NL, Shapiro MZ, Sabra A, et al. [2021]. Cardiovascular disease in the World Trade Center Health Program General Responder Cohort. Am J Ind Med *64*(2):97–107, https://doi.org/10.1002/ajim.23207	Yes
	3. Remch M, Laskaris Z, Flory J, et al. [2018]. Post-traumatic stress disorder and cardiovascular diseases: A cohort study of men and women involved in cleaning the debris of the World Trade Center complex. Circ Cardiovasc Qual Outcomes *11*(7):e004572, https://doi.org/10.1161/CIRCOUTCOMES.117.004572	Yes
	4. Berry C, Duncker DJ [2020]. Coronary microvascular disease: The next frontier for Cardiovascular Research. Cardiovasc Res *116*(4):737-740, https://doi.org/10.1093/cvr/cvaa035	No
Petition 056	1. Sloan NL, Shapiro MZ, Sabra A, et al. [2021]. Cardiovascular disease in the World Trade Center Health Program General Responder Cohort. Am J Ind Med *64*(2):97–107, https://doi.org/10.1002/ajim.23207	Yes
Petition 058	1. Lin S, Gomez MI, Gensburg L, et al. [2010]. Respiratory and cardiovascular hospitalizations after the World Trade Center disaster. Arch Environ Occup Health *65*(1):12–20, https://doi.org/10.1080/19338240903390230	Yes
	2. Sloan NL, Shapiro MZ, Sabra A, et al. [2021]. Cardiovascular disease in the World Trade Center Health Program General Responder Cohort. Am J Ind Med *64*(2):97–107, https://doi.org/10.1002/ajim.23207	Yes
	3. Mueller AK, Cohen H, Singh A, et al. [2024]. Self-reported cardiovascular disease in career firefighters with and without World Trade Center exposure. J Occup Environ Med *66*(2):135–140, https://doi.org/10.1097/JOM.0000000000003007	Yes

Petition Number	Information Provided in Each Petition	Medical Basis[1] (Yes/No)
Petition 058 (cont.)	4. Cohen HW, Zeig-Owens R, Joe C, et al. [2019]. Long-term cardiovascular disease risk among firefighters after the World Trade Center disaster. JAMA Network Open *2*(9):e199775, https://doi.org/10.1001/jamanetworkopen.2019.9775	Yes
Petition 067	1. Lin S, Gomez MI, Gensburg L, et al. [2010]. Respiratory and cardiovascular hospitalizations after the World Trade Center disaster. Arch Environ Occup Health *65*(1):12–20, https://doi.org/10.1080/19338240903390230	Yes

1 Medical basis must be scientific in nature and provide a positive association between the September 11, 2001, terrorist attacks and the condition to be added through published, peer-reviewed literature that has not been previously evaluated by the Program. For more information, please *see* NIOSH [2026b].

Table 1b. Studies that Provided Sufficient Medical Basis Information and Whether They Met High-Quality Study Criteria, by Petition.

	Petition 024	Petition 042	Petition 046	Petition 047	Petition 051	Petition 056	Petition 058	Petition 067	Met High Quality Study Criteria
Brook et al. [2010]				☑					
Lin et al. [2010]							☑	☑	
Newby et al. [2015]				☑					
Kaufman et al. [2016]				☑					
Alper et al. [2017]		☑		☑					☑
Cohen et al. [2017]				☑					
Thurston et al. [2017]				☑					
Cascio and Long [2018]				☑					
Jordan et al. [2018]				☑					☑
Remch et al. [2018]		☑		☑	☑				☑
Cohen et al. [2019]	☑	☑	☑	☑	☑		☑		☑
EPA [2019]				☑					
Newman et al. [2020]				☑					
Sloan et al. [2021]		☑		☑	☑	☑	☑		☑
Mears et al. [2022]		☑							
Li et al. [2023]				☑					☑
Mueller et al. [2024]							☑		☑

Table 2. Major 16, Diseases of the Heart.[1]

Minor Cause	Description	ICD 10th Revision 1999-Present
053	Rheumatic heart disease, including fever	I00-I09
054	Hypertension with heart disease	I11,I13
055	Ischemic heart disease	I20-I22, I24-I25
056	Chronic disease of endocardium	I34-I38
057	Cardiomyopathy	I42, I52.8
058	Conductive disorder	I44–I49, R00.1, R00.8
059	Other disease of the heart	I30–I33, I40, I50, I51[2], I52.0–I52.1, I97.0–I97.1, I97.8–I97.9

1 Abstracted from NIOSH LTAS 119-cause map with modification.
2 I51.3 and I51.6 have been moved to Minor Cause 059 for this evaluation.

Abbreviations: ICD, International Classification of Diseases, 10th Revision.

Table 3. Classification of Minor 055, Ischemic Heart Disease.[1]

ICD 10 code	Description
I20	Angina pectoris
I21	Acute myocardial infarction
I22	Subsequent ST elevation (STEMI) and non-ST elevation (NSTEMI) myocardial infarction
I24	Other acute ischemic heart diseases
I25	Chronic ischemic heart disease (e.g., coronary atherosclerosis, ischemic cardiomyopathy)

1 The NIOSH LTAS 119-cause map for Minor 055 also includes I51.3, intracardiac thrombosis, not elsewhere classified, and I51.6, cardiovascular disease, unspecified. These conditions were moved to Minor 059 for this evaluation to align with ICD subgroups.

Abbreviations: ICD, International Classification of Diseases, 10th Revision.

Table 4. Identified Studies Evaluated by the Science Team from Previous Petitions.

Author	Follow-up	Population	Health Condition	Characteristics	Confounding controls	9/11 Injury[1]	Dust Exposure[2]
Jordan et al. [2011a]	2003-2009	WTCHR	CVD mortality, DCERT records-based	longitudinal cohort; 41,3903 (13,337 rescue/ recovery) enrollees; 24% female (rescue recovery); 59% female (survivors)	SMRs: age, sex (by stratification) race/ethnicity, calendar period. Cox proportional hazards regression models: age, sex, race and ethnic origin, income, smoking, WTCHR recruitment source (self-identified vs list-identified), history of pre-9/11 heart disease or diabetes	+	-
Jordan et al. [2011b]	2003-2008	WTCHR	heart disease (angina, heart attack, or any other heart condition); incidence, self-report	longitudinal cohort; 39,324 adult enrollees; 38.4% female	age, sex (by stratification) race/ ethnicity, education, marital status, smoking, hypertension, diabetes mellitus, PTSD	+	+
Jordan et al. [2013]	2003-2010	WTCHR	heart disease (hypertension, acute and chronic CAD, dysrhythmia, and congestive heart failure), CAD; incidence, records-based	longitudinal cohort; 46,346 enrollees; 40.3% female	age, sex, race/ethnicity, education, smoking, hypertension, diabetes mellitus	-	+
Mani et al. [2013]	NR	GRC	multi contrast MRI and DCE-MRI, ankle-brachial index	cross-sectional; 31 law enforcement personnel; 10% female	NR	NR	+
Brackbill et al. [2014]	2003-2008[3]	WTCHR	heart disease (angina, heart attack, or any other heart condition); prevalence, self-report	cross-sectional; 14,087 adult enrollees aged <64 years, present south of Chambers Street on 9/11, and completing Waves 1 and 2; 40% female	age, sex, race/ethnicity, education, hypertension, smoking	+	+

1. Studies defined injury as having experienced at least one of the following on 9/11: cut, abrasion or puncture wound, sprain or strain, burn, broken bone or dislocation, and concussion or head injury.
2. A plus sign (+) indicates at least one statistically significant positive association, minus sign (-) indicates no associations.
3. Data collection period for administered questionnaires.

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CVD, cardiovascular disease; DCE-MRI, dynamic contrast enhanced magnetic resonance imaging; DCERT, death certificate; FDNY, Fire Department of the City of New York; EMS, emergency medical services; GRC, General Responders Cohort; IHD, ischemic heart disease; MI, myocardial infarction; MRI, magnetic resonance imaging; NR, not reported; PTSD, post-traumatic stress disorder; and WTCHR, World Trade Center Health Registry.

Table 5. Identified High-Quality Studies Not Previously Evaluated by the Science Team.

Author	Follow-up	Population	Health Condition	Characteristics	Confounding controls	9/11 Injury[1]	Dust Exposure[2]
Brackbill et al. [2006]	2003-2004[3]	WTCHR	CAD, angina, MI, stroke; incidence, self-report	cross-sectional; 8,418 adult survivor enrollees occupying damaged or collapsed buildings and completing Wave 1; 45.8% female	angina–age, sex, recruitment mode, race/ethnicity, psychological distress, smoking; CAD and MI–sex, recruitment mode	NR	-
Alper et al. [2017]	2003-2012	WTCHR	IHD (angina or MI); incidence, self-report	longitudinal cohort; 8,701 enrollees; 49% female; 69% non-Hispanic White; aged 18-64 years on 9/11	age, sex, race/ethnicity, education, smoking, hypertension, PTSD, study recruitment source, BMI	+	-
Jordan et al. [2018]	2003-2014	WTCHR	CVD mortality, DCERT records-based	longitudinal cohort; 68,923 (29,280 rescue/recovery) enrollees; 21.9% female (rescue recovery); 53.3% female (survivors)	age, sex, race/ethnicity, education, smoking, diabetes mellitus, pre-9/11 diabetes mellitus and heart disease	NR	-
Remch et al. [2018]	2012-2016	GRC	CVD (MI, stroke); incidence, self-report	longitudinal cohort; 5,971 general responders enrolled in 2012-2013; 20.8% female; 54% White; average age 51 years	age, sex, race/ethnicity, smoking, hypertension, diabetes mellitus, BMI	NR	-
Cohen et al. [2019]	2001-2017	FDNY	CVD (MI, stroke, unstable angina, coronary artery surgery or angioplasty, congestive heart failure, or CVD death); incidence, records-based	longitudinal cohort; 9,796 male firefighters; average age 40.3 years	age, sex, race/ethnicity, smoking, hypertension, diabetes mellitus, BMI, cholesterol, protective services	NR	+
Colbeth et al. [2020]	2001-2017	FDNY	CVD mortality, DCERT records-based	longitudinal cohort; 15,431 firefighters and EMS (exposure-response restricted to 15,058); 3.2% female; 87.2% non-Hispanic White; median age 39.9 years on 9/11;	age, sex, race/ethnicity, smoking, BMI, work assignment	NR	-
Alper et al. [2021]	2002-2015	WTCHR	IHD (heart attack); incidence, self-report and hospital discharge data	longitudinal cohort; 18,206 enrollees; 40% female; 70% non-Hispanic White; 51% aged 25-44 years on 9/11	age, sex, race/ethnicity, education	+/-	-

Author	Follow-up	Population	Health Condition	Characteristics	Confounding controls	9/11 Injury[1]	Dust Exposure[2]
Sloan et al. [2021]	2002-2019	GRC	CVD (CAD, MI, stroke, or congestive heart failure); incidence, self-report	longitudinal cohort; 37,725 responders; 13.7% female; 53.7% White; median age 37 years (19-80);	age, sex, race/ethnicity, smoking, hypertension, diabetes mellitus, BMI, cholesterol	NR	+
Li et al. [2023]	2001-2016	FDNY, GRC, WTCHR	CVD mortality, DCERT records-based	longitudinal cohort; 60,631 rescue/recovery workers; 15.9% female; median age 39.0 years on 9/11	age, sex, race/ethnicity, smoking status at enrollment	NR	+
Mueller et al. [2024]	2019-2021[3]	FDNY	CVD (CAD or stroke), stroke, CAD; prevalence, self-report and records-based	cross-sectional; 9,789 male FDNY firefighters and 2,729 unexposed controls; average age 40.0 years on 9/11; 94.1% non-Hispanic White	age, race/ethnicity, smoking, hypertension, diabetes mellitus, BMI	NR	+
Krasnov et al. [2025]	2003-2021	GRC	CAD; incidence, self-report	longitudinal cohort; 47,795 GRC members; 13% female; average age 40.0 years on 9/11; 52% White	age, sex, race, education, marital status, BMI, neighborhood sociodemographic variables	-	-

1. Studies defined injury as having experienced at least one of the following on 9/11: cut, abrasion or puncture wound, sprain or strain, burn, broken bone or dislocation, and concussion or head injury.
2. A plus sign (+) indicates at least one statistically significant positive association, minus sign (-) indicates no associations.
3. Data collection period for administered questionnaires.

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CVD, cardiovascular disease; DCERT, death certificate; FDNY, Fire Department of the City of New York; EMS, emergency medical services; GRC, General Responders Cohort; IHD, ischemic heart disease; MI, myocardial infarction; NR, not reported; PTSD, post-traumatic stress disorder; and WTCHR, World Trade Center Health Registry.

Table 6. Adjusted hazard ratios for heart-disease-related mortality. Adapted from Jordan et al. [2011a].

Exposure	HR (95% CI)[1]
Dust cloud exposure (all enrollees)	
Low	Reference
High	1.04 (0.77, 1.42)
Overall level of WTC exposure (non-rescue and non-recovery participants only)[2]	
Low	Reference
Intermediate	1.21 (0.80, 1.83)
High	2.06 (1.10, 3.86)

1. Models included age, sex, race and ethnic origin, income, smoking, history of pre-9/11 heart disease or diabetes. Models for non-rescue and non-recovery participants also included WTCHR recruitment source (self-identified vs list-identified).
2. *High exposure*: reported two or more injuries on 9/11; for residents in zip codes including Canal Street and south, in lower Manhattan, did not evacuate their home on 9/11; for school students and school staff south of Canal Street, were present at school on 9/11. Low exposure: reported no injuries on 9/11; for residents in zip codes including Canal Street and south, in lower Manhattan, evacuated their home on 9/11 (for any amount of time); for school students and school staff south of Canal Street, were not present at school on 9/11. Intermediate exposure: participants whose exposure level fell between high and low.

Abbreviations: CI, confidence interval; HR, hazard ratio.

Table 7. Associations between measures of 9/11 exposure and self-reported heart disease[1] among WTCHR participants aged ≥ 18 on September 11, 2001 (*n* = 39,324), New York, 2003–2008. Adapted from Jordan et al. [2011b].

	Women			Men		
Exposure	**Cases**	**HR (95% CI)[2]**	**PY**	**Cases**	**HR (95% CI)[2]**	**PY**
9/11 dust cloud exposure (all enrollees)						
Intense	141	1.28 (1.02, 1.61)	13,357	243	1.14 (0.97, 1.34)	20,371
Some	48	0.83 (0.60, 1.14)	4,247	90	1.00 (0.79, 1.25)	8,500
None	171	Reference	22,237	412	Reference	37,511
9/11 dust cloud exposure and probable PTSD (all enrollees)						
Intense	136	1.17 (0.92, 1.48)	13,002	238	1.09 (0.93, 1.29)	19,902
Some	47	0.80 (0.58, 1.11)	7,078	89	1.00 (0.80, 1.26)	8,307
None	165	Reference	21,610	400	Reference	36,816
Probable PTSD						
Yes	101	1.62 (1.26, 2.07)	7,062	126	1.56 (1.27, 1.91)	7,061
No	247	Reference	34,628	601	Reference	57,965
Injured on 9/11 (all enrollees)						
Yes	186	1.46 (1.19, 1.79)	16,298	348	1.33 (1.15, 1.53)	26,551
No	195	Reference	27,928	433	Reference	42,529
Time of arrival (rescue/recovery workers)						
9/11, on pile	4	2.25 (0.79, 6.40)	292	87	1.39 (1.04, 1.86)	7,452
9/11, another WTC site	19	1.94 (1.10, 3.40)	1,298	71	1.21 (0.89, 1.63)	5,846
9/12 – 9/17	39	1.76 (1.11, 2.77)	3,404	216	1.24 (0.98, 1.56)	17,420
9/18 – 6/2002	44	Reference	6,186	112	Reference	9,293
Damage to workplace (area workers)						
Heavy layer of dust and damage	21	1.35 (0.85, 2.14)	1,822	31	1.55 (1.03, 2.31)	2,075
Damage without heavy dust layer	31	1.23 (0.82, 1.82)	3,178	29	1.12 (0.75, 1.69)	2,864
None	128	Reference	15,501	124	Reference	13,792
Damage to home (area residents)						
Heavy layer of dust and damage	12	1.23 (0.63, 2.42)	1,543	18	2.05 (1.15, 3.67)	1,152
Damage without heavy dust layer	13	1.69 (0.87, 3.25)	1,213	7	1.09 (0.48, 2.48)	841
None	34	Reference	6,369	39	Reference	4,666

1. Heart disease defined as self-reported physician-diagnosed angina, heart attack, or other heart problem first reported on the 2006–2008 Wave 2 survey.
2. Models adjusted for age, race/ethnicity, education, marital status, smoking, hypertension, and diabetes mellitus.

Abbreviations: CI, confidence interval; HR, hazard ratio; PTSD, post-traumatic stress disorder; PY, person-years; WTC, World Trade Center; WTCHR, World Trade Center Health Registry.

Table 8. Associations of 9/11 exposures with heart disease and CAD hospitalization among WTCHR enrollees residing in New York State, 2003–2010. Adapted from Jordan et al. [2013].

	Women (n = 18,551)		Men (n = 27,511)	
Exposure	**events**	**HR (95%CI)**	**events**	**HR (95% CI)**
Heart disease hospitalizations[1]				
9/11 dust cloud exposure (all enrollees)				
Yes	178	0.96 (0.75, 1.22)	450	0.96 (0.84, 1.11)
No	118	Reference	402	Reference
Injured on 9/11 (all enrollees)				
Yes	126	0.93 (0.74, 1.19)	377	1.11 (0.97, 1.28)
No	170	Reference	478	Reference
Overall level of exposure (rescue/recovery workers: 3,634 women, 16,137 men)				
High	5	3.29 (0.85, 12.69)	82	1.82 (1.06, 3.13)
Intermediate	34	1.72 (0.60, 4.94)	407	1.63 (0.99, 2.69)
Low	4	Reference	16	Reference
p for trend		0.09		0.05
Overall level of exposure (non-rescue/recovery workers: 15,045 women, 11,530 men)				
High	20	0.88 (0.54, 1.43)	22	0.94 (0.60, 1.47)
Intermediate	125	0.94 (0.71, 1.25)	140	0.92 (0.72, 1.16)
Low	98	Reference	164	Reference
CAD only hospitalizations[1]				
9/11 dust cloud exposure (all enrollees)				
Yes	83	0.89 (0.63, 1.25)	304	1.06 (0.89, 1.25)
No	60	Reference	252	Reference
Injured on 9/11 (all enrollees)				
Yes	56	0.80 (0.57, 1.13)	247	1.11 (0.94, 1.32)
No	86	Reference	312	Reference
Overall level of exposure (rescue/recovery workers: 3,634 women, 16,137 men)				
High	2	5.52 (0.48, 63.30)	54	1.94 (0.98, 3.83)
Intermediate	19	3.61 (0.48, 27.41)	270	1.76 (0.94, 3.32)
Low	1	Reference	10	Reference
p for trend		0.14		0.11
Overall level of exposure (non-rescue/recovery workers: 15,045 women, 11,530 men)				
High	9	0.78 (0.38, 1.60)	18	1.19 (0.72, 1.98)
Intermediate	60	0.91 (0.61, 1.36)	85	0.85 (0.62, 1.15)
Low	47	Reference	104	Reference

1. Outcomes and ICD-9 codes for heart disease hospitalizations included: hypertension (401–405), acute CAD (410, 411), chronic CAD (412–414), dysrhythmia (427), and congestive heart failure (428). Outcomes and ICD-9 codes for all CAD were 410–414.

Abbreviations: CAD, coronary artery disease; CI, confidence interval; HR, hazard ratio; ICD, International Classification of Diseases; WTCHR, World Trade Center Health Registry.

Table 9. Odds ratios for associations between heart disease and probable PTSD, injuries, and dust cloud exposure in WTCHR enrollees. Adapted from Brackbill et al. [2014].

Risk factor	Events (angina, heart attack, other heart disease)	OR (95% CI)
No. injuries, subject without probable PTSD		
0	270	Referent
1	51	1.6 (1.2, 2.3)
2	15	1.5 (0.8, 2.8)
≥ 3	3	1.8 (0.5, 5.9)
No. injuries, subject with probable PTSD		
0	79	2.4 (1.8, 3.2)
1	17	2.2 (1.3, 3.8)
2	10	3.3 (1.6, 6.8)
≥ 3	3	2.9 (0.8, 10.2)
Dust/debris exposure		
Intense	238	1.3 (1.05, 1.6)
Some/none	203	Referent

Abbreviations: CI, confidence interval; OR, odds ratio; PTSD, post-traumatic stress disorder; WTCHR, World Trade Center Health Registry.

Table 10. Odds ratios[1] for self-reported cardiovascular conditions among WTCHR adult enrollees by exposure type, 2003–2004. Adapted from Brackbill et al. [2006].

		Dust and debris cloud (yes vs no) (*n* = 8,374)	Time of evacuation (before vs after collapse of the first building) (*n* = 7,873)	Building type occupied (collapsed vs damaged) (*n* = 8,418)
Self-reported exposure[2]	Number of cases[3]	OR (95% CI)	OR (95% CI)	OR (95% CI)
Coronary heart disease	40	1.6 (0.8, 3.3)[4]	0.5 (0.1, 2.2)[4]	0.8 (0.4, 1.6)[4]
Angina	31	1.0 (0.4, 2.2)	0.7 (0.2, 3.1)[4]	0.8 (0.4, 1.6)
Heart attack	30	1.7 (0.8, 3.9)[4]	ND	2.1 (0.9, 4.9)[4]

1. Logistic regression adjusted for mode of recruitment, age, race/ethnicity, sex, level of serious psychological distress, and smoking status at time of interview.
2. Names of conditions shown as reported. The Science Team considered "coronary heart disease" as CAD, and "heart attack" as MI.
3. Case numbers shown for the total study group (*n* = 8,418). Case numbers among analysis groups were not provided.
4. Adjustment limited to mode of recruitment and sex.

Abbreviations: CAD, coronary artery disease; CI, confidence interval; MI, myocardial infarction; ND, not determined; OR, odds ratio; WTCHR, World Trade Center Health Registry.

Table 11. Predictors of self-reported angina/MI (*n* = 92 events) for directly exposed WTCHR enrollees (*n* = 8,701). Adapted from Alper et al. [2017].

Exposure	HR (95% CI)[1]
Dust cloud exposure (all enrollees)	
Intense	0.8 (0.5, 1.3)
Some/none	Reference
Number of 9/11 injuries	
3+	6.8 (2.0, 22.6)
2	3.1 (1.2, 7.9)
1	2.0 (1.1, 3.6)
0	Reference
p for trend	< 0.0001
Probable PTSD at WTCHR Wave 1 survey	
Yes	0.9 (0.5, 1.6)
No	Reference

1. Model included all variables shown and adjusted for study recruitment source, age, sex, race/ethnicity, and education.
Abbreviations: CI, confidence interval; HR, hazard ratio; MI, myocardial infarction, PTSD, post-traumatic stress disorder, WTCHR, World Trade Center Health Registry.

Table 12. Associations of 9/11 exposures with heart disease mortality[1] among WTCHR enrollees, 2003–2014. Adapted from Jordan et al. [2018].

9/11-related exposure	Rescue/recovery participants (*n* = 28,303) HR (95% CI)[2]	Community participants (*n* = 36,533) HR (95% CI)[2]
High	1.44 (0.76, 2.74)	1.14 (0.76, 1.73)
Intermediate	1.40 (0.89, 2.20)	1.19 (0.95, 1.51)
Low	Reference	Reference
p for trend	0.21	0.21

1. Heart disease deaths were defined as the underlying cause of death within the major category of Diseases of the Heart (Major 16) of the NIOSH LTAS 119-cause rate file.
2. Models adjusted for age, sex, race/ethnicity, education, smoking, pre-9/11 diabetes mellitus, and pre-9/11 heart disease.

Abbreviations: CI, confidence interval; HR, hazard ratio; WTCHR, World Trade Center Health Registry.

Table 13. Associations between WTC dust exposure and self-reported MI and stroke combined[1] in 5,971 responders, 2012–2016. Adapted from Remch et al. [2018].

Exposure	HR (95% CI)[2]
In lower Manhattan	
Yes	1.08 (0.59, 1.95)
No	Reference
Directly in the dust cloud	
Yes	0.76 (0.32, 1.88)
No	Reference
Worked on the pile	
Yes	1.30 (0.69, 2.46)
No	Reference
First day on site	
9/11 without dust cloud exposure	1.45 (0.59, 3.57)
9/12–9/13	1.05 (0.43, 2.54)
9/14	0.90 (0.34, 2.54)
9/11 + cloud	Reference
Summary exposure[3]	
High	0.88 (0.29, 2.65)
Intermediate	1.21 (0.57, 2.54)
Low	Reference

1. Analyses included 70 MIs (56.9%) and 53 strokes (43.1%).
2. From a multivariable model adjusted for age, sex, blood pressure, total cholesterol, BMI, smoking, respirator use, and probable PTSD.
3. Ordinal exposure categories for "summary exposure" were listed but not defined by study authors.

Abbreviations: BMI, body mass index; CI, confidence interval; HR, hazard ratio; MI, myocardial infarction; PTSD, post-traumatic stress disorder; WTC, World Trade Center.

Table 14. Associations between WTC dust and CVD in 9,796 FDNY firefighters, September 11, 2001, to December 31, 2017. Adapted from Cohen et al. [2019].

Exposure Indices	HR (95% CI)[1]
Time of arrival	
Morning of 9/11	1.44 (1.09, 1.90)
Afternoon of 9/11	1.24 (1.00, 1.54)
9/12–9/24	Reference
p for trend	0.009
Duration on WTC site	
≥ 6 months	1.30 (1.05, 1.6)
< 6 months	Reference

1. Models adjusted for age, race/ethnicity, and baseline values of BMI, hypertension, hypercholesterolemia, diabetes mellitus, smoking, and PTSD.

Abbreviations: BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; FDNY; Fire Department of the City of New York; HR, hazard ratio; MI, myocardial infarction; PTSD, post-traumatic stress disorder; WTC, World Trade Center.

Table 15. Odds ratios for associations between heart attack and dust cloud exposure, injuries, traumatic events, and PTSD in WTCHR enrollees, comparing self-report and SPARCS-derived hospitalizations. Adapted from Alper et al. [2021].

Exposure[1]	n	Self-report OR (95% CI)[2]	SPARCS OR (95% CI)
Caught in cloud dust	10,262	1.1 (1.0, 1.3)	1.1 (0.9, 1.4)
One or more injuries on 9/11	2,641	1.3 (1.1, 1.6)	1.0 (0.7, 1.4)
Witnessed 3 or more traumatic events	6,823	1.3 (1.1, 1.5)	1.2 (1.0, 1.6)
PTSD	2,666	2.3 (1.9, 2.8)	1.7 (1.2, 2.2)

1. The referent for each category had no exposure to the item in that category
2. Adjusted for age, race/ethnicity, sex, and education.

Abbreviations: CI, confidence interval, OR, odds ratio; PTSD, post-traumatic stress disorder; SPARCS, New York State Department of Health's Statewide Planning and Research Cooperative System.

Table 16. Associations between 9/11 arrival time/dust cloud exposure and CVD in 37,725 general responders, 2002–2019. Adapted from Sloan et al. [2021].

Exposure	Women (*n* = 5,186) HR (95% CI)[1]	Men (*n* = 32,539) HR (95% CI)[1]
Very High	2.17 (1.50, 3.14)	1.29 (1.16, 1.44)
High	1.49 (1.04, 2.13)	1.33 (1.20, 1.47)
Low/Intermediate	Reference	Reference
After adjusting for protective services employment		
Very High	1.61 (1.10, 2.36)	1.04 (0.93, 1.17)
High	1.18 (0.82, 1.70)	1.16 (1.05, 1.28)
Low/Intermediate	Reference	Reference

1. Models adjusted for race/ethnicity, smoking, cholesterol, hypertension, diabetes mellitus, and BMI.

Abbreviations: BMI, body mass index; CI, confidence interval; CVD, cardiovascular disease; HR, hazard ratio.

Table 17. Adjusted HR and 95% CI for heart disease mortality exposure-response associations among groups of WTC rescue and recovery workers, 2001–2016. Adapted from Li et al. [2023].

Exposure by Group	HR (95% CI)[1]
Date of arrival: 9/11/2001 vs 9/18/2001–6/30/2002	
FDNY	0.50 (0.23, 1.08)
GRC	1.91 (0.98, 3.72)
WTCHR	1.37 (0.88, 2.13)
Date of arrival: 9/12/2001 vs 9/18/2001–6/30/2002	
FDNY	0.81 (0.36, 1.83)
GRC	1.25 (0.59, 2.65)
WTCHR	1.42 (0.91, 2.20)
Date of arrival: 9/13/2001–9/17/2001 vs 9/18/2001–6/30/2002	
FDNY	0.61 (0.26, 1.43)
GRC	1.37 (0.66, 2.84)
WTCHR	1.50 (1.01, 2.23)
Work on the pile vs no work on the pile	
FDNY	0.42 (0.25, 0.69)
GRC	1.13 (0.73, 1.76)
WTCHR	1.42 (0.98, 2.05)

1. Models adjusted for age, sex, race/ethnicity, and smoking.

Abbreviations: CI, confidence interval; FDNY, Fire Department City of New York; GRC, General Responder Cohort; HR, hazard ratio; WTC, World Trade Center, WTCHR, World Trade Center Health Registry.

Table 18. Odds ratios from external comparisons of CAD, comparing FDNY firefighters with non-WTC-exposed firefighters (referent). Adapted from Mueller et al. [2024].

Exposure[1]	Model 1 OR (95% CI)[2]	Model 2 OR (95% CI)[3]
Ever/never	1.25 (1.06, 1.47)	1.03 (0.87, 1.21)
High	1.48 (1.18, 1.86)	1.20 (0.95, 1.51)
Mod	1.32 (1.10, 1.57)	1.09 (0.91, 1.31)
Low	1.03 (0.84, 1.26)	0.85 (0.69, 1.05)
linear trend	$p < 0.0001$	$p = 0.03$

1. Non-WTC-exposed firefighters from Chicago, Philadelphia, and San Francisco, used as the referent group.
2. Model 1, adjusted for age, race, and BMI.
3. Model 2, Adjusted for age, race, BMI, high cholesterol, diabetes mellitus, hypertension, and smoking (ever/never).

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; FDNY, Fire Department of the City of New York; OR, odds ratio; WTC, World Trade Center.

Table 19. Odds ratios[1] from internal comparisons of CAD among FDNY firefighters. Adapted from Mueller et al. [2024].

Exposure[1]	Self-reported OR (95% CI)	Validated OR (95% CI)[2]
High	1.38 (1.09, 1.75)	1.29 (0.98, 1.69)
Mod	1.28 (1.07, 1.54)	1.17 (0.95, 1.44)
Low	Reference	Reference
linear trend	$p < 0.01$	$p = 0.06$

1. Models adjusted for age, race, BMI, high cholesterol, hypertension, diabetes mellitus, and smoking.
2. Self-reported case status that was confirmed by medical record review.

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; FDNY, Fire Department of the City of New York; OR, odds ratio.

Table 20. Associations between various 9/11 exposures and self-reported CAD in 47,795 GRC members, 2003-2021. Adapted from Krasnov et al. [2025].

Exposure Indices	HR (95% CI)[1]
WTC Exposure Index	
High	1.20 (0.97, 1.48)
Intermediate	1.18 (0.98, 1.42)
Low	Reference
Hours on-site in Sept. 2001[2]	1.03 (0.93, 1.14)
Presence in Lower Manhattan on 9/11 (yes/no)	1.07 (0.95, 1.20)
Days on-site (Oct. 2001 — June 2002)[2]	1.01 (0.95, 1.08)
Sustained a 9/11 injury[3]	1.15 (0.97, 1.37)
Lost someone (yes/no)	1.11 (0.99, 1.25)
Witnessed horror[3]	0.97 (0.85, 1.11)

1. Models adjusted for sex, age, race, education, marital status, BMI, and neighborhood sociodemographic variables during the first year of follow-up.
2. The associations with the total number of hours on-site in September 2001 and total number of days on-site during October 2001–June 2002 are presented per interquartile range increments (176 hours and 68 days).
3. The models assessing the risks associated with having injuries and witnessing horror during the attack were weighted by the inverse probability of being included in the analytical data set to minimize selection bias attributable to/because of/owing to a high percentage of missing values.

Abbreviations: BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; GRC, General Responders Cohort; HR, hazard ratio; WTC, World Trade Center.

Table 21. Summary of Bradford Hill Criteria used in Evaluation and Evidence Synthesis.

Aspect of Association ("Bradford Hill Criteria") [Hill 1965]	Evaluation Findings
Strength of Association (and estimate of precision)	There were 14 high-quality studies identified for this evaluation [Brackbill et al. 2006; Jordan et al. 2011b; Jordan et al. 2013; Brackbill et al. 2014; Alper et al. 2017; Jordan et al. 2018; Remch et al. 2018; Cohen et al. 2019; Colbeth et al. 2020; Alper et al. 2021; Sloan et al. 2021; Li et al. 2023; Mueller et al. 2024; Krasnov et al. 2025]. Among these 14 studies, eight reported at least one statistically significant positive association between 9/11 exposures and IHD. Among positive associations, effect measures were modest (RR < 2.0) and the set of potential modifying factors (e.g., mediators, moderators, and confounders) was exceedingly large. Small effects and multifactorial causes give rise to estimate errors; therefore, the internal validity of existing risk estimates is uncertain. For example, more information is needed to understand the joint effects of 9/11 exposures and PTSD (or other comorbidities) on cardiovascular risk in the 9/11-exposed population to parse out any causal association between WTC dust exposure and IHD.
Consistency	Seven studies reported at least one significantly positive association between a measure of WTC dust exposure and an outcome including IHD [Jordan et al. 2011b; Jordan et al. 2013; Brackbill et al. 2014; Cohen et al. 2019; Sloan et al. 2021; Li et al. 2023; Mueller et al. 2024] compared with seven studies that did not [Brackbill et al. 2006; Alper et al. 2017; Jordan et al. 2018; Remch et al. 2018; Colbeth et al. 2020; Alper et al. 2021; Krasnov et al. 2025]. Only three longitudinal studies examined specific IHD outcomes [Jordan et al. 2013; Alper et al. 2017; Alper et al. 2021], and none of the three reported significant excess IHD risk from WTC dust exposure. Results were mixed in two cross-sectional studies that examined specific IHD outcomes [Brackbill et al. 2006; Mueller et al. 2024]. Fewer studies examined the association between the 9/11 agent, "sustained injury on 9/11" and CVD outcomes. Findings were mixed within and between studies. Four studies reported at least one significant positive association [Jordan et al. 2011b; Brackbill et al. 2014; Alper et al. 2017; Alper et al. 2021] with injury while two studies found no evidence of an association [Jordan et al. 2013; Krasnov et al. 2025] in multiple analyses. Negative findings from the two studies using hospital discharge records [Jordan et al. 2013; Alper et al. 2021] were inconsistent with the positive findings in the previous studies using self-reported outcomes [Jordan et al. 2011b; Alper et al. 2021]. Mixed findings might result from differences in the definitions of health conditions, exposure measures, populations at risk, case ascertainment, as well as observing modest effects, among other possible explanations. There was evidence of potential bias from residual confounding (e.g., comparison of Model 1 and Model 2 in Mueller et al. 2024). Most studies defined cardiovascular outcomes as broad categories of self-reported, loosely related circulatory system conditions. Errors in ascertainment from self-report appeared slightly attenuated and non-differential in Alper et al. [2021], but substantial in Mueller et al. [2024]. Patterns of inconsistency over time suggested that variability among studies decreased with increasing time since exposure. This suggests that improvements in data quality from extended follow-up will benefit risk assessment moving forward. Further benefits may be achieved by improving definitions of health conditions used in future studies.

Aspect of Association ("Bradford Hill Criteria") [Hill 1965]	Evaluation Findings
Temporality	Longitudinal studies have generally taken steps to exclude prevalent CVD cases. In contrast, steps taken to alleviate general limitations of cross-sectional designs were poorly described; therefore, these cross-sectional studies merit cautious interpretation [Brackbill et al. 2006; Brackbill et al. 2014; Mueller et al. 2024]. In all studies, subclinical health conditions may have manifested prior to 9/11 in some individuals, or the events of 9/11 may have triggered CVD in persons with relevant pre-9/11 conditions.
Biological Gradient	Exposure-response findings were inconsistent. However, findings from multiple studies that examined exposure-response reported evidence suggestive of modestly increasing CVD or IHD risk across increasing categories of 9/11 exposure.
Biological Plausibility, Coherence, and Analogy	An association between WTC dust exposure and IHD is coherent with the available evidence. There is large uncertainty in an analogy comparing a proposed causal association between WTC dust exposure and IHD and the established causal relationship between $PM_{2.5}$ and IHD. The latter is supported by a large body of evidence linking both short- and long-term exposures to ambient air pollution to increased CVD risk. Chronic exposure to $PM_{2.5}$ in air pollution and acute exposure to WTC dusts are largely dissimilar. There is sparse evidence available on the relevant etiologic period for late cardiovascular effects from $PM_{2.5}$ exposure; therefore, the biological plausibility of these effects remains largely uncertain. There is considerably less evidence supporting a causal association between sustaining injury on September 11, 2001, and cardiovascular disease. It is posited that the trauma of sustaining injuries during the 9/11 attacks initiates stress-related psychological and biological mechanisms that might lead to increased cardiovascular disease risk. It has also been suggested that injury could alter physical function, which might adversely affect cardiovascular health. However, biological mechanisms of injury-related IHD in the absence of physical disability and chronic stress are not currently known. Information refuting the biological plausibility of 9/11 injury or WTC dust as causal agents was not found.
Representativeness	There was representation of all groups of 9/11-exposed populations.

Abbreviations: CVD, cardiovascular disease; IHD, ischemic heart disease; PTSD, post-traumatic stress disorder; RR relative risk.