

October 30, 2023

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Surface Transportation Board
Office of Environmental Analysis
395 E St SW
Washington, D.C., DC 20423

Via electronic mail

RE: Draft Environmental Assessment Docket No. FD 36616 – Savage Tooele Railroad Company – Construction and Operation – Line of Railroad in Tooele County, Utah

Dear Environmental Protection Specialist Poole:

Multiple environmental, public health, and civic nonprofits have serious concerns about more development and population growth in Tooele, Utah, which informs our concern about the proposed Savage Tooele Railroad (STR) rail line. Thank you for this opportunity to comment on this Draft Environmental Assessment (EA).

Utah Physicians for a Healthy Environment was formed in 2007 and is one of the largest civic organizations of healthcare professionals in the Western United States. We focus on the public health consequences of various types of environmental degradation, especially air pollution. Great Salt Lake Audubon is dedicated to protecting and enhancing habitat for wild birds, animals and plants, and to maintaining healthy and diverse environments for wildlife and people throughout the state.

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The Great Basin Water Network (GBWN) is a 501(c)3 non-profit that has decades of experience working in the nation's second-driest state, representing a diverse cohort of water advocates concerned with protecting the public welfare — with board members, staff and supporters who earn a living, reside and recreate in Salt Lake City.

The Center for Biological Diversity is a non-profit environmental organization dedicated to the protection of native species and their habitats through science, policy, and environmental law. These scoping comments are submitted on behalf of the Center's 1.6 million staff, members, and online activists, including those that live in and near the impacted area.

The Youth Coalition for Great Salt Lake is a group of high school and college age youth that use our powerful voices to advocate for environmentally just solutions to address the crisis facing Great Salt Lake. We focus on: educating ourselves and the public, collaborating with diverse stakeholders and supporting our elected officials in legislating in ways to effectively address this crisis.

The proposed approval of STR's construction and operation of 11 miles of a new rail line in Tooele County would be a large contributor to a cascade of development consequences having far reaching, undesirable effects, not only there, but throughout the major urban areas of the Wasatch Front where 80% of Utah's population, over 2.5 million people live.

The Draft EA fails to acknowledge that the true purpose of this rail line is to incentivize development of over 35 million square feet of industrial development on land that is currently open space, uplands, playa and wetlands and in some places less than a mile from Great Salt Lake, a critical water body on the verge of ecological collapse. The EA does not take a hard look at the consequences of this, in a valley that is facing a growing environmental crisis with regard to air pollution, and water quality and quantity.

The Draft EA is profoundly incomplete, riddled with contradictions, and a denial of the impact the project will have on the most affected communities and the most heavily populated communities of Utah. The standard for when an Environmental Impact Statement (EIS) should be prepared is: "An agency shall issue an environmental impact statement with respect to a proposed agency action requiring an environmental document that has a reasonably foreseeable significant effect on the quality of the human environment." 42 U.S.C. sec. 4336(b)(1).

We believe that standards are easily met in this case. What follows is a critique of the Draft EA and a request that the project be denied, or at the very least, trigger a full EIS.

1. Stated Purpose and Need Contrary to STB's Statutory Obligation

The Draft EA states that the "purpose of the Proposed Action is to provide rail service to tenants of the Lakeview Business Park" (LBP). In other words, the Surface Transportation Board (STB) is being asked by a private business to approve a project that will have a profound impact, much of it negative, on the community at large, purely for the benefit of investors in the business park: "STR states that many of the companies seeking to locate in the LBP desire rail service for their facilities." ¹

As a public, taxpayer funded agency, the STB should prioritize serving the public good, not private business interests, especially when those two objectives conflict as they do in this case.

¹ Draft Environmental Assessment, Docket No. FD 36616, Savage Tooele Railroad Company – Construction and Operation – Line of Railroad in Tooele County, Utah.

The STB's posture as stated in the Draft EA of "accommodating the rapid growth of manufacturing and warehousing facilities across the country, and specifically in the Greater Salt Lake City area, including Tooele County," is at odds with the current and future public interest in Tooele County, the Great Salt Lake ecosystem and the biological resources therein, the residents of the greater Salt Lake City area, and the state of Utah.

The Draft EA states, "The project's purpose and need should be informed by both the goals of STR as the project's applicant and the agency's enabling statutes." The enabling statutes are the laws that create and empower the STB - 49 USC 10101 through 11908, and the Interstate Commerce Act as amended by the ICC Termination Act, which includes whether the construction of the railway is "inconsistent with the public convenience and necessity," U.S.C.A. §10901. The Rail Transportation Policy identified in 10101 includes the policy to operate rail facilities without detriment to the public health and safety. We believe STR's proposal represents not only a detriment to public health and safety, but a profound degradation of quality of life in the most affected communities.

The Draft EA goes on to state that manufacturers and distributors of goods are adding manufacturers and warehousing capacity in the United States. While that statement is certainly true, it is conspicuous that the Draft EA ignores the evidence that communities where that "added capacity" is being sited, are becoming victims of the trend, not beneficiaries. The Inland Empire in Southern California is a good example. Based on the warehouse capacity in that district and the number of truck trips associated with it, if the LBP is built to capacity with warehouses, we could reasonably extrapolate that the STR would be a primary enabler of tens of thousands of new daily truck trips and overall vehicle trips in the area.

Also, the Office of Environmental Analysis (OEA) makes a questionable assumption about the market for warehouse space. If Great Salt Lake continues its ecological collapse, the market for anything in northern Utah will be collapsing too. Also, the two planned industrial projects connected to the STR are not "market based" as they are planning on receiving significant public subsidies from the Utah Inland Port Authority (UIPA).

2. The Draft EA Fails to Inform the Public of Significant Environmental Consequences

NEPA's "twin aims" are to ensure that the agency (1) "consider[s] every significant aspect of the environmental impact of a proposed action, and to consider reasonable alternatives that could mitigate those impacts"; and (2) "inform the public that it has indeed considered environmental concerns in its decision-making process." *Balt. Gas & Elec. Co. v. Natural Res. Def. Council*, 462 U.S. 87, 97 (1983) (citation omitted). "By focusing both agency and public attention on the environmental effects of proposed actions, NEPA facilitates informed decision-making by agencies. . . ." and "public involvement" in those decisions. *N.M. ex rel. Richardson v. BLM*, 565 F.3d 683, 703 (10th Cir. 2009).

The Draft EA prepared by OEA falls short of these aims in multiple respects:

3. The Draft EA Fails to Disclose the Project's Purpose and Effect of Increasing Industrial Development

The Draft EA fails to acknowledge the very purpose of the project, which is to incentivize industrial development in Tooele County, by providing another transportation method for freight. As a result, the Draft EA does not consider the reasonably foreseeable effects of accelerated industrial development in an area that is immediately adjacent to the ecologically imperiled Great Salt Lake, and in an area with issues of declining water quality and quantity, that also fails to meet federal clean air quality standards.

Also, the scope of this proposed industrial development is far larger than what is addressed in the Draft EA.

Another developer, Zenith Bolinder LLC, has entered the picture and is planning a 162.74-acre industrial development (that they would eventually like to double in size) on the shores of the imperiled Great Salt Lake. This is not even mentioned in the Draft EA, even though the Utah Inland Port Authority [cites the Savage Tooele Rail line several times in the draft Project Area Plan](#) for the location next to the proposed rail line.²

Furthermore, there is an on-going legal dispute between the newly incorporated city of Erda, and Grantsville City regarding several thousand acres of land in Great Salt Lake wetlands, on the south side of the proposed rail line that developers also want to turn into an industrial area.

The OEA needs to take a hard look at this new information.

4. The Proposed Savage Tooele Rail Line is Contrary to the Public Interest

In multiple communities where inland ports and/or massive logistics warehouse farms have been developed, the impact on residents' health has become obvious, and residents have derisively nicknamed their own neighborhoods as [“diesel death zones.”](#)³ Studies are showing that turning the Inland Empire into a gigantic warehouse farm is very harmful to residents health and quality of life.

² Utah Inland Port Authority, Tooele Valley Draft Project Area Plan and Budget, September 22, 20023, p.7. <https://inlandportauthority.utah.gov/wp-content/uploads/DRAFT-Tooele-Valley-Project-Area-Plan.pdf>

³ Barboza, Tony, As 'diesel death zones' spread in California, pollution regulators place new rules on warehouse industry', *Los Angeles Times*, May 10, 2021. <https://phys.org/news/2021-05-diesel-death-zones-california-pollution.html>

Recognizing the creation of these diesel pollution hot spots, California’s South Coast Air Quality District voted in 2021 to apply various new rules on warehouse development and operations to mitigate the associated pollution. “[Under the rules](#), warehouses 100,000 square feet or larger—about the size of two football fields—must take steps to cut or offset emissions associated with their operations or pay a mitigation fee to fund similar air quality improvements nearby... Under the rules, facilities must choose from a menu of pollution reduction and mitigation options, such as using electric or natural-gas-fueled trucks, installing charging stations, erecting rooftop solar panels or putting air filters in neighboring schools and child-care centers.”⁴

There are no plans or even discussions for pollution mitigation from UIPA or developers of the two industrial zones to be served by STR. And as pointed out after the establishment of these mitigation rules adopted in California, “some board members [complained](#) [the new rules] would not reduce pollution, only exposure to it.”⁵ The obvious reality is that it is far better to prevent pollution in the first place rather than attempt mitigation after institutionalizing its creation. These rules were reactive, adopted only many years after the unfettered exposure had been allowed to damage the health of the residents. Many of the health consequences of even short-term pollution exposure can be permanent, especially to children and the unborn, because their organ systems are in critical developmental stages, leading to the axiom that public health protection delayed is protection denied. Furthermore, pollution mitigation does not eliminate the health risk, obviously, it only reduces it.

Approval of this project would open the door to the creation of diesel death zones in Grantsville and Erda. But the downstream effects would extend far beyond because the area is part of the airshed of the Salt Lake Valley, and because the project would add tens of thousands of daily truck trips to roads in the greater Salt Lake City area. Consequently, it would also add to pollution-caused death and disease for millions more.

We find the following statement in the Draft EA contradictory to itself, contradictory to reality, and to the disposition of the majority of Grantsville and Erda residents. “Like Tooele County, Erda seeks to halt rapid population growth while also attracting commercial opportunities that would improve the quality of life for residents. The Proposed Action would be consistent with the Erda general plan and with the Tooele County general plan because it would not add population to the Tooele Valley and would support new commercial opportunities in an area designated for growth while preserving the natural character of the remainder of the county.”

We agree with only this part of that statement, that affected residents do not want to see population growth. But economic “growth” fostered by the rail line can be reasonably expected to lead to population growth, and both lead to consumption of natural resources, in particular

⁴ Id

⁵ Id.

water consumption, and usually energy consumption, both of which will have significant adverse impacts on the quality of life in the community. Indeed, establishing infrastructure for more water consumption flies in the face of the scientific evidence of future worsening, climate crisis-related drought for the entire Intermountain region.

5. The Draft EA Fails to Consider Upstream and Downstream Environmental/Public Health Consequences

The Board's determination that an EA rather than Environmental Impact Statement was appropriate is in error because the Board limited the scope of the environmental/public health issues to what could be directly attributed to the building and conducting of the rail line, and did not include the upstream and downstream effects of the rail line, i.e. all the development and consequent traffic, and pollution that would be stimulated by the existence of the rail line. To use a medical analogy, that is as inappropriate as trying to control the COVID pandemic by focusing only its pathophysiology on individual patients, and ignoring its community transmission.

Language in STB's enabling statutes requires that it consider the public's "convenience and necessity." Even without any new warehouse capacity in Tooele, construction of distribution warehouses has exploded in the Salt Lake Valley, and is poised to extend that rapid growth throughout the Wasatch Front given the recent taxpayer subsidies and plans of UIPA. Virtually any consumer item can already be ordered and delivered within a day or sometimes less to Utah residents. Given the associated truck pollution with distribution warehouses, there is no net societal benefit of even further massive expansion of warehouse capacity in Tooele or the Wasatch Front.

In order to approve the project, the Board must find that the project's transportation merits, and therefore economic merits outweigh its environmental harms. See *Eagle County, Slip Op. at 34* (citing 49 U.S.C. §§ 10501(c), 10901(b); *Alaska R.R.—Constr. & Operation Exemption—Rail Line Between Eielson Air Force Base & Fort Greely, Alaska (Alaska Railroad)*, S.T.B. Fin. Docket 34658, 2007 WL 2875687, at *1 (STB served Oct. 4, 2007)).

We believe that the transportation merits do not come close to outweighing the environmental harm of the proposal.

Recently, in a case in which some of our groups were plaintiffs regarding a proposed railway in Utah's Uinta Basin, the D.C. Circuit Court of Appeals held that the STB was required to analyze the indirect and cumulative impacts of an oil railway, which was proposed to deliver hundreds of

thousands of barrels of oil to the Gulf Coast daily. See *Eagle Cnty. v. Surface Transp. Bd.*, __4th__, 2023 U.S. App. LEXIS 21649 (D.C. Cir. Aug. 18, 2023).⁶

Specifically, the Court found the STB failed to adequately analyze (1) the Railway’s “upstream” impacts, including the effects of drilling thousands of new oil and gas wells that would be induced by the Railway on the Uinta Basin’s vegetation and special-status species, and (2) its “downstream” impacts—the effects of refining the oil in Gulf Coast communities, including Houston, Port Arthur, Texas, and Louisiana.⁷

These impacts were “reasonably foreseeable,” because “[t]he undisputed purpose of the railway is to expand oil production in the Uinta Basin, by enabling it to be brought to market via the proposed rail line connecting the Basin to existing lines that run to Gulf Coast refineries.” *Id.* at 34. Further, the EIS estimated “the number of oil wells that would need to be constructed and operated [in the Basin] to satisfy the expected increased oil production volume scenarios,” *id.* at 31; and it identified “specific regions that will receive the oil based on expected train traffic . . . and a limited number of refineries in those regions that would have the available capacity to process and refine the Uinta Basin’s waxy crude oil.”⁸

The Court also held the Board “cannot avoid its responsibility under NEPA to identify and describe the environmental effects of increased oil drilling and refining on the ground that it lacks authority to prevent, control, or mitigate those developments.” *Id.* at 34. This is because the Board “has authority to deny an exemption to a railway project on the ground that the railway’s anticipated environmental and other costs outweigh its expected benefits.”⁹

In other words, the Court held that the STB erred in not considering all the pollution, public health and climate consequences of the new railway stimulating massive increases in oil and gas extraction and production on both the upstream and downstream communities. The STB has made the same type of mistake in this case and in doing so has severely underestimated the consequences.

6. Claims of Reducing Truck Traffic and Pollution Defy Reason and Empirical Evidence

The Draft EA states, “STR indicated that rail service under the Proposed Action to business park tenants would mean that large volumes of commodities and goods could be transported into and

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https://www.biologicaldiversity.org/programs/public_lands/energy/dirty_energy_development/pdfs/Uinta-Basin-Railway-75-Opinion-2023-08-18.pdf?_gl=1*a9wypx*_gcl_au*NTQzOTM3ODg5LjE2OTUyMzExNjQ

⁷*Id.* at 28-35

⁸*Id.* at 32

⁹ *Id.* at 34-35

out of the County without tying up local roads and highways with commercial trucks.”

The entire purpose of the rail line would be to serve two new proposed industrial zones, likely to be largely warehouse farms, directly stimulating the growth of the Lakeview Business Park (LBP). Based on the amount of truck traffic per square foot of warehouse space in the Inland Empire, between these two industrial zones an additional 30,000 daily truck trips could be generated.

But as noted in the Draft EA, the LBP contracted its own Traffic Impact Study (TIS) in 2021. That TIS concluded that “the total network wide daily added trips,” 50,726 [vehicles], would be generated just by one of the two STR served industrial zones, the LBP, at full build out. If we hypothesized a similar volume of car and truck traffic generated by the UIPA proposed Zenith-Bolinder industrial zone, that would represent a massive influx of new traffic and associated air pollution, completely transforming the character of Grantsville and Erda from rural or semi-rural to heavily urbanized and industrialized communities.

From the description of the traffic volume anticipated on the rail line, only 12-20 cars would be on a typical train, and that the first year they expect to transport 1,200 cars per year, increasing to an eventual 8,000 car loads per year. At even the latter number, that would only be 22 rail cars per day. The carrying capacity of one rail car is the equivalent of no more than 4 trucks. So, a fully operational rail line would only reduce the on road truck inventory by a paltry 88 trucks at the most, not even a proverbial drop in the bucket of the over 30,000 daily truck trips or well over 50,000 vehicle trips modeled in the TIS from just the one industrial zone. So how could anyone claim that the rail line would be responsible for any measurable decrease in air pollution, traffic congestion, or energy consumption compared to no rail line?

But the claim is even more preposterous given the amount of pollution generated by the two diesel locomotive engines. Heavy equipment diesel engines produce enormous amounts of pollution. According to Emissions Based Maintenance (EBM) in Lehi, Utah, diesel mechanics and emissions experts, two tier 0+ diesel locomotive engines of the size suggested in the EA, will produce the equivalent in direct PM_{2.5} of what would be expected from 500,000 average cars, equal to half of all the cars registered in the state.

Making the diesel pollution from this proposal even worse are two facts. Unlike automobiles and personal pick-up trucks, engines larger than 750 hp are never inspected once they are on the road or tracks, and there is no state or federal law requiring it. Steve Forbush, owner of EBM, states that in their experience these diesel engines in the real world perform even worse. Furthermore, diesel engines produce a disproportionate amount of ultrafine particulate matter (UFP), by far the most toxic subset of the inventory of atmospheric particulate matter. Importantly, UFP contributes only a negligible amount to PM mass measured at PM_{2.5} monitors

within Utah's and the nationwide EPA network, but dominates the particle number, which is the [most relevant metric](#) of PM human health toxicity.¹⁰ In other words, estimating tons of emitted PM2.5 and other pollutants from the project as a surrogate for its air pollution related health hazard is not adequate or accurate.

7. *The Savage Tooele Rail Line Would Dramatically Degrade Quality of Life in Adjacent Communities*

It is obvious that if the developers of these industrial zones and the STR achieve their lofty ambitions, it would thoroughly degrade the rural character of the towns of Tooele, Grantsville and Erda and become a massive new air pollution and traffic burden. This kind of development is inconsistent with improving quality of life in the area, and inconsistent with the STB's statutory requirement to prioritize "public convenience and necessity." Indeed, many people live in Tooele, Grantsville, and Erda, not just because the land is comparatively cheap, but because they prefer a non-urban environment and lifestyle. This development would transform their community dramatically, and we believe for most people that transformation would be a marked net negative. Several community referendums have been conducted on this issue and based on that experience the overwhelming majority of residents of both Erda and Grantsville do not want these industrial projects.

8. Air Quality/Public Health Impact Would Not be "De Minimis"

The EA is completely absent in addressing other sources air pollution beyond the trucks and rail locomotives. Turning tens of thousands of acres of open space and grasslands into seas of asphalt and concrete contributes to air pollution irrespective of the vehicles that travel on them.

Not surprisingly, laying hot asphalt releases toxic VOCs. But even long after, i.e. years, when exposed to sunlight and summer temperatures, asphalt continues to emit toxic VOCs and "secondary organic aerosols" (SOC) which are major components of PM2.5. In fact, this phenomenon was [calculated as equal to, or even exceeding](#) the contribution of tailpipe emissions to summertime PM2.5 in Los Angeles.¹¹ Obviously, this is a source of pollution that will not be reduced or eliminated by future fleet electrification. Furthermore, [recent studies](#) have shown that

¹⁰ Seny Damayanti, Roy M. Harrison, Francis Pope, David C.S. Beddows, Limited impact of diesel particle filters on road traffic emissions of ultrafine particles, Environment International, Volume 174, 2023 <https://www.sciencedirect.com/science/article/pii/S0160412023001617>

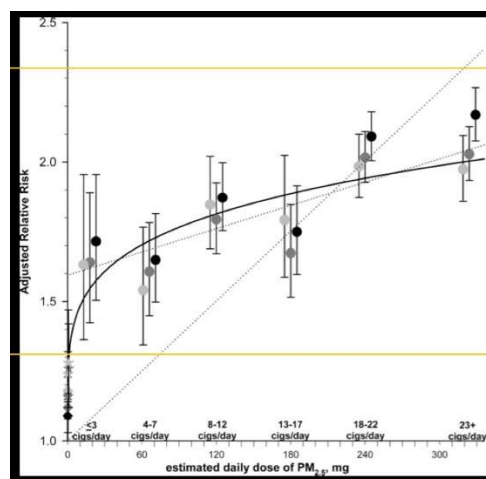
¹¹ Peeyush Khare *et al.*, Asphalt-related emissions are a major missing nontraditional source of secondary organic aerosol precursors. *Sci. Adv.* **6**, eabb9785(2020). DOI: [10.1126/sciadv.abb9785](https://doi.org/10.1126/sciadv.abb9785)

PM2.5 just from tire, brake, and road surface wear, and other vehicle mechanical friction probably also exceed the PM2.5 from tail pipes. Electric vehicles generally produce more of this category of pollution because they are heavier.

Through another path, water consumption secondary to this project will increase ozone formation. More water consumption will further deplete the size of the Great Salt Lake. Among the many consequences of that trend (and addressed more later on) is an increase solar reflectivity which is a catalyst for the formation of ozone.

As part of the Wasatch Front airshed, Tooele County is already in an area that chronically violates the EPA's air quality standards (NAAQS) for both PM2.5 and ozone. Any increase in pollution sources will harm not only residents of Tooele County, but those throughout the entire airshed of which it is part, and that includes a majority of Utah's population.

Tooele is part of the airshed that violates the EPA's NAAQS for 24 hr. PM2.5, ozone, and sulfur dioxide. In other words, new pollution sources created in Tooele, affect not only Tooele, but the greater Great Salt Lake area, home to nearly 2 million people. More air pollution has severe public health consequences, even in those parts of the country that meet the NAAQS. Notwithstanding those standards, thousands of medical studies have concluded there is no safe level of any of the pollutants for which the EPA sets standards. In fact, the relationship between pollution concentration, in particular PM2.5 and ozone, two of the three pollutants for which the Greater Salt Lake City area is in perpetual violation of the standards, is not linear but hyperbolic, as illustrated in this graph that plots adverse health outcomes vs. PM2.5 concentrations.



(Peters, A. Air Quality and Cardiovascular Health: Smoke and Pollution Matter. Circulation. 2009: 120:924-927)

This hyperbolic relationship has been established repeatedly with virtually all types of pollution.

That means small increments in both pollutants have large impacts on public health, especially when background pollution levels are low or modest.

In the attached document heavily referenced to the medical literature, Utah Physicians for a Healthy Environment (UPHE) make the scientific case that even EPA's proposed tightening of the annual PM_{2.5} is not adequate to protect public health, and that its 24 hr. PM_{2.5} standard, for which pollution in Tooele contributes to the ongoing violation in the Salt Lake Valley, is profoundly inadequate. The document details why several unmistakable trends suggest air pollution will be a steadily larger health burden in the future, including for the state of Utah and the greater Salt Lake Valley. The clear implication is that in reality, the likely end result of the pollution and public health consequences implied in the EA will be much more significant than "de minimis."

Not addressed in the attached document is an analysis of the health consequences of the other most important high-volume pollutant—ozone. The EPA's standard for ozone is 70 parts per billion. The potency of ozone, and the inadequacy of EPA's standards are illustrated by [a recent study](#) published in a highly respected medical journal that found that exposure to an increase of just 3 ppb ozone for ten years was associated with as much deterioration of lung tissue and function as smoking a pack a day of cigarettes for 29 years.¹²

As with PM_{2.5}, the EPA's regulatory thresholds notwithstanding, there is [no safe level of ozone](#). Furthermore, not only is Tooele County part of the greater Salt Lake Valley airshed and therefore a contributor to air pollution's health hazards for a much larger population, but the precursors of ozone, VOCs and NO_x, can travel hundreds of miles and form ozone far removed from where the precursors originate.¹³ Diesel truck emissions include both precursors, and therefore a significant increase in truck traffic in Tooele County will increase ozone levels far removed from the industrial zones served by the STR.

9. Inadequate assessment of harms to biological resources

The study area OEA used to assess impacts to biological resources is too small to be useful for any science-based analysis of the impacts to biological resources, yet the potential for impacts is significant. Just half a mile away from the project area is Great Salt Lake, and adjacent to the project area wetlands in each direction (but particularly to the south).

¹² Wang M, Aaron CP, Madrigano J, et al. Association Between Long-term Exposure to Ambient Air Pollution and Change in Quantitatively Assessed Emphysema and Lung Function. *JAMA*. 2019;322(6):546–556. doi:10.1001/jama.2019.10255

¹³ Boehland, J. (2006, April 3). Study Finds No Safe Level of Ozone. Retrieved from <https://www.buildinggreen.com/newsbrief/study-finds-no-safe-level-ozone>

OEA also doesn't take into account the scope of intended industrial development incentivized by the rail line which will destroy significantly more habitat.

In the immediately adjacent areas, there is habitat identified by [Utah's 2015 Wildlife Action Plan](#) for 16 Utah Species of Greatest Conservation Need.¹⁴ These are species the state has prioritized for special attention because of the threats they face, and to stave off potential Endangered Species Act listings.

In close proximity to the proposed rail line and the industrial development it will help induce, is habitat for white faced ibis, American white pelican, snowy plover, peregrine falcon, burrowing owl, greater sage grouse, bald eagle, ferruginous hawk, golden eagle, flammulated owl, caspian tern, Lewis's woodpecker and kit fox.

Given that Great Salt Lake is on the verge of ecological collapse, protecting habitat for these species is all the more important as resources and habitat for wildlife are becoming more scarce. The stress on these species from habitat loss and degradation increase the potential for listings under the Endangered Species Act.

Other than looking for golden eagle habitat in the narrowly defined project area, the Draft EA failed to examine what impacts might occur to the immediately adjacent landscape and the Species of Greatest Conservation Need habitat in and adjacent to Great Salt Lake.

Finally, the proposed STR is within the line the state drew, establishing land eligible for Great Salt Lake wetland mitigation funds, demonstrating that the area deserves great scrutiny.

From a biological standpoint, a line drawn on a map is meaningless, as when looking at this project in the context of the eco-region it sits in. Thus, OEA needs to examine the eco-region impacts to biological resources. The OEA needs to examine the broader habitat impacts of the industrial development that will be induced by the proposed STR.

10. The Draft EA Fails to Assess Cumulative Impacts

Under NEPA, cumulative impacts are defined as “the impact on the environment, which results from the incremental impact of the action when added to other past, present, and reasonably foreseeable future actions regardless of what agency (federal or non-federal) or person undertakes such other actions” (40 C.F.R. § 1508.7).

The OEA did not fully examine the impact of all of the industrial development the STR is designed to incentivize.

11. Meaningful Discussion of Climate Change Impacts Is Lacking.

¹⁴ Utah Division of Wildlife Resources, Utah Wildlife Action Plan, 2015-2025.
https://wildlife.utah.gov/pdf/WAP/Utah_WAP.pdf

The Draft EA fails to evaluate the significance of the project's direct, indirect, and cumulative greenhouse gas emissions on climate change, and relies on a STR propaganda piece saying:

“Specifically, STR focuses on supporting sustainable supply chains, aiding the energy transition to renewable sources, promoting sustainable farming practices, and restoring and protecting the environment (STR 2021). STR is also committed to promoting the transition to a lower-carbon economy.”

In fact STR is a project of Savage Companies, which also promotes refinery services, handling of chemicals “from sulphur, petroleum coke, crude oil, sulphuric acid, liquid petroleum gas, and benzyne,” as well as “From plastics and dilutions to corrosives, flammables, and combustibles, Savage handles a wide variety of dry and liquid bulk chemicals. We load or transload hundreds of thousands of railcars of chemical and petrochemical products annually, including 40,000 railcars of polymers each year.”¹⁵ They are also involved in oil and gas industry activity, as well as mining. This is not a company that cares about carbon emissions as a significant percentage of their business is in the fossil fuel and chemical industries.

12. Utah Drought Cannot Sustain This Level of Industrial Development

Ground water is the sole source of drinking water in the Tooele Valley.¹⁶ Well water levels are dropping valley wide. Further industrial growth in Tooele, and growth of the Tooele population attendant to the creation and expansion of the two industrial zones to be served by the STR project would exacerbate water demand. The Draft EA acknowledges, “The current U.S. Drought Monitor shows that 100 percent of Tooele County is in severe drought conditions and that 47 percent of the county is in extreme drought conditions.” Pushing a massive industrial project in area suffering from decades long and likely worsening severe drought in the future related to the climate crisis, is the epitome of short sightedness and reality denial. The Draft EA addresses the reality of the climate crisis only as it might affect the stability and safety of rail line infrastructure. Incredibly it does not address the impact of the climate crisis on the sustainability of the increased population, economic activity, and water demand stimulated by the rail line.

The town of Stockton in Tooele County already has a building moratorium because springs have dried up and drastically cut their water supply.¹⁷ Numerous other towns throughout Utah have

¹⁵ <https://savageco.com/>

¹⁶ Scientific Investigations Report 2009-5154 Hydrology and Simulation of Ground-Water Flow in the Tooele Valley Ground-Water Basin, Tooele County, Utah
<https://pubs.usgs.gov/sir/2009/5154/pdf/sir20095154.pdf>

¹⁷ O'Donoghue, Amy Joi, Utah drought takes toll on water systems, drying up springs, wells: Towns ask Utah Legislature to provide a 'financial' fix for dried-up communities, *Deseret News*, Jan 26, 2023.

had similar moratoriums on growth because of a lack of water resources. With the climate crisis, that problem will almost certainly grow and intensify. Adding more industrial zones in Tooele, no matter what types of businesses operate in those zones, will only increase water demand and exacerbate the water crisis.

There is a high likelihood that a hydrological connection exists between wells in Tooele County and the Great Salt Lake (GSL). More water consumption in Tooele, stimulated by more industrial and population growth, is very likely to add to water loss in the Great Salt Lake. The steady loss of GSL surface area and increasing dust storms originating from the expanding dry lake bed is looming as the most serious environmental crisis in the modern history of the state. There is every reason to believe that this project will only add to that crisis.

13. The Draft EA is Inherently Contradictory

The EA states, “Without the availability of freight rail service, these commodities would either ship on commercial trucks, or possibly, the businesses would not choose to locate in Tooele County.” Elsewhere in the EA the STB states, “However, according to the traffic study provided by STR, the efficiency of rail to and from the LBP will reduce the need for trucks that would otherwise access the site.” These claims are contradictory. On the one hand the EA claims that not having the rail line may cause businesses not to locate in Tooele, on the other hand the EA implies that the same amount of goods will be moved regardless of the means of transport, so there will be a reduction in truck traffic benefiting the community. Here again the Draft EA is irrational in denying the role that the rail line will play in creating much more commodity movement and therefore truck traffic. It is not a matter of the same amount of shipping of goods will occur no matter what transportation mode is available.

As noted above, the STB is required to assess “cumulative” impacts of the proposal. Again, the Draft EA is self-contradictory in that on the one hand it claims a rail line would be an important contributor to LBP’s viability, but on the other hand, it states in section 3.13.3 that it would not contribute to a cumulative impact on “air quality, energy use, land use, zoning, or local plans.”

14. Voluntary Measures Provide No Public Protection

In numerous places in the Draft EA, the STB relies heavily on “voluntary measures by the applicant” to mitigate its harms. Observing the current frenzied construction activity of warehouse builders in the Northwest Quadrant of Salt Lake City and their total disregard for any and all environmental concerns, there is no reason to believe any volunteer measures that cost STR money will be adopted. In the same vein, we find the Draft EA statement below hollow, and of no value in protecting the community from collateral damage from the proposed rail project. “OEA also encourages applicants to negotiate mutually acceptable agreements with

affected communities and other government entities. Negotiated agreements can be with neighborhoods, communities, counties, cities, regional coalitions, states, and other entities.”

15. Tooele County is Not in Need of Employment Stimulus

Since April, 2023, the average unemployment rate in Tooele County has been 2.7%. That is near an [historic low](#) going back to 1990.¹⁸ More jobs alone will add little to the economic strength of the county, especially if most of those jobs are low paying warehouse distribution and fulfillment jobs, often without benefits, as is the case in other logistics centers. The impact on the overall economy can even be a net negative because many of those workers require various forms of public assistance.

The Draft EA cites a letter from a Representative from Tooele County, Douglas Sagers, stating that over 8,000 Tooele Valley residents commute back and forth to the Salt Lake Valley daily, and that employment at the LBP will reduce that number. Conveniently, the letter mentions that the developer, The Romney Group, LLC forecasts that between 8,000 and 10,000 jobs will be created by the LBP. While it is difficult if not impossible to project how many of those people would find acceptable, similar, or higher paying employment at either industrial zone served by the STR, the history of job creation in other logistics centers offers no reason to be optimistic that the numbers would be significant. The speculation offered by Rep. Sagers is void of any supporting evidence beyond his pure conjecture.

Conclusion

We believe the Draft EA fails in assessing the full extent of the environmental and public health harm that will be unleashed by approving the project. We believe this project does not meet the criteria for approval because of the transportation merits, and therefore the economic merits benefit only a very small number of developers at the environmental, public health, and quality of life expense of a much larger number of people.

We urge the OEA to address the issues we raise in these comments.

Sincerely,

Dr. Brian Moench
President, Utah Physicians for a Healthy Environment

¹⁸ <https://fred.stlouisfed.org/series/UTTOOE5URN>

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Utah Physicians for a Healthy Environment (UPHE) is one of the largest civic organizations of healthcare professionals in the Western US, including about 450 physicians, some of whom are academics and researchers, but most of whom are clinicians, and 3,500 members of the lay public. We practice on the front lines of public health, 24/7, 365 days per year. Our patient care responsibilities provide us with a different perspective on pollution's health consequences from what EPA might get from other environmental groups or non-clinicians doing only research. We submit these comments for the purpose of demonstrating that EPA's proposed changes to the PM_{2.5} National Ambient Air Quality Standards (NAAQS) are inadequate to protect public health, do not reflect an overwhelming body of relevant science (most of which EPA already has at hand), and do not satisfy EPA's legal obligations to do both. We urge the EPA to adopt a 24-hour standard of 20 μ g/m³ and an annual standard of 8 μ g/m³ for PM_{2.5}.

Executive Summary

A. Introduction

B. Trends suggest air pollution will be an even larger health burden to the US population in the future.

1. The US population is aging.
2. The urban migration increases air pollution exposures.
3. The climate crisis is increasing multiple types of pollution.
4. Like previous research trends, future research is likely to show greater health impacts and show them with more accuracy.
5. Airborne plastic nanoparticles are adding to toxicity of particulate pollution (PM).
6. Incidence of cancer in young people is increasing. They will need more protection from PM.
7. PM increases morbidity and mortality from COVID, a disease likely to become endemic.
8. Life expectancy is dropping, and air pollution is connected to several contributing trends.

C. EPA's methodology is flawed.

1. The EPA standard for declaring causality is extreme.

2. Medical organizations have long called for stricter standards than the EPA eventually adopts; this proposal is an example of this disparity.
3. The form used to establish the 24-hour standard must be changed to 99th percentile.
4. The standard for nitric oxide and nitrogen dioxide (NO_x, the nitrogen oxides most relevant for air pollution) has been virtually ignored; updating the PM_{2.5} standard will have ripple effect on NO_x.

D. Clean Air Act (CAA) mandates that EPA establish stricter standards.

1. “Adequate margin of safety” is required, including for the public to engage in outdoor activities.
2. The EPA may not consider cost or feasibility.
3. The precautionary principle applies: the EPA must protect the public from “known” hazards and those about which there is still scientific uncertainty.
4. Setting standards is an expression of a value system, not just of science.

E. EPA Looks at the right science but draws the wrong conclusions.

1. Some EPA conclusions are wrong on their face and even defy common sense.
2. EPA methodology is arbitrary and eliminates too many valuable studies.
 - a. There is no reason to eliminate studies outside of North America.
 - b. Insisting on a common “ambient exposure” standard eliminates outliers such as Utah.
 - c. Over emphasizing co-pollutant confounding is counterproductive to protecting public health.
 - d. EPA seems to ignore critical autopsy studies.
 - e. EPA is inconsistent in their consideration of heterogeneity of studies.
 - f. EPA should act as caregivers must, with less than perfect knowledge.
 - g. EPA inappropriately discounts morbidity studies.
 - h. EPA gives inappropriate weight to controlled human exposure studies.
 - i. EPA is wrong to discount biochemical and histological studies and studies of subtle clinical outcomes.
 - j. The Clean Air Scientific Advisory Committee (CASAC) is correct that EPA is wrong to over emphasize the use of the “mean” in exposure studies.
 - k. CASAC is right in criticizing EPA for excluding areas impacted by wildfires and winter inversions.
3. We agree with CASAC that lowering the annual standard alone will leave many communities and subgroups without protection from short-term pollution hazards.
4. By relying on PM_{2.5} mass measurements, EPA is likely underestimating the toxicity of PM.
5. EPA’s standard for declaring causality is arbitrary and extreme.

F. A small fraction of the studies that compel stricter standards:

1. Supralinear dose/response relationship at low exposures.
2. PM_{2.5} and mortality:
 - a. Mortality and long-term exposure.

- b. Mortality and short-term exposure.
 - c. Association with infant mortality.
 - d. Association with ICU and COVID mortality rates.
- 3. PM2.5 and the cardiovascular system:
 - a. PM2.5 is a key contributor to atherosclerosis, arteriole narrowing, plaque rupture, and cardiac ischemia.
 - b. Effect on heart electrophysiology.
 - c. Effect on blood pressure.
 - d. Association with pulmonary hypertension.
 - e. Association with heart failure (HF), morphologic changes, and blood clots.
- 4. PM2.5 and the brain and nervous system:
 - a. Interferes with brain development.
 - b. A significant contributor to stroke.
 - c. Impaired cognition.
 - d. Association with Parkinson's Disease.
 - e. Association with dementia and Alzheimer's Disease.
 - f. Association with multiple psychiatric and tic disorders.
 - g. Anatomic brain changes.
- 5. PM2.5 and reproductive toxicity, fetal development/chromosomal integrity:
 - a. Preconception toxicity impairs fertility, organogenesis.
 - b. Quantitative consequences of preconception exposure.
 - c. Prenatal exposure increases the risk of birth defects.
 - d. Prenatal exposure is associated with chromosomal damage and decreased telomere length.
- 6. PM2.5 and pregnancy and birth outcomes:
 - a. Impairs fetal growth.
 - b. Is associated with premature birth.
 - c. Other pregnancy, birth complications.
- 7. PM2.5 and the lung:
 - a. PM2.5 and parameters of lung function.
 - b. PM2.5 and COPD and asthma.
 - c. Association with respiratory infections.
 - d. PM2.5 and idiopathic pulmonary fibrosis.
- 8. PM2.5 and Cancer:
 - a. PM2.5 and increased risk of cancer.
 - b. Decreased rate of cancer survival.
- 9. PM2.5 and Metabolic, Endocrine, and Kidney Disease:
 - a. PM2.5 and risk of type II diabetes and glucose intolerance.
 - b. Obesity, metabolic syndrome, and thyroid dysfunction.
 - c. Chronic kidney disease.
- 10. PM2.5 and miscellaneous health impacts.
- 11. PM2.5 and environmental justice.

G. Economic considerations

1. The economic benefits of tightening the annual standard is overwhelmingly positive, nationally and in Utah
Cost benefit analysis favors annual standard of 8 ug/m³ over 9-10.
2. Economic benefits to the heavily populated areas of Utah

H. Conclusion

A. INTRODUCTION

On March 8, 2023, a worldwide news headline read, “Almost everyone in the world breathes unhealthy air.”²¹⁵ The report referenced a study published in *Lancet Planetary Health* that showed that virtually everyone across the globe is exposed to air pollution that exceeds the standards proposed by the World Health Organization (WHO).²¹⁶ The WHO states, “Air pollution is the greatest environmental threat to health and well-being at the global scale, and all populations are affected....”³⁴⁰ It is from that general assessment that WHO makes recommendations for much stricter standards than EPA. In the three documents that form the scientific basis of EPA’s proposed changes, *2019 Integrated Science Assessment for Particulate Matter*, *2022 Supplement to the 2019 Integrated Science Assessment for Particulate Matter*, and *Preamble to the Integrated Science Assessments*, we see no scientific justification for EPA to adopt the standards they are proposing.

Although a wealth of science is available to guide EPA’s decision, in the end, setting the NAAQS is a discretionary act. The decision will be one of judgement and values, not technical analyses of the quality of the data. For the last 16 years, UPHE has kept very close track of the world’s air pollution and health research. When we see that time and again, EPA, under both Republican and Democratic administrations, makes standards that we and most other medical organizations believe to be too weak, standards that don’t adequately reflect the science that we are familiar with, we feel obligated to speak out.

Our interaction with patients and their families compels us to see this issue not on the abstract level of morbidity and mortality statistics and causality probabilities, but on the level of the human faces behind those numbers and equations. We interact personally with air pollution’s victims and their families. They experience real diseases, real economic losses and disability, loss of quality of life, real suffering, and sometimes irreversible tragedy and death from air pollution.

What are the risks and benefits of EPA’s options in establishing PM_{2.5} NAAQS? EPA’s current proposal contradicts any reasonable risk/benefit analysis. If EPA sets NAAQS at 8 µg/m³ annual and 20 µg/m³ daily averages or lower, that would be unequivocally supported by current science, even if an argument can be made that the supportive science is still incomplete. If it turns out the science behind that decision was wrong or merely premature, and the end result was 330 million people breathed cleaner air than necessary or cleaner air than polluting industries were willing to acquiesce to in court, what is the societal cost? At the very most, a

slim possibility of a reduction in some kinds of economic activity. However, EPA's own cost analysis found that the benefits of pollution reductions afforded by EPA's enforcing the Clean Air Act from 1990 to 2020 paid off at a rate of 30 to 1.¹ Is it logical that a slightly overzealous NAAQS PM2.5 would have a reverse economic impact? The medical and economic literature certainly doesn't support such a scenario.

From a public health standpoint, there is obviously no such thing as air that is too clean. There would also be a co-benefit of reducing CO₂ emissions, and we could ask another absurd rhetorical question, "Is there such a thing as too much climate protection?"

On the other hand, if EPA sets NAAQS that are too weak, it also risks economic consequences from increased healthcare costs, decreased worker productivity, and lost employment, but it obviously also risks quality of life, increased morbidity, shortened life expectancy, and directly increased mortality.

To be simpler and more direct, EPA failed to do its job in allowing 11 years and 17 years, respectively, to elapse since the annual and 24-hour PM2.5 NAAQS were last updated. As with justice, "public health protection delayed is public health protection denied." When the EPA errs on the side of NAAQS that are too weak or delays updating them, public health consequences on a massive scale are the result. Tens of thousands of lives are shortened or lost, millions are victimized with life-altering morbidities, and virtually every US resident suffers to some degree, even if, for some, it is subclinical and not quantifiable. Even worse, establishing regulations that indisputably allow this as an end result codifies a cynicism and disrespect for human life into federal agency regulatory actions that tend to be perpetuated and normalized. Much of the world looks to EPA for guidance on environmental and public health protection, so the consequences of weak or delayed regulations reverberate throughout the world, affecting billions of lives.

B. TRENDS SUGGESTING AIR POLLUTION WILL BE A STEADILY LARGER HEALTH BURDEN IN THE FUTURE

B1. The US population is aging. By 2050, the number of Americans over the age of 65 will double to nearly 90 million.⁴ Overall, the US population five and ten years from now will be increasingly more vulnerable to the health consequences of air pollution from this demographic shift.

B2. Urban migration increases air pollution exposures. Globally, the world's population is drifting toward urban centers. While this trend has slowed in the US, urban areas are still growing denser, and that means more people are exposed to more air pollution of all types. Among the fastest-growing US cities, growth from 2010 to 2020 ranged from 11% to 26%. As a result, other things being equal, the residents of these cities will all be experiencing higher concentrations of PM2.5 attributable to the urbanization trend.

B3. The climate crisis is increasing multiple types of pollution. In setting PM2.5 NAAQS, **EPA must consider the contribution of the climate crisis to future pollution exposure.** Global temperatures will undoubtedly continue to increase, and heat waves will have a dual enhancing effect on pollution and health. Warmer atmospheric temperatures will increase ground-level ozone globally. In Utah, for example, rural communities are experiencing ozone as high as Los Angeles, but many contributors to that problem are beyond the reach of state or federal regulations. Ozone's health hazards largely overlap with those from PM2.5. Higher temperatures and drought in the US, especially in the Western US, are leading to increased pollution from wildfires, including PM2.5. Numerous studies have found that the consequences of PM are enhanced in a setting of higher temperatures. A study of populations in Japan, Korea, and Taiwan found a synergistic effect between high temperature and air pollution on mortality, using a multicity time-series analysis.²⁹⁹ A meta-analysis of 56 studies found moderate quality evidence for a synergistic adverse effect of high temperatures and air pollution.¹³⁴ In a study of over 2 million adults in New England, increasing temperature extremes and temperature variability had a synergistic effect with short-term PM2.5 on hospital admissions.²⁸⁹

EPA should also factor into its decision that control of PM2.5 will derive the co-benefit of reducing atmospheric greenhouse gas emissions, contributing to mitigation of the climate crisis. It will also produce the co-benefit of reduction of other criteria pollutants, such as NOx and cobalt (CO), and other hazardous air pollutants such as polycyclic aromatic hydrocarbons (PAHs) and heavy metals. There is evidence that synergism exists in the adverse health effects precipitated among criteria pollutants. Reducing PM2.5 will help address those possible synergists effects.¹³⁶

As temperatures and atmospheric carbon dioxide rise, both will contribute to increased air pollution from natural sources like plants and dust. On their own, biogenic volatile organic compounds (BVOCs) are benign. However, once they react with oxygen, they produce toxic organic aerosols. The organic aerosols and dust will increase PM2.5. A recent study found that an increase in global temperatures of 2° C will increase BVOCs and global dust (largely from the Sahara Desert) about 7%.²³⁶

B4. Like previous research trends, future research is most likely to show greater health impacts and with more accuracy. The history of pollution/health research has steadily moved in only one direction. **The more research advances, the stronger the association with death and the broader its association with disease.** The overwhelming likelihood is that research five or ten years from now will show that the standards that EPA is proposing are inadequate. Yet EPA's approach is almost purely reactive, insisting on an unrealistic standard of biological proof of harm before taking action. Proactive anticipation of that research trend's continuing should provide more impetus for a stricter standard. Not only does research continuously move in the direction of finding ever-greater harm from air pollution, but the research steadily becomes more accurate, especially regarding estimating concentrations of exposure. Populations in newer studies are more than ten times larger than those in studies used for previous reviews.²

B5. Airborne plastic nanoparticles are adding to toxicity of particulate pollution. When criteria pollutants became part of EPA's regulatory mandate, airborne plastic nanoparticles were not a recognized part of the toxic potential of air pollution. Now, however, we know that **plastic fragments of 5 microns in size and smaller are a ubiquitous component of global air, water, and soil pollution and are an increasing source of human health hazards.**¹⁴¹ Exposure is possible through inhalation, ingestion, and dermal absorption. Thousands of different chemicals are used in manufacturing different plastics and are attached to these plastic fragments. Furthermore, they absorb other toxins, like PAHs and heavy metals, once released into the environment,¹⁴² and can serve as a vector for microbial pathogens.¹⁴³

Plastic nanofibers are resistant to biodegradation much like asbestos is, and can be deposited in terminal bronchioles, alveolar ducts, and alveoli, resulting in chronic inflammation, granulomas, or fibrosis. They are now detected in human stool, blood,¹⁴⁴ and many human organs.¹⁴⁵ The toxic potential of airborne microplastics is beyond the scope of our comments, but their presence is reason enough to engage in mitigation of the problem. EPA should consider that PM2.5 control will also help control human contamination by airborne plastic nanoparticles, a problem that is likely to accelerate, given the rate of global plastic use and production.

B6. The incidence of cancers in people under 50 years old—breast, colorectum, endometrium, esophagus, extrahepatic bile duct, gallbladder, head and neck, kidney, liver, bone marrow, pancreas, prostate, stomach, and thyroid—has increased dramatically in multiple countries.⁵ Air pollution has been implicated in multiple cancers (to be addressed later in our comments), but it has also been implicated in decreased survival rates from cancer in general.⁶ Stricter PM2.5 NAAQS would help tens of thousands of these young cancer victims survive.

B7. Air pollution, PM2.5 in particular, has been shown numerous times to contribute to increased rates of hospitalization and death from COVID.^{7,8,9} A Harvard Chan study found an 11% increase in mortality with each 1 µg g/m³ increase in long-term PM2.5 exposure.¹⁰ The chances are high that COVID will become endemic to the United States, and other pandemics are likely to emerge, but stricter PM2.5 standards will save the lives of some who contract COVID. One new study has found that even in a setting of low pollution, median annual PM2.5 of 6.39 µg/m³, the risk of developing long COVID is increased with small increases in long-term PM2.5. For a PM2.5 increase of just 0.65 µg/m³, the odds of long COVID increased about 30%.³⁷¹

B8. Air pollution is among the reasons that life expectancy in America has been dropping, down almost three years since 2025.³ Many countries that are poorer than the United States now have higher life expectancies. American life expectancy is now nine years lower than Japan's. While COVID, vaccine misinformation, drug overdoses, and gun violence are contributing to the majority of that decline, increasing cardiovascular disease, metabolic disorders like obesity and diabetes—all morbidities significantly connected to air pollution—are as well. Even violence and crime have a connection to air pollution. For many Americans, a poor healthcare system contributes to this disturbing trend, and unfortunately, will likely continue to

do so, given the current political climate and lack of political will to improve or expand it. In this setting, air pollution has an even larger impact.

C. EPA'S METHODOLOGY IS FLAWED

C1. The EPA standard for declaring causality is extreme. Time and again, EPA's scientific reviews are characterized by being overly cautious in drawing conclusions that would force enhanced regulatory action. While we cannot expect that setting the NAAQS is an exercise in exact science, it is obvious that EPA often functions more as a political agency than as a public health agency. This was particularly true during the Trump Administration when, flying in the face of overwhelming evidence, the NAAQS were not strengthened. Notably, it was during that time that CASAC was dismantled and reassembled with political appointees rather than public health and research experts.

EPA's methodology for establishing causality (and presumably, therefore, proof of benefit from intervention) is arduous, excessive, and incompatible with providing best available healthcare and public health protection. It is likely that EPA adopts this methodology as a precaution for the eventuality of being sued by polluting industries. But that will happen regardless of the standards adopted, and if those standards are no stronger than those proposed, health groups will almost certainly sue as well. In establishing NAAQS, EPA should function with the same focus on the best available information that physicians have to use.

C2. EPA has a long history of repeatedly setting standards that the vast majority of the medical specialty societies and other health organizations believe are inadequate to protect public health. At virtually every opportunity for engagement, the American Lung Association, American Thoracic Society, and the California Air Resources Board have called on EPA for stricter NAAQS than what EPA eventually adopts. This year, the following organizations have called for NAAQS stronger than what the EPA has proposed: Allergy & Asthma Network, Alliance of Nurses for Healthy Environments, American Academy of Pediatrics, American Lung Association, American Psychological Association, American Public Health Association, Asthma and Allergy Foundation of America, Children's Environmental Health Network, Health Care Without Harm, Medical Society Consortium on Climate and Health, Medical Students for a Sustainable Future, National Association of Pediatric Nurse Practitioners, National League for Nursing, Physicians for Social Responsibility, and Public Health Institute. That alone is strong evidence that EPA's proposal is inadequate. UPHE joins these and other groups in that assessment for this proposal. The World Health Organization's recommendation of a 24-hour standard of 15 and an annual standard of 5 may be unachievable, but it is thoroughly scientifically defensible.¹³

C3. We also join these other groups in calling for EPA to revise the form of the short-term standard to the 99th percentile to effectively capture acute, short-term exposures. The current form at the 98th percentile dates to 1997 and allows nearly 22 days in the 3-year

review period to exceed the standard limit, in addition to days exempted for exceptional events, such wildfires.

C4. It should be noted that **the annual standards for nitrogen oxides and carbon monoxide have not been updated since their inception in 1971, over 52 years ago.** An arguably far-too-weak, one-hour daily standard for NO_x was only added in 2010, and the last time the CO was even reviewed was in 1994. This is a profound failure on EPA's part. Because both the sources and health hazards of these other toxins greatly overlap with PM_{2.5}, by selecting stricter standards for PM_{2.5}, EPA also has a chance to add the co-benefit of simultaneously reducing nationwide NO_x and CO to a more appropriate level.

D. THE CAA MANDATES THAT EPA ESTABLISH STRICTER STANDARDS

D1. Under Section 109 of the Clean Air Act, **the primary NAAQS must be set at a level requisite to protect the public health with an adequate margin of safety** in order to prevent not just known, but even reasonably anticipated health-related effects from air pollution. It further mandates that EPA set the NAAQS at a level that allows the public to spend time outdoors engaged in their normal activities and that air will be clean enough to "protect the public's health with an adequate margin of safety" during those outdoor activities.

This mandate "carries the promise that ambient air in all parts of the country shall have no adverse effects upon any American's health." 116 Cong. Rec. 81 (Dec. 18, 1970, remarks of Senator Muskie, floor manager of the conference agreement). Indeed, EPA has previously recognized this to be the case:

"Standards must be based on a judgment of a safe air quality level and not on an estimate of how many persons will intersect given concentration levels. EPA interprets the Clean Air Act as providing citizens the opportunity to pursue their normal activities in a healthy environment."

44 Fed. Reg. at 8,210

D2. The CAA sets significant limits on the discretion granted to EPA in selecting a level for the NAAQS. **The EPA must err on the side of protecting public health and may not consider cost or feasibility** in connection with establishing the NAAQS. The D.C. Circuit summed up EPA's mandate two decades ago in a suit by the American Lung Association:

D3. "Based on these comprehensive [air quality] criteria and taking account of the 'preventative' and 'precautionary' nature of the act, **the Administrator must then decide what margin of safety will protect the public health from the pollutant's adverse effects – not just known adverse effects, but those of scientific uncertainty or that research has not yet uncovered.**" Then, and without reference to cost or technological feasibility, the Administrator must promulgate national standards that limit emissions sufficiently to establish that margin of safety."

The CAA expressly requires EPA to consider the advice of the “statutorily-created” CASAC and rationally explain any important departure from their recommendations.

The precautionary and preventative nature of the NAAQS requires EPA to set standards that protect against health consequences that may go beyond those impacts that their analysis finds causally established by science. As the D.C. Circuit noted in another case, limited data cannot be an excuse for failing to establish the level at which there is an absence of adverse effect. To the contrary:

“Congress’ directive to the Administrator to allow an ‘adequate margin of safety’ alone plainly refutes any suggestion that the Administrator is only authorized to set primary air quality standards which are designed to protect against health effects that are known to be clearly harmful.”

EPA is legally bound to prioritize public health protection, not economic activity, industrial profit making, or societal convenience. It could be reasonably argued that given the strong evidence that there is no safe level of particulate pollution, having a standard at all actually backfires. Often, the standard is used to defend industry and proposed polluting projects and public policy with modeling that shows a certain standard will not be exceeded. The rationale of setting a standard (which is inadequate) is to ensure that by meeting this standard, public health will be protected. Meeting an inadequate standard does not promote safety.

D4. Given that a pollution standard will never fully protect public health, what is “adequate” protection must be used instead. **EPA standards then are not scientific expressions that establish thresholds differentiating between health and illness, but value system expressions, i.e., how much pollution can a society accept to maintain the normal activities of modern civilization?** To that extent, EPA standards must reflect what is reasonably possible to achieve, not what is easy, convenient, or inexpensive to achieve.

E. EPA LOOKS AT THE RIGHT SCIENCE BUT DRAWS THE WRONG CONCLUSIONS

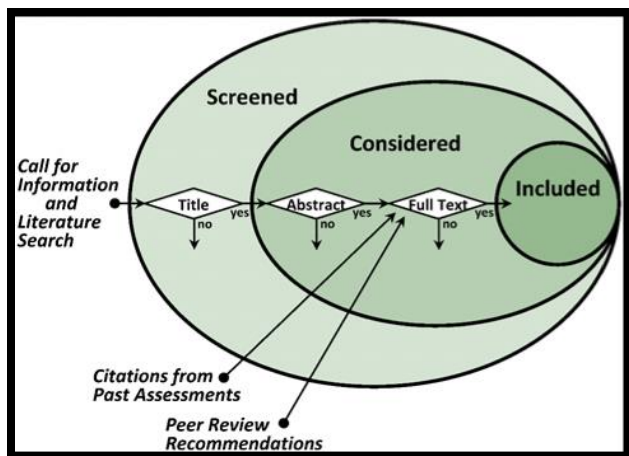
E1. Some EPA conclusions are wrong and even defy common sense. In the EPA’s trio of documents presumably used as the basis for their PM2.5 NAAQS proposal, the *2019 Integrated Science Assessment for Particulate Matter*, the *2022 Supplement to the 2019 Integrated Science Assessment for Particulate Matter*, and the *Preamble to the Integrated Science Assessments*, **we see a recurring pattern of referring to many of the appropriate scientific studies, yet being overly cautious in drawing conclusions from that science that should be driving regulatory action.**¹⁶

We find it ironic that EPA managed to compile over 2,300 pages in these companion documents that are highly detailed, with many hundreds of studies referenced, most of which we are familiar with, and still found a way to draw the wrong conclusions.

Some of the assertions in these documents are stunning to healthcare professionals. For example, on page 1-1 of the *2019 Integrated Science Assessment for Particulate Matter* it states, “Inadequate evidence exists to determine whether having diabetes, being in an older life stage (i.e., older adults), residential location (including proximity to source and urban residence), sex, or diet increase the risk of PM_{2.5}-related health effects.” Every part of that statement contradicts the vast majority of relevant studies and the experience of virtually every front-line clinician.

Many of the recent, large, air-pollution epidemiologic studies are specific to the elderly, i.e., those on Medicare. For example, one study looked at the entire Medicare-eligible population of seven states and found that mortality increased 2.1% for each 1µg/m³ increase in PM_{2.5}. The risk decreased with age. It also found increased risk for those that lived in lower-income zip codes, higher urban density, or had any of several chronic diseases or previous hospitalizations.⁴⁷ EPA’s statement above also ignores the growing evidence that increased risk of diabetes itself is associated with air pollution.

E2. EPA methodology is arbitrary and eliminates too many valuable studies. Figure 3 in the *Preamble to the Integrated Science Assessments* offers a good example of EPA’s flawed methodology.



What the figure above implies is that EPA sifts through the volume of relevant literature, and through a process of elimination, presumably by quality, narrows down the research they will consider to only small number of studies to draw the conclusions used to establish the NAAQS. But weight of evidence is related to both quality and quantity of the research. If EPA starts out with 100 studies and grades 60 of them C, 30 of them B, and 10 of them A, and ultimately only allows the A studies to be considered, then it is completely eliminating a great deal of available,

important evidence. While quality of research is important and should be given a premium in consideration, quantity of research is also important, especially if the conclusions are in line with those considered of highest quality. To just eliminate the vast majority of “slightly lower quality” serves only to justify weaker standards.

The result of EPA’s overly cautious approach to study inclusion and data/design scrutiny provides a veneer of scientific rationale for EPA to routinely offer only tepid public health protection.

E2(a). In a similar vein, **we are disturbed by EPA’s apparent policy to downplay or even dismiss epidemiologic research that originates outside of North America.** The *Supplement to the 2019 Integrated Science Assessment for Particulate Matter* states, “studies examining associations outside the U.S. or Canada reflect air quality and exposure patterns that may be less typical of the U.S., and thus less likely to be informative for purposes of reviewing the NAAQS. Therefore, within this Supplement the studies considered for inclusion are limited to those studies conducted in the U.S. and Canada.” We consider that policy and the rationale behind it scientifically inexplicable and indefensible.

The unwritten but implied EPA assumption is that pollution from other countries is often higher than in the US, sometimes significantly so, and that those studies, therefore, have no value in establishing EPA standards. While North American air pollution may have components and overall chemical composition slightly different than exists in other countries, to our knowledge there is no literature to support a contention that the toxic profile of foreign pollution is so different from domestic pollution that we can justify wholesale dismissal of research that examines foreign populations and foreign atmospheric-pollution data. The supralinear dose response relationship (more about that later) that has been repeatedly established in both the US and foreign-based research is more reason to consider studies of concentrations higher than are common in the US because they provide more data points on those same dose response curves.

Furthermore, this policy is inconsistent with other EPA policies. EPA states, “multicity studies can provide insight on potential confounding through the use of a consistent method to analyze data from across locations with different concentrations of copollutants and other covariates.” If “multicity” studies can provide insight, “multi-country” studies should be able to provide the same strength and quality of data benefit.

No other branches or specialties of medical care, diagnosis, and treatment would discard large bodies of well-done research merely because it was done in other countries on foreign populations. Indeed, nearly all drug makers routinely conduct early-stage drug trials outside the US because it is often less expensive. In fact, “a STAT analysis found that 90 percent of new drugs approved this year were tested at least in part outside the U.S. and Canada.”¹⁴

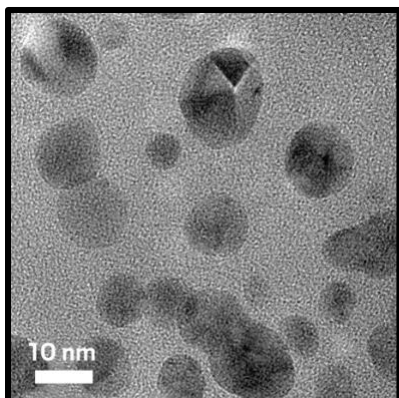
We do not see that kind of American exclusivity being applied to scientific research in non-medical disciplines. For EPA to limit what they regard as relevant or qualifying research to what

is generated from North America seems like an ironic, hypocritical, unscientific excuse to restrict available scientific evidence.

E2(b). In many places, EPA states that it prioritizes studies that analyze conditions “at or near conditions relevant to ambient exposures.” But doctors part of Utah Physicians for a Healthy Environment practice medicine in a geographic area characterized by severe spikes in PM2.5 that are not typical of “ambient exposures” in many other places of the country. Those spikes sometimes represent the some of the highest PM2.5 levels in the world. What is relevant “ambient exposure” in New York is not more relevant to Utah than ambient exposure in Beijing would be. **EPA should not be limiting the research it “considers” to what is typical of ambient exposures for most of the US.** Indeed, it is those areas that may be exposure outliers that need the most protection, given that the largest source of PM2.5 in some Western states is now wildfire PM2.5, with exposure delivered in short-term spikes.

E2(c). **Over emphasizing copollutant confounding is counterproductive to protecting public health.** EPA makes repeated reference to the importance of eliminating confounders and attributes much of the uncertainty in many studies that could be used to infer “causality” to the presence of “copollutant confounding.” While that concern is valid to a certain extent, that emphasis can be overwrought. For example, attributing health outcomes to one type of pollution, like PM2.5, when the atmosphere is also contaminated with other types of pollution, like NOx, may weaken the quality of the study because NOx would be considered a confounder. But both the sources and physiologic effects of the different pollutants significantly overlap. Furthermore, in most cases, regulatory control of sources of one type of pollution also provides control of other pollution components. If the goal is actually to protect public health, then this kind of obsessive differentiation does not serve that goal, but instead, is being used as an excuse to discount numerous valuable studies.

E2(d). **EPA demonstrates little consideration of the growing number of autopsy and tissue studies that have proven beyond any reasonable doubt that particulate pollution nanoparticles now contaminate virtually all human critical organs.** The first of these studies found high-temperature-combustion nanoparticles (magnetites), at the rate of millions per gram of tissue, in the brains of every human examined from two different cities, including the brains of children.¹³⁷



This electron microscopy image shows magnetite particles extracted from a human brain sample.

That should be considered prima fascia evidence of unmitigated biological harm. In fact, EPA's own review gives a detailed physiologic and biochemically plausible explanation of mechanisms of harm from this nanoparticle contamination of human organs, but ultimately downplays its significance and the significance of all the other epidemiologic and laboratory studies on brain function, labeling PM2.5 only "likely to be causal" in neurotoxicity (more about that below). The review even makes the case that 10% of particles landing on nasal mucosa would "translocate to the olfactory bulb," and that is only a "small fraction," of those landing on the nasal mucosa, again downplaying its significance.

Subsequent studies have found even greater particulate pollution contamination of human heart tissue,¹³⁸ knee joints,³⁵⁰ the placenta, including the fetal side of the placenta,¹³⁹ and black carbon nanoparticles in the lungs, livers, and brains of unborn, otherwise normally progressing fetuses.¹⁴⁰ The large surface area-to-volume ratio of the smallest PM allows them to be often saturated with other toxins like heavy metals, PAHs, and pathogens, allowing the PM to act as a Trojan horse carrying other co-pollutants into the body. Moreover, the attached co-pollutants may alter the surface of particles, increasing their reactivity and enhancing their intracellular bioaccessibility.³⁵¹ This information should be treated as clear justification for the tightest PM2.5 regulations possible, i.e., as a regulatory five-alarm fire, yet it doesn't seem to factor into EPA decision making.

E2(e). EPA is inconsistent in their consideration of heterogeneity of studies. There are likely slightly different toxic profiles of PM2.5 from one region in the US to another, from one state to another, from one county to another, even from one neighborhood to the next. Yet, in establishing regulatory thresholds, EPA does not make customized standards for each of these jurisdictions. We know full well there are different toxic profiles of PM2.5 depending on the source. Yet in state implementation plans, EPA allows state agencies to equate all types of PM2.5 as interchangeable in pursuing regulatory compliance.

Moreover, EPA explicitly recognizes there is significant heterogeneity in susceptibility among the US population. Therefore, there is also heterogeneity in causality. A criteria pollutant may

be “causal” for heart disease in person A, but it may not be in person B. Nonetheless, EPA has an obligation to protect both.

We acknowledge that it would be absurd for EPA to have standards for each individual in the country, despite each individual’s having their own susceptibility risk, even if that risk is quantitatively unknown. Likewise, It would be impractical to have separate NAAQS for each subgroup of vulnerability, even though that would provide better protection. For example, a set of NAAQS for pregnant mothers and a different one for adolescents is impossible even though it would make scientific sense. So on the one hand, EPA accepts heterogeneity of risk within the population, while having to establish a uniform standard that is required to be broadly protective of all. But inexplicably and arbitrarily, EPA rejects heterogeneity of populations and pollution characteristics in the studies that it will consider valid or informative based solely on the country of origin.

EPA states in its Nov. 2015, *Preamble to the Integrated Science Assessments*, “Consistency of findings across studies is informed by the repeated observation of effects or associations across multiple independent studies. Further strength is provided by reproducibility of findings in different populations under different circumstances.” Yet EPA arbitrarily eliminates research that would accomplish exactly that.

E2(f). EPA cannot do its job functioning as an engineering firm, it must act with less than perfect knowledge. Healthcare decisions seldom can be made with the same precision as physics or engineering decisions. Biologic systems are too complex to be accurately or adequately evaluated using merely mathematical equations. Physicians and patients don’t have the luxury of waiting until all uncertainty calculations have been satisfied and all doubt is removed before diagnosis and treatment options must be engaged. As caregivers, we have to function on the basis of the best available information at the time, not perfect information or indisputable facts. The science often steers us toward multiple treatment options, with each one having competing risks and benefits. In evaluating knowledge offered by research and in establishing NAAQS, EPA should look at their responsibility in the same way healthcare providers do, as public health advocates do, not as engineering firms do.

E2(g). The CASAC review of the afore-mentioned documents implies that **EPA considers almost exclusively only mortality-based risk assessments, giving little consideration to morbidity risk.** It is bewildering and indefensible that EPA would arbitrarily limit their review to such a narrow adverse health outcome. A similar criticism was levied by the Natural Resources Defense Council against the EPA when it declined to strengthen the ozone standards. They said, “EPA’s near-exclusive focus on lung function decrements demonstrated in controlled human experiments on healthy young adults arbitrarily overlooks important factors and sensitive populations for whom the standards must be protective with an adequate margin of safety.”¹⁵ We echo that criticism and go further. Ozone’s adverse impact on the pulmonary system is only one small part of ozone’s overall health consequences. Ozone has nearly as broad an influence on health as does PM2.5, affecting virtually every organ system, including having a mortality impact.

E2(h). **We also echo CASAC’s critique on EPA’s relying on controlled human exposure studies to identify a minimum concentration for which health can be expected from a 24-hour PM2.5 standard.** Those studies do not and cannot involve those most vulnerable to air pollution, i.e., the elderly, those with cardiovascular and pulmonary morbidities, children, and those in utero. **Most of those studies involved exposures much shorter than 24 hours, and none of those studies involve PM2.5 spikes that last several days in a row, as is typical in Utah.** They almost always involve a single pollutant, hardly ever matching a real-world pollution spike, and the concentrations required to elicit a response in the short term are usually unrealistically high.

E2(i). **EPA is wrong to discount biochemical and histological studies and studies of subtle clinical outcomes.** We disagree with this statement from the EPA and its implications in their decision-making process: “It is more difficult to determine the extent of change that constitutes adversity in more subtle health measures. These more subtle health effects include a wide variety of responses, such as alterations in markers of inflammation or oxidative stress, changes in pulmonary function or heart rate variability, or alterations in neurocognitive function measures.”¹⁶ Each one of these clinically subtle or biochemical outcomes is directly associated with definitive disease and disability. If A=B, and B=C, then A=C. By discounting the value or significance of these kinds of biochemical studies, the EPA is unnecessarily and inappropriately limiting the evidence for stricter standards.

Furthermore, EPA’s statement, “The committee also observed that elevations of biomarkers, such as cell number and types, cytokines, and reactive oxygen species, may signal risk for ongoing injury and clinical effects *or may simply indicate transient responses that can provide insights into mechanisms of injury, thus illustrating the lack of clear boundaries that separate adverse from nonadverse effects*”¹⁶ (italics added).

This kind of characterization of the relevance of biochemical and histological hallmarks of injury and inflammation, and the claim that this “illustrates the lack of clear boundaries separating adverse from nonadverse effects” reflects a poor understanding or a deliberate discounting of their connection with real clinical disease. Injury at the microscopic level means injury at the macroscopic level, even if it is difficult to measure.¹⁷ For example, repeated episodes of airway inflammation may provoke airway remodeling, which occurs in asthma, and leads to irreversible reductions in lung function. Indeed, chronic or repeated episodes of inflammation are the ubiquitous root cause of atherosclerotic vascular disease.¹⁸

E2(j). We agree with CASAC’s critique that the **EPA is being overly conservative for emphasizing use of “the mean” to define where the data provide the most evidence,** since quality data clearly indicate adverse effects below the mean in concentration-response functions.

E2(k). **CASAC is right in criticizing EPA for excluding areas impacted by wildfires and winter inversions.** CASAC’s review states, “in an effort to exclude areas influenced by wildfire PM, areas where the 24-hour PM2.5 standard is controlling due to wintertime stagnation and/or

home heating by woodstoves were also excluded.” Utah is a perfect example of EPA exclusion of major sources of our pollution. But in the same way, EPA is also ignoring the PM produced by “prescribed burns,” which produce PM every bit as toxic as that from wildfires. In some parts of the country, EPA acknowledges that prescribed burns are the largest source of particulate pollution.¹³⁵

E3. Many communities and subgroups will not be protected from short-term pollution hazards by lowering the annual standard alone. We join CASAC in disputing that the annual standard guarantees or even implies adequate protection from short-term PM_{2.5} spikes. A simple analogy is worth considering. A home in Oklahoma’s tornado alley could be destroyed by 10 seconds of 240 mph tornado winds, yet the average wind speed at the front door of that house over a 24-hour period might be completely normal. Regulating wind speed in Oklahoma based on an annual average would accomplish nothing. **PM_{2.5} is a key component in abrupt spikes in pollution related to winter versions, wildfires, and industrial accidents and bypass events.** Independent of chronic exposure, it can result in multiple morbidity and mortality events, such as status asthmaticus, infections like pneumonia, cardiac arrhythmias and arrest, ischemic cardiac events, strokes, and other outcomes related to venous and arterial thrombi or to the disruption and friability of atherosclerotic plaque. Even brief exposures to air pollution triggering inflammation can have life-long consequences if they occur at the earliest life stages, i.e., in utero during organogenesis. The genesis of all these listed events is not related to annual averages, and that fact is the reason there is a 24-hour PM 2.5 standard in the first place.

Most UPHE physicians are based in Utah on the Wasatch Front, where 2.5 million people live. Because of unique geographic circumstances, the majority of Utah’s population lives in the greater Salt Lake Valley with mountain ranges on both sides. Therefore, most of Utah’s population is subjected to significant short-term spikes of PM_{2.5}. Because of that geography, our physicians group is particularly concerned that EPA is not proposing a tightening of the 24-hour standard.

A recent study found that Utah air pollution causes between 2,480 and 8,000 premature deaths every year, shortens median life expectancy up to 3.6 years, and triggers economic losses of \$750 million to \$3.3 billion annually, up to 1.7% of the state’s gross domestic product.¹¹ This large impact on Utah’s population is mostly due to short-term, i.e., days’ to-weeks’ long PM_{2.5} spikes from weather inversions, and where the nation’s worst air pollution may be found for weeks at a time. Our state does not violate the annual average standard. In fact, we would likely not have violated the annual standard even if it were lowered to 9µg/m³. **Utah citizens will receive virtually no protection from only reducing the annual standard.**

We also believe that the EPA should not be allowing exemptions from the standards for “exceptional events.” Utah’s exceptional events are primarily regional wildfires. With the increasing intensity and duration of Western wildfires, exceptional events are no longer exceptional. In California, wildfire emissions nearly equal all their transportation emissions.¹²

Utah is heading in the same direction, with wildfire pollution now becoming a larger source of particulate pollution than our historic winter-inversion PM_{2.5} spikes. The belief of some EPA staff and a few CASAC members that tightening the annual standard would be enough to reduce the 24-hour standard is contrary to the experience in Utah. If you were to ask Utah's population, "Should the EPA do more to prevent or ameliorate our short-term pollution spikes?" you would almost certainly get nearly 100 percent responding adamantly, "Yes." We believe both the legal mandate via the Clean Air Act and the science compel the EPA to do exactly that.

In discounting the need to tighten the 24-hour standard and in EPA's afore mentioned documents, we see inadequate consideration of fetal, infant, and children's exposure to PM_{2.5}. These are the critical developmental stages through which everyone must pass. A standard that is not sufficiently protective of these universal life stages cannot be considered acceptable from any standpoint. Children experience greater exposure for a given atmospheric concentration because of their higher metabolic rate, higher heart rate, and higher respiratory rate relative to adults. The adverse influence of pollution spikes on lifetime chronic disease vulnerability is also greater because of the ongoing organ development during all these early life stages.³⁰

It is reasonable to conclude that the greatest public health impact of air pollution comes from its adverse impact during in-utero stages of development, considering the impact on organogenesis and genetic and epigenetic function. Many of the studies that assess these connections found specific, sometimes short windows of vulnerability, e.g., during certain weeks of gestation.³² Protection against these kinds of outcomes will be provided only by tightening the 24-hour standard.

To those EPA staff and CASAC members that argue against tightening the 24-hour standard, we say such a position implies an **unacceptable philosophy of "how much harm can citizens tolerate?" rather than a philosophy consistent with EPA's mandate, which is, "how much harm can we prevent?"**

E4. By relying on PM_{2.5} mass measurements, EPA is likely underestimating the toxicity of PM. We disagree with EPA's assertion that "the evidence does not indicate that any one source or component is more strongly related with health effects than PM_{2.5} mass."³¹ Ultrafine particles (UFPs) are now widely recognized as the most toxic subset of PM_{2.5}.^{20, 44} Particle number concentration (PNC) is a common metric to measure smaller particles with little mass and are a much better marker of ultrafine concentration, and therefore, are a better marker of health hazard. This is common sense, given the axiom that the smallest particles are the most easily inhaled, the most difficult to exhale, the most easily translocated to the blood stream, and in turn, are the ones that most easily penetrate cellular membranes, including the nucleus of the cell. The majority of particles contributing to PNC in typical atmospheric systems are UFPs.

Therefore, measurement of PM_{2.5} via capture of PM_{2.5} mass on filters does not accurately reflect the toxicity of particulate pollution because it does not accurately reflect PNC or the surface area of the PM_{2.5}. Regulating PM_{2.5} mass as a surrogate for PNC has been found to be

inadequate because it correlates poorly with PM2.5 mass.²¹ The study's authors stated that the two metrics, "are not representative of each other; and regulating PM2.5 does little to reduce PNC."

As long as EPA continues to use PM2.5 mass and not PNC as the regulatory benchmark, it is flying blind in determining the true health hazard of particulate pollution. This adds urgency to the need for EPA to tighten PM2.5 standards as much as possible in the hope of reducing PNC until it starts changing regulations based on PNC. Other studies draw similar conclusions.⁴⁵ PM2.5 tends to be more homogeneous within cities, impacted predominantly by regional and long-range transport. PNC is usually more variable, influenced by in-city sources, especially traffic emissions, things that are more amenable to local public policy control.

Furthermore, measuring merely PM2.5 mass also doesn't distinguish between the different toxic profiles of the various elemental components of PM2.5⁴⁶ or the source. For example, for multiple physiologic and mechanistic reasons, wood smoke is the most toxic of the various types of PM2.5 that the average person is ever exposed to. Yet EPA conducts a certification program that perpetuates and even implicitly endorses wood stoves as acceptable sources of heat.

EPA's regulatory framework allowing states to consider all sources equally toxic fails to provide the public health with protection afforded by prioritizing control of the most toxic sources and types of PM.

E5. The EPA standard for declaring causality is arbitrary and extreme. We strongly disagree with many of the conclusions on causality in table ES-1, page ES-9 of EPA's *2019 Integrated Science Assessment for Particulate Matter*. Of all the organ systems and disease categories, the only ones that EPA acknowledges have an unequivocal causal relationship to short- and long-term particulate pollution are the cardiovascular system and mortality. The table labels the respiratory system for both short- and long-term exposure as only "likely to be causal." It labels the nervous system for long-term exposure only as "likely to be causal," and for short-term exposure only "suggestive of, but not sufficient to infer." It labels "metabolic effects," "male and female reproductive, and fertility" as "suggestive of, but not sufficient to infer," pregnancy and birth outcomes as "suggestive of, but not sufficient to infer," and cancer as "likely to be causal."

Given our familiarity with the many hundreds of epidemiologic studies from around the world that have firmly established strong connections with these outcomes, and the autopsy, biochemical, histologic, and animal toxicologic studies that provide biological plausibility, we consider EPA's standards for declaring "causality" far too rigid, arbitrary, and unscientific. They are an excuse to not pursue stricter standards. To put this in context, it is not possible to say in any one individual who is a lifetime smoker and got lung cancer, that smoking was the cause. Even though smoking increases the risk of lung cancer by at least 15 times, about 25-30% of lung cancers are triggered by air pollution (more about that later), and 3-14% are caused by radon. If the EPA was that patient's physician, using EPA's regulatory standard for establishing

causality, Doctor EPA would not be willing to tell that patient they must “regulate smoking,” that is, stop smoking, because there might have been another cause.

EPA’s rigid causality standard contributes to its over emphasis on cardiovascular disease and mortality while discounting all the other endpoints and providing cover for a weak proposal. Again, to us this suggests an underlying strategy more consistent with a philosophy of, “how much pollution-related harm can we tolerate?” rather than “how much can we prevent?”

We note that in that same document, other health outcomes associated with particulate pollution are left out. There is no mention of the hundreds of studies that show connection to infections, inflammatory bowel disease, arthritis, immunosuppression, skin disorders, and acceleration of the aging process. There is inadequate attention paid to infant mortality or sudden infant death syndrome (SIDS).

F. A SMALL FRACTION OF THE STUDIES THAT COMPEL STRICTER STANDARDS

The totality of adverse health effects from particulate air pollution is staggering from both mortality and morbidity. Our comments in the remainder of this document are based on approximately 1,800 studies that we have reviewed. However, we cite here only those specific studies that were the most directly policy relevant, that provide quantitative exposure-response relationships, and that could be interpreted to specifically address the issue of whether to lower the annual and 24-hour PM_{2.5} standards.

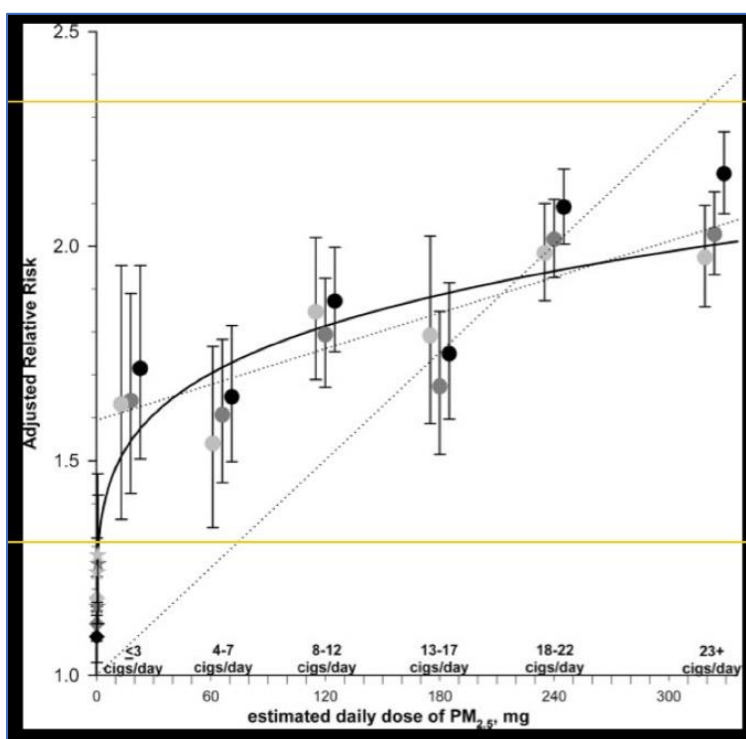
Specifically, we excluded those that measured PM₁₀ even though 50-70% of PM₁₀ consists of PM_{2.5} in most cases.¹⁹ We eliminated studies that only measured common co-pollutants of PM_{2.5}, such as hazardous air pollutants (HAPs), black carbon, or PAHs, or studies that only measured certain sources of PM, such as diesel exhaust or pollution surrogates such as traffic density or distance from heavily trafficked roads, or only measured subsets of PM_{2.5}, such as UFPs. Nonetheless, EPA should take into account that many studies of air pollution suggest that toxic chemicals like PAHs, although not regulated as criteria pollutants, are the most important hazards of a typical urban air pollution mix.²²

We eliminated almost all animal studies. These other types of studies could be extrapolated to indict PM_{2.5} and should be considered in rule making. Our comments then are based on only a small fraction of the worldwide medical literature that reveals the extent of the public health hazard of PM_{2.5}.

There is the temptation to look at these PM_{2.5} health outcomes in isolation. But regulators must keep in mind that there are additional adverse outcomes from ozone, NO_x, sulfur oxides (SO_x), VOCs, HAPs, etc., and that the overall nationwide health burden from air pollution is far greater than and much worse than the statistics we cite in the following pages. The EPA should

not look at regulating PM2.5 in isolation. Regulating PM2.5 should be looked at as only one step of many needed to protect the public from the much larger overall air pollution hazard.

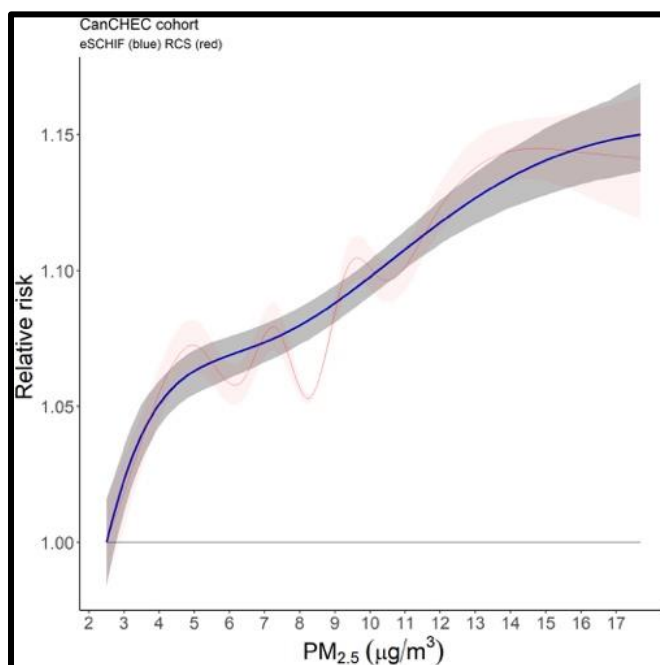
F1. Supralinear dose/response relationship at low exposures: Fundamental to setting the PM2.5 NAAQS at an appropriate level is the concept repeatedly confirmed by research over the last 15 years, that the relationship between disease and particulate air pollution is not linear but is supralinear. As this graph illustrates, from research published in 2009 in the journal *Circulation*, plotting concentration of three different types of air pollution (first-hand cigarette smoke, second-hand cigarette smoke, and community PM2.5), versus disease risk, it is clear that there is no safe level of air pollution, and that reducing pollution levels by a fixed amount has the greatest benefit at the lowest background levels.³⁵ The inclusion of smoking in this discussion is appropriate because smoking is merely personalized air pollution.



Many other studies have confirmed the same supralinear relationship.³⁶ For example, a meta-analysis found an RR of 1.08 per 10 $\mu\text{g}/\text{m}^3$ PM2.5, but also found a supralinear relationship at lower levels.³⁷ An analysis of European cohorts found the same pattern for “(1) natural- and cause-specific mortality including cardiovascular and nonmalignant as well as malignant respiratory and diabetes mortality; and morbidity measured as (2) coronary and cerebrovascular events; (3) lung cancer incidence; and (4) asthma and chronic obstructive pulmonary disease (COPD) incidence.... Associations mostly showed steeper slopes at low exposures with no indication of a threshold.”³³⁰

Most recently, a population-based cohort study of 7.1 million Canadian adults in one of the world’s cleanest environments for air pollution, followed between 1991 and 2016, revealed a

supralinear concentration-response relationship between outdoor PM_{2.5} and mortality at concentrations below 5 µg/m³. The mean PM_{2.5} was 8.5 µg/m³, and 13.3% of the person-years in the cohort had outdoor PM_{2.5} concentrations below 5 µg/m³. Each 10 µg/m³ increase in long-term, average outdoor PM_{2.5} concentration was associated with an 8.0% increased risk of nonaccidental mortality.³⁶⁷ The dose mortality response curve is copied below.



A meta-analysis of 141 cohort studies found smoking one cigarette per day is nearly half as much cardiovascular and stroke risk as smoking an entire pack per day.³⁸ The risk of a premature death from smoking just one cigarette per day is 64% higher than if a person didn't smoke. By smoking just one cigarette per day, a person has a nine times greater risk of dying from lung cancer than a non-smoker has, while smoking ten cigarettes a day results in a 12 times greater risk.³⁹ These studies don't just speak to the risks of very light smoking, they are reflective of studies that correlate community PM_{2.5} levels in a supralinear dose-response relationship with disease.

This same supralinear relationship is at the heart of the conclusions of the report commissioned by Environmental Defense Fund that concluded that an annual PM_{2.5} standard of 8 µg/m³ would save nearly 20,000 lives compared with an annual standard of 10 µg/m³ that would save only 4,800 lives.²³

Whether the annual standard should be tightened and to what degree is specifically addressed by a study of US veterans that found nine different causes of death were associated with air pollution (cardiovascular disease, cerebrovascular disease, chronic kidney disease, chronic obstructive pulmonary disease, dementia, type 2 diabetes, hypertension, lung cancer, and pneumonia), and that 99% of air pollution deaths occurred in counties where the annual PM_{2.5}

levels met current EPA standards.⁴⁰ This study is another reflection of the supralinear relationship between PM_{2.5} dose and adverse health outcomes.

The knowledge that there is no safe level of air pollution, there is no threshold below which health effects are not seen, and that per unit of exposure, most major health consequences are greater at low concentrations calls into question not only the adequacy of current standards but also the efficacy of even having standards.

For example, in Utah and undoubtedly other states, invariably pollution discussions with state agencies end up at whether a proposal allows a community to be compliant with NAAQS. If modeling suggests that compliance will be achieved or maintained, then a project that will expose the community to more air pollution is almost certainly approved by the state. The existence of the standard in such a case provides a shield behind which state regulators can hide in approving more pollution. Instead of protecting public health, the standards actually undermine it. Because of that, the issue is not whether a new standard will be tight enough to eliminate public health impacts—no new standard ever will be. The issue is what does the society value? How much constraint of industry and personal fossil fuel use will society accept in pursuit of improved health?

There is a significant difference between genders and demographic groups on their risk of poor health outcomes from particulate pollution. Several studies show women have higher risk of cardiovascular disease from air pollution compared with men,^{41,42} something that should be factored into the NAAQS. Reductions in PM_{2.5} are associated with increased life expectancy.⁴³

F2. PM_{2.5} and mortality: PM_{2.5} has been identified as the sixth leading cause of premature death.³⁴ The scope of the of diseases and organ system damage from particulate pollution is nearly as broad as that from smoking cigarettes.

F2(a). Mortality and long-term exposure: The report commissioned by the Environmental Defense Fund mentioned above²³ also found that low-income Americans would see a 30% higher mortality benefit per capita from an 8 µg/m³ standard than a 10 µg/m³ standard.

In the largest study of its kind, using a cohort of over 60 million US Medicare beneficiaries followed for 12 years, with 460,310,521 person-years of follow-up, researchers found the risk of death from a 10 µg/m³ increase in PM_{2.5} was 7.3%. But when the analysis was restricted to person-years of less exposure than 12 µg/m³, the same increase was associated with a 13.6% increase in risk of death. Subsets of that population—men, blacks, and Medicaid-eligible people had an even greater risk of death. This study is particularly striking because it provides information on the health effects of long-term exposure to low levels of PM_{2.5} in smaller cities and rural areas and among minorities or persons with low socioeconomic status.⁴⁸ This study also supports the supralinear dose/response relationship addressed above. In a study of similar size, each daily increase of 10 µg/m³ in PM_{2.5} was associated with an increase in daily mortality rate of 1.05%.⁴⁹

In an 11-year follow-up study of the famous Harvard Six Cities study, the authors found each average 10 $\mu\text{g}/\text{m}^3$ increase in PM2.5 was associated with increased risk of all-cause mortality of 14%. The concentration-response relationship was linear down to PM2.5 concentrations of 8 $\mu\text{g}/\text{m}^3$.⁵³

A Canadian cohort study of over 2 million people found similar results. Notable about this study was that exposures were predominantly lower than in previous studies: mean PM2.5 exposure was 8.7 $\mu\text{g}/\text{m}^3$.⁵⁵

F2(b). Mortality and short-term exposure: Another study found an 18% increase in all-cause mortality, a 3% increase in cardiovascular disease, a 22% increase in heart attacks, a 76% increase in stroke, and a 71% increase in respiratory deaths in association with a mere 10 $\mu\text{g}/\text{m}^3$ increase in 2-day averaged PM2.5.⁵⁴

Analyzing long-and short-term PM2.5 via satellite, researchers found that even annual concentrations < 10 $\mu\text{g}/\text{m}^3$ and daily concentrations < 30 $\mu\text{g}/\text{m}^3$ were associated with increased mortality: 9.28% and 2.14% respectively. The relationship appeared to be linear for short-term exposure, but on annual exposure, a greater effect per unit of exposure appeared with concentrations above 6 $\mu\text{g}/\text{m}^3$.⁵⁶

Other studies of daily PM2.5 and daily deaths in Boston found that the association was almost certainly causal.⁵⁷ Causal modeling of PM2.5 in 135 US cities found that PM2.5 from local pollution increased daily deaths 1.5% per 10 $\mu\text{g}/\text{m}^3$ PM2.5 increase. Restricting the analysis to days with pollution below 25 $\mu\text{g}/\text{m}^3$ yielded a 1.7% increase, supporting again the supralinear association and that the current 24-hour PM2.5 standard is not providing enough protection.²⁹⁰

An increase of 10 $\mu\text{g}/\text{m}^3$ PM2.5 on the day of and the day prior to death is associated with a 1.56% increase in daily deaths. This association was found even in zip codes that meet the EPA's current annual standard. The effect of PM2.5 below both EPA daily and annual standards was 2.08%. This study highlights that PM2.5 affects even rural populations with low air pollution levels.⁵⁸ Schwartz, et al, estimated that a PM2.5 increase of 6.32 $\mu\text{g}/\text{m}^3$ increased daily death totals by .9%, even when all days with PM2.5 concentrations > 30 $\mu\text{g}/\text{m}^3$ were eliminated.⁵⁹

In a nationwide study in Italy, data on causes of death were extracted for three years and correlated to daily PM2.5. levels. There was a positive association with mortality from natural, cardiovascular, cardiac, respiratory, and nervous-system causes. For example, mortality from nervous system–related causes increased by 4.55% for 10 $\mu\text{g}/\text{m}^3$ increases in PM2.5, lag 0-5 days.³³⁵

F2(c). Association with infant mortality: The United States has one of the highest rates of SIDS of all middle and high income countries in the world. PM2.5 is also associated with infant mortality, such as SIDS, and respiratory mortality. In a Korean study of 2.5 million births, an increase of 10 $\mu\text{g}/\text{m}^3$ PM2.5 during the first two trimesters was associated with a 20% increased risk of SIDS.⁷³ A Massachusetts study of infant mortality among 466,000 births and

postnatal lifetime PM2.5 found a much stronger association with after-birth exposure. Per 1.3 µg/m³ increase in PM2.5, the rates of total, respiratory, and SIDS mortality increased 266%, 336%, and 250% respectively.²⁸⁵

In a study of nearly 1 million African infants, a 10 µg/m³ increase in PM2.5 concentration is associated with a 9% rise in infant mortality. The authors noted, “This effect has not declined over the last 15 years and does not diminish with higher levels of household wealth.”²⁹¹ In another study of 360,000 births in Korea, an increase in gestational PM2.5 exposure of 3.15 µg/m³ was associated with a 53% increase in all-cause infant mortality, 315% for respiratory infant mortality, and 42% increase for SIDS.¹⁷³

F2(d). Association with ICU and COVID mortality rates: Mortality rates in the intensive care unit are related to short-term PM2.5 exposures. Per 10 µg/m³ increase in PM2.5, mortality within 30 days increased 18%.³⁰⁵

As previously noted, COVID is likely to become endemic to the world’s population. It is still the third leading cause of death in the US. Numerous studies found PM2.5 was associated with increased mortality from COVID. In 32 European cities, from 2020 through 2022, the highest death rates occurred during pollution peaks and varied in proportion to their intensity. A 550% increase in mortality was observed when PM2.5 concentrations got close to 45 µg/m³. But an increase of just 1 µg/m³ was associated with a 10% increase in mortality.⁵⁰ Other studies on short-term PM2.5 exposure found similar results.^{312,337}

Finally, reductions in PM2.5 are associated with increased life expectancy.⁴³ Using 16 years of data on 68 million Medicare enrollees, a decrease in long-term PM2.5 by 10 µg/m³ was causally linked to a mortality decrease of 6-7%.³⁰⁸

The totality of adverse health effects from particulate air pollution is staggering from both mortality and morbidity. Taking into account the numerous studies that show genetic and epigenetic damage, which suggests transgenerational effects, makes the case even stronger for acting more aggressively than the EPA proposal on both the annual and 24-hour standard.

F3. PM2.5 and the cardiovascular system: Air pollution’s impact on cardiovascular disease accounts for about 80% of air pollution–related mortality.³²³ The pro-atherogenic influence of PM is based on several related pathophysiological processes: endothelial dysfunction,³⁵⁸ impaired lipid metabolism,³⁵⁶ increased oxidative stress and inflammatory reactions, and enhanced thrombogenesis and plaque friability. In addition, PM2.5 causes subclinical damage to cardiac muscle cells by several mechanisms: apoptosis, oxidative stress, and decreased oxygen delivery due to coronary atherosclerosis and ischemic damage of myocytes.³²⁴ Particulate pollution is a key contributor to accumulation of atherosclerosis. On the other hand, small reductions in PM2.5, 1 µg/m³, over less than five years, are associated with a slowing of atherosclerosis progression.⁸⁴

As with cigarette smoke, the PM effects can be almost immediate. Within 15 minutes, inhaled pollution nanoparticles are detectable in the blood and urine and can still be detectable 3 months later. The amount detectable is inversely proportional to the size of the particles.⁵² This implies that brief exposure to pollution nanoparticles can have prolonged inflammatory-based health consequences. This alone makes for a strong argument to reduce the 24-hour PM2.5 as much as possible.

Furthermore, these nanoparticles preferentially accumulate at sites of vascular inflammation: in other words, at the worst possible locations.⁸⁷ This provides a plausible mechanism for the endothelial prothrombotic changes and friability of atherosclerotic plaques that are often the cause of strokes and heart attacks.

Other impacts of short-term PM2.5 exposure include alteration of electrical signaling within the heart, starting as early as infancy. Rates of arrhythmias, heart attacks, and strokes increase abruptly with air pollution spikes and are the primary cause for increased community mortality rates. Those rates correspond to hourly pollution concentrations and stay elevated for as long as 30 days after the exposure has ended. In patients who suffer from heart failure, short-term air pollution spikes reduce cardiac function further.

The studies referred to below provide quantitative information relevant to where PM2.5 NAAQS should be established.

F3(a). PM2.5 is a key contributor to atherosclerosis, arteriole narrowing, plaque rupture, and cardiac ischemia. The relationship between PM2.5 and cardiovascular disease is striking. Following over 136,000 healthy participants with no known previous history of cardiovascular disease for approximately 7 years, the risk of major cardiovascular events increased with higher PM2.5 in a linear relationship, 36% per 1 µg/m³ chronic PM2.5 exposure. The air pollution effect was comparable to that from hypertension and diabetes mellitus.⁶⁰

This winter, PM2.5 levels in the heavily populated areas of Utah were often above 50 µg/m³, a common wintertime occurrence. For one weekend, Utah had 7 of the top ten worst polluted cities in the country. Based on this study, the risk of heart attacks for most of Utah's population was increased by over 12% by short-term exposure to our winter inversion PM2.5 pollution.

In a review and meta-analysis of 12 global studies, angina pectoris risk increased .66% on the second day of exposure to a 10µg/m³ increase in PM2.5.³⁶¹ Another meta-analysis showed a near-term increase in risk of heart attack of 2.5% for each increase of 10 µg/m³ in PM2.5.⁵¹

Implementation of the first NAAQ for PM2.5 allowed researchers to track the difference in rates of cardiovascular (CV) mortality from before the standard was implemented and afterward. They found a 10% decrease in CV mortality for each 1 µg/m³ decrease in long-term PM2.5. But counties with the greatest baseline pollution, and therefore the greatest reduction in PM2.5 after implementation saw the smallest reduction in CV mortality per unit decrease of PM2.5.⁶¹

This is further evidence of the supralinear relationship between PM2.5 concentration and disease and further supports the need to continue tightening the PM2.5 standards.

The retina is the only place where direct vision of arterial vasculature is possible. This lends itself to valuable observations relevant to the entire arterial system. The value in reducing PM2.5 by even small amounts was illustrated by a study showing that the diameter of arterial retinal vessels was reduced by an amount equivalent to 7 years of aging from chronic exposure to just 3 µg/m³ PM2.5. The value of reducing even short-term exposure by 9 µg/m³, as determined by PM2.5 levels on the day prior to the exam, was associated with a reduction in vessel diameter equivalent to 3 years of aging.⁶²

Rates of heart attacks are associated with exquisitely small increments in chronic PM2.5 exposure. Just .59 µg/m³ increase in PM2.5 was associated with a 16% increase in the incidence of acute heart attacks.⁶³

In a retrospective cohort study of 3.7 million California adults followed for 10 years, there was a 12% increased risk of acute heart attack (acute myocardial infarction [AMI]), a 21% increased risk of ischemic heart disease (IHD) mortality, and an 8% increased risk of cardiovascular mortality associated with a 10 µg/m³ increase in 1-year mean PM2.5. PM2.5 exposure at concentrations 10.0 to 11.9 µg/m³ was associated with a 6% increased risk of AMI and 7% increased risk of IHD mortality compared with concentrations less than 8 µg/m³.³⁶⁴

A retrospective study of 3.7 million people followed over 10 years found that chronic PM2.5 exposure was associated with an increased risk of heart attack, ischemic heart disease mortality, and cardiovascular disease mortality; these associations were more pronounced in low socioeconomic status communities. **PM2.5 exposure at moderate concentrations (10.0 to 11.9 µg/m³) was associated with increased risks of incident AMI (6% [95% confidence interval (CI), 3%-10%]) and IHD mortality (7% [95% CI, 2%-12%]) compared with exposures < than 8 µg/m³.⁶⁴**

Elevated PM2.5 contributes to the onset of acute coronary events, especially ST-segment elevation heart attacks. In a study done of Utah patients, researchers found that a same-day 10 µg/m³ increase of PM2.5 to a level greater than 25 µg/m³ increased the risk of an ST-segment elevation myocardial infarction 15%.⁶⁵ A 5 µg/m³ increase in annual mean PM2.5 was associated with a 13% increased risk of coronary events.⁶⁶ In another study of fatal heart attacks, long-term PM2.5 increases of 5.3 µg/m³ were associated with a 35% increase risk.⁶⁷ Even hourly PM2.5 concentrations of 36 µg/m³ increase the risk of heart attack,⁶⁸ which speaks to the inadequacy of EPA's form used to calculate the 24-hour standard.

F3(b). Effect on heart electrophysiology: It is increasingly recognized that complex chronic diseases have their roots in early life development. Air pollution's effect on the heart begins in utero.

Normal heart rate variability is an indicator of a healthy heart's ability to respond to stress and is essential for optimal functioning of the cardiovascular, respiratory, and digestive systems and is also connected to psychological well-being and the ability to handle lifetime emotional stress. Decreased heart-rate variability, i.e., lower resting vagal tone, is an important indication of a heart's inability to respond appropriately to stress and is associated with increased risk of SIDS, heart attack, arrhythmias, hypertension, metabolic syndrome, and psychological disorders in older childhood, adolescence, and adulthood.^{70, 71, 72} **Examining heart and respiratory rates of six-month-old babies, and correlating that to air pollution levels inhaled by the mother during the pregnancy, a 1 µg/m³ increase in PM_{2.5} was associated with a 3.53% decrease in respiratory sinus arrhythmias, i.e., lower resting vagal tone.⁶⁹ This is an example of an important study with long-term implications that the EPA would likely not consider, given their arbitrary inclusion criteria.**

In adults, long-term PM_{2.5} increases of 10 µg/m³ increases the risk of abnormal heart electrical activity by 60-70%, depending on the type of abnormal rhythm.⁷⁴ Research on out-of-hospital cardiac arrest helps make the case for a stricter 24-hour standard. These typically fatal events occur 4% more often with an increase of 10 µg/m³ in the day of and the day before the event.⁷⁵ Other studies showed similar results, such as the risk's increasing significantly with even a mild elevation of PM_{2.5} (10-15 µg/m³) and further increasing with higher levels.⁷⁶

F3(c). Effect on blood pressure: The relationship between air pollution and high blood pressure begins in utero. Prenatal air pollution exposure is associated with higher blood pressure in newborns. Increases in maternal PM_{2.5} exposure of just 5 µg/m³ was associated with a 2.4 mm mercury (Hg) higher systolic and a 1.8 mm Hg higher diastolic blood pressure (BP) at birth.⁷⁷ Another study showed similar results.⁷⁸ These are examples of studies excluded by EPA from consideration, but they have significant clinical implications.

Less than three days' exposure to 3.6 µg/m³ PM_{2.5} is associated with an increase in arterial stiffness in elderly men.⁷⁹ That, in turn, contributes to spikes in blood pressure. Elevated blood pressure is a health hazard both acutely and chronically, because it contributes to multiple adverse cardiovascular outcomes, like strokes and heart attacks. Short-term increases of 5.2 µg/m³ PM_{2.5} are associated with an 8.2 mm Hg higher mean systolic BP and 5.8 mm Hg higher mean diastolic BP.⁸⁰ Within just two hours of exposure to multiple types of pollution, including multiple sizes of particulate matter, BP rises.⁸² Each 10 µg/m³ increase in long-term PM_{2.5} is associated with a 3% increased risk of hypertension.⁸¹

F3(d). PM_{2.5} is also highly associated with pulmonary hypertension. Just a 3 µg/m³ increase in chronic exposure is associated with a 438% increase in the risk of death or lung transplant from pulmonary hypertension.⁸³

F3(e). Association with heart failure (HF), morphological changes, and blood clots: PM is also associated with HF. A highly cited meta-analysis found that a mean reduction of chronic PM_{2.5} of 3.9 µg/m³ would prevent 7978 HF hospitalizations and save a third of a billion US dollars per year just in HF expenses.⁸⁵ In a nationwide study by county, increased ambient PM_{2.5}

concentration level was associated with increased incidence of HF hospitalizations and mortality across the US. Every 1 $\mu\text{g}/\text{m}^3$ increase in annual PM_{2.5} concentration was associated with an increase of 0.51 HF hospitalizations/1,000 Medicare beneficiaries, and 0.74 HF deaths/100,000 residents.³⁴⁹

PM_{2.5} is associated with increased risk of deep-vein thrombosis and pulmonary embolism, even in locations that meet the current annual standard of 12 $\mu\text{g}/\text{m}^3$.⁸⁶

In addition to atherosclerotic coronary artery disease, rhythm abnormalities, heart failure, and hypertension, chronic PM_{2.5} exposure is also associated with cardiac morphological abnormalities reflective of impaired pumping mechanisms. Using a cohort of almost 4,000 people without known cardiovascular disease, researchers estimated PM_{2.5} exposure five years prior to cardiac imaging studies. The mean PM_{2.5} value was 9.86 $\mu\text{g}/\text{m}^3$. Per PM_{2.5} increase of 1.32 $\mu\text{g}/\text{m}^3$, left ventricular end systolic volume increased 1.28%.⁸⁸ This cardiac parameter change is an indication of impaired heart function.

Studies of hospitalizations make a similar strong case for reducing the annual standard to 8 $\mu\text{g}/\text{m}^3$. In a nationally representative sample of Medicare enrollees, increasing exposure to PM_{2.5} from less than 8 $\mu\text{g}/\text{m}^3$ to between 8 and 12 $\mu\text{g}/\text{m}^3$ increased all-cause hospitalization rates by 15%.⁸⁹

F4. PM_{2.5} and the brain and nervous system: As with the cardiovascular system, particulate air pollution is associated with increased oxidative stress and inflammation in both the peripheral and central nervous system. In addition to the vascular system and crossing the blood brain barrier (BBB), PM_{2.5} and UFPs can directly access the central nervous system via the nasal mucosa and the olfactory nerves, and likely after oral ingestion, through the GI tract carried by the vagus nerve. These auxiliary pathways make the brain uniquely vulnerable to particulate pollution. Moreover, the systemic inflammation precipitated by PM causes a loss of BBB integrity and an increase in BBB permeability, initiating a vicious cycle of adverse impact on the brain.⁹⁰ Once UFPs penetrate brain parenchyma, their accumulation triggers local induction of oxidative stress and inflammatory responses, primarily manifested by reactive microgliosis and neuronal damage.

F4(a). PM_{2.5} interferes with brain development: PM nanoparticles can cross the placenta and interfere with brain development throughout intrauterine life. In a study where almost all PM_{2.5} measurements were below current NAAQS, prenatal exposure to small increments of PM_{2.5} (3 $\mu\text{g}/\text{m}^3$) was inversely associated with multiple metrics of functional neurodevelopment at two years. Exposures during mid to late pregnancy may be especially detrimental to neurodevelopment, which suggests the need for limiting air-pollution exposure, especially during the latter half of pregnancy.¹¹³

In a Chinese study of 2,435 infant mother pairs, increments of every composition of PM in prenatal exposure of 10 $\mu\text{g}/\text{m}^3$ PM_{2.5} [primary particles (black carbon, mineral dust, and sea salts) and secondary particles (NH₄⁺, NO₃⁻, SO₄²⁻ and organic matter)] was negatively

associated with gross-motor and personal-social scores, and especially problem solving for all infants measured at age one.³³⁶

Neurodevelopmental disorders have repeatedly been shown to correlate with PM2.5 exposure during pregnancy. A 10 µg/m³ increase in PM2.5 was associated with a 33% increased risk of Autism Spectrum Disorder (ASD) in children. PM1 was even more tightly associated, with an increase of 10 µg/m³ during pregnancy and the first year of life being associated with an increased risk of 364%.¹¹⁵

Other studies found similar results, such as a 15% increased incidence with an increased PM2.5 exposure of 4.68 µg/m³.^{116,117} and even higher correlations, as high as 232% for an increase of 10 µg/m³.^{118,119}

The association of PM2.5 with ASD is much stronger in boys, corresponding to the much higher incidence of ASD in males. Per 6.5 µg/m³ increase in PM2.5 during the entire pregnancy, the risk increased 17%, and when occurring during the first year of life, the risk increased 21% and was specific to boys.¹²⁰

Not only is PM2.5 associated with ASD, it is associated with long-term variations and disruptions in mitochondrial physiology in children with ASD.³⁵⁴ The effect on mitochondria may be the route by which PM2.5 precipitates neurodevelopmental regression (NDR) in children with ASD, i.e., when a child loses previously acquired skills and develops ASD symptoms. A triggering event may or may not be involved. In a case control study, the risk of NDR was related to higher PM2.5 during 3 to 6 weeks of the NDR-event period, particularly in those without a trigger. Those that experienced NDR had a higher average exposure to PM2.5, both during the NDR-event period and reference periods, 12.2 µg/m³ versus 11.2 µg/m³. Furthermore, those that had an NDR demonstrated a significant change in PM2.5 during the NDR event period relative to the reference period. The odds of having NDR without a trigger were significantly elevated when PM2.5 was higher, OR 1.041, per 1 µg /m³.³⁵⁵

Early-stage brain development is dependent on placental expression of appropriate genes, such as those that control the production of the brain-derived neurotrophic factor (BDNF)—signaling pathway. Prenatal exposure to PM2.5 impairs BDNF production. A 5-µg/m³ increase in residential PM2.5 exposure during the first trimester of pregnancy was associated with a 15.9% decrease in expression of placental BDNF at birth.¹²¹

F4(b). PM2.5 is a significant contributor to stroke: A landmark study of PM2.5's association with four outcomes precipitating hospitalizations (stroke, cardiac arrhythmias, pneumonia, and heart attack) using a causal-model approach, accounting for multiple pollutants, identified important trends.³⁰⁹ First, supporting the supralinear concept, the greatest increase in the risk of admissions per unit change in exposure occurs at lower concentrations of air pollutants for all four types of admissions. Second, PM2.5's association with increased risk for all four types of hospitalizations was especially true for elderly patients, contradicting an EPA as noted earlier. There was a nearly 1% increase in the risk of stroke for each 1 µg/m³ increase in annual PM2.5.

Elevated levels of PM_{2.5} may trigger not only cerebrovascular events via short-term exposures but also increase the risk of future events via long-term average exposures.³⁵³

Particulate pollution contributes to about one-third of the global stroke burden and about one-fifth of the global burden of dementia.⁹¹ Like heart attacks, strokes are highly associated with PM_{2.5}. An increase of 6.6 µg/m³ on the day of the stroke is associated with an increase in the risk of ischemic stroke of 10%.⁹² A meta-analysis of long-term exposure to PM_{2.5} as a risk factor for stroke found a 6.4% (95% CI, 2.1–10.9%) increase in the hazard of admission for each 5-µg/m³ increase in PM_{2.5} levels.³¹⁰

In another study, the risk of stroke increased 34% following a 24-hour period of PM_{2.5} 15 µg/m³ to 40 µg/m³, i.e., what is currently classified as moderate pollution and largely below the current 24-hour PM_{2.5} standard. The increase risk was greatest between 12 and 14 hours after exposure and was most closely associated with markers of traffic pollution, which suggests that ultrafine PM is a primary culprit. The same study found that as a continuous variable, 6.4 µg/m³ PM_{2.5} increased stroke risk by 11%.⁹³ PM_{2.5} is also associated with the progression trajectory of strokes. A UK study of stroke incidence, post-stroke cardiovascular diseases, and subsequent death found that each 5 µg/m³ increase in annual PM_{2.5} was associated with a hazard ratio (HR) for stroke of 1.24, and an HR of transition from pre-stroke to death of 1.30.³³²

F4(c). PM_{2.5} is a significant contributor to impaired cognition: Impaired cognition is a well-established consequence of both acute and chronic PM_{2.5} exposure at levels relevant to the issue of tightening the NAAQS. In a study of Salt Lake City, Utah, school children who were exposed to an average PM_{2.5} level of just over 8 micrograms per cubic meter, impaired school performance in math and English was associated with both chronic PM_{2.5} and short-term spikes that only reached as high as 23 µg/m³, well under the current 24-hour standard. Short-term spikes had a greater impact on academic performance than chronic levels.⁹⁴ An increase in PM_{2.5} exposure during adolescence of 7.73 µg/m³ is associated with a loss of performance IQ of 3.08 points.¹¹⁴

In a study of nearly 58,000 3-4 year olds in low- and middle-income countries, a 5 µg/m³ increase in annual PM_{2.5} was associated with an OR of cognitive delay of 1.17.³⁴⁷

In a meta-analysis of 86 studies, a 1 µg/m³ increase in PM_{2.5} exposure was associated with reduced performance in general cognition, lower verbal fluency, and a decrease in executive functioning.³⁴² In a Chinese population of infants up to age 3, exposed to high levels of PM_{2.5}, an increase of 16 µg/m³ PM_{2.5} exposure was associated with a .19 decrement in motor-performance scores, and an OR of 1.06 for being diagnosed with “developmental coordination disorder” a neurodevelopmental disorder that affects children’s ability to execute coordinated motor actions, resulting in slow, clumsy, or inaccurate motor performances.³⁴³

In a study of workers in 6 different countries, over 12 months, office workers exposed to higher PM2.5 and lower ventilation rates demonstrated worse cognition. Each increase of 8.8 µg/m3 was associated with slower response times and reduced accuracy for 8 out of 10 cognition-test metrics.⁹⁵

PM2.5 adversely affects cognition in all age groups, but older adults are the most widely studied. In a racially diverse sample of older adults, an increase of 10 µg/m3 annual average PM2.5 was associated with a 50% increase in cognitive errors on a mental-status questionnaire.¹²² A 1.1 µg/m3 increase in long-term PM2.5 exposure was associated with a decline in cognitive performance equivalent to about 14 months of aging.¹²³

In a population of 19,409 US women aged 70 to 81 years, long-term exposure of 10 µg/m3 PM2.5 was associated with a cognitive decline equivalent to 2 years of aging.⁹⁶ Another study of older women found that a three-year average PM2.5 increase of just 4.04 µg/m3 was associated with associated accelerated declines in verbal learning and free-recall memory.⁹⁷ A meta-analysis of longitudinal studies involving over 12 million people found a risk of cognitive impairment of 8% per 5 µg/m3 increments in exposure to PM2.5.⁹⁸

F4(d). PM2.5 is associated with Parkinson's Disease (PD): PD is associated with PM2.5. The deposition of α-synuclein (α-Syn) in the brain is the pathological hallmark of PD. PM2.5 promotes the fibrillization of α-Syn and the formation of α-Syn fibrils with enhanced seeding activity and neurotoxicity.³²⁸

A population-based geographic study reported just weeks ago involving 22 million Medicare beneficiaries found not only an association, but there were geographic hotspots. The incidence of PD increased 25% with an annual average increase in PM2.5 exposure of 14 µg/m3.²⁷⁶ This study found a “ceiling effect” at PM2.5 12 to 19 µg/m3 consistent with the supralinear effect addressed earlier.

F4(e). Association with dementia and Alzheimer's Disease (AD): In a study of nearly 3,000 people with a mean age of 74.1 years, the risk of dementia increased 54% in association with an increase of .88 µg/m3 PM2.5 during the previous 5 years at their residential address.⁹⁹

Numerous other studies of dementia and long-term PM2.5 exposure showed a strong correlation. In a study with a mean 10-year average PM2.5 exposure of 10.1 µg/m3, each 1 µg/m3 increase was associated with a 16% increased risk of dementia.¹⁰⁰ A meta-analysis of 12 studies found the risk of dementia increased 3% for each 1 µg/m3 increase in long-term PM2.5.³⁶⁸

On the other hand, reduction in PM2.5 in later years reduced the risk of dementia. Older women free of dementia were followed for six years. A reduction in PM2.5 of 1.78 µg/m3 was associated with a 20% reduction in the risk of dementia, equivalent to the risk reduction expected from being 2.4 years younger.¹⁰¹ Other studies found similar, if less dramatic results.^{102,103}

AD is significantly associated with PM2.5. A meta-analysis of nine studies showed long-term exposure of 10 µg/m³ was associated with a 95% increased risk of AD.¹⁰⁴ Another study found a 138% increased risk of AD per increase of 4.34 µg/m³ in PM2.5 over nine years.¹⁰⁵ In older females, averaging PM2.5 over three years, each of increase of 2.81 µg/m³ declines in learning and immediate recall were accelerated by 19.3%. Those same increments were associated with progressive atrophy of grey matter, as shown by MRI scans, indicative of increased AD risk.¹⁰⁶

A meta-analysis of 49 studies published just weeks ago showed a positive association between 10 µg/m³ increases in long-term PM2.5 and all-cause dementia, AD and PD, with pooled OR of 1.3, 1.65, and 1.17 respectively.³⁶³

Amyloid-β (Aβ) plaques are considered an anatomic finding of AD. In a study that included more than 18 000 US participants with cognitive impairment who received an amyloid PET scan, air pollution was estimated 14 years before the scan and again 1 year before the scan. Living in areas with higher estimated PM2.5 concentrations was associated with a 10% higher likelihood of amyloid PET scan positivity per 4 µg/m³ increase in chronic PM2.5.¹⁰⁷

In a study of North Carolina residents, those living with chronic PM2.5 > 10 µg/m³ were compared with a control group living with PM2.5 ≤ 7.61µg/m³. The group with greater exposure were found to have higher rates of mortality and hospital admissions for AD, non-AD dementia, and PD, including a pronounced increase in AD mortality (323/100,000 versus 257/100,000, respectively).¹⁰⁸ Another study tracked the relationship between long-term exposure to PM2.5 and time to first hospitalization for three common neurodegenerative diseases—dementia, AD, and PD. An increased risk for all three was found, ranging from 8% to 15% per 1 µg/m³ increase in annual PM2.5.¹⁰⁹ Other studies tracked similar outcomes with short-term PM2.5. For each 10 µg/m³ increase in two days' average of PM2.5, researchers found statistically significant increases in hospital admissions for PD 3.23% and for diabetes 1.14%.¹¹⁰ Another study found an increase of 61% for the risk of hospitalization for PD, per 10 µg/m³ increase in PM2.5 averaged over an eight-day period.¹¹¹

Tracking the relationship between long-term PM2.5 and dementia, researchers found that a 4.8 µg/m³ increase in PM2.5 was associated with a 4% increase in dementia over a 12-year period.¹¹²

F4(f). Association with multiple psychiatric and tic disorders: Air pollution is significantly associated with increased risk of psychiatric disorders. Multiple types of mental illness are highly associated with PM2.5. An increase of 10 µg/m³ over 3 years was associated with an increased risk of depression of 44%.¹³¹ In pregnant women, PM2.5 in the first 3 months of pregnancy was associated with increased risk of anxiety and depression, 23% and 25% respectively for a 10 µg/m³ increase in daily PM2.5.³³⁹ In a population-based longitudinal cohort study of nearly 9 million US Medicare enrollees older than 64 years, each 5 µg/m³ increase in long-term mean exposure to PM2.5 was associated with an adjusted percentage increase in depression risk of 0.91%.³⁶²

On a daily basis, PM2.5 levels are associated with increases in emergency room visits for psychiatric disorders during the next three days. A 10 µg/m³ increase in PM2.5 was associated with an increased risk of 7%.¹³² In a French study, for periods of 6 days with PM2.5 above 20 µg/m³, hospital admissions for psychotic disorders was significantly increased.³¹⁹ Suicide risk is increased 4% per 6 µg/m³ increase in PM2.5 two days before the event.²⁷⁰

Several studies have shown that particulate air pollution is associated with increased anti-social, aggressive behavior and crime. For example, one study found that over an eight-year period, a 10% increase in daily PM2.5 was associated with a 0.14% increase in violent crime, costing society \$1.4 billion. Notably, the effects increase until 20 µg/m³ and then level off,¹³³ suggesting other pollution-related health outcomes with a supralinear relationship to dose.

Tic disorders in children are associated with PM2.5 exposure. In a Taiwan study of nearly 6,000 cases, tic disorders were positively associated with a 10 µg/m³ increase in PM2.5 in a non-linear relationship. During pregnancy, the HR was 1.09, and during infancy it was 1.12. The vulnerable time window for infants with increased risk of tic disorders was 6-52 weeks after birth.³⁴⁸

F4(g). Anatomic brain changes related to PM2.5: Anatomic brain changes related to numerous pollution components, including PM2.5, have been documented even in children. Structural neuroimaging and cognitive function were investigated at 6 to 10 years of age in nearly 800 children and correlated with PM2.5 exposure of the mother during pregnancy. For each 5 µg/m³ PM2.5 exposure, brain scans showed thinner cortex in several brain regions of both hemispheres, but primarily in the right prefrontal cortex.³²⁹ These anatomic changes correlated to impaired childhood inhibitory control.¹²⁴

MRI brain scans of 8-12 year olds were compared based on PM2.5 exposure of the mother during the third trimester of the pregnancy. A 7 µg/m³ increase in PM2.5 was linked to a 5% decrease in corpus callosum volume. This anatomic aberration was associated with a higher rate of hyperactivity.¹²⁵

In a study of 332 youth ages 6-14 years, brain imaging was correlated with PM2.5. "Researchers found progressively higher exposures were associated with greater disruptions in local volumes, tissue organization, metabolite concentrations, and blood flow throughout cortical and subcortical brain regions and the white matter pathways interconnecting them. Together these affected regions comprise cortico-striato-thalamo-cortical circuits, which support the regulation of thought, emotion, and behavior."¹²⁶

In a study evaluating susceptible windows of exposure, from conception to preadolescence, via brain imaging of 9-12 year olds, markers of neurodevelopmental aberrations (fractional anisotropy and mean diffusivity) on MRI scans correlated with 5 µg/m³ increases in PM2.5 during pregnancy and childhood.³⁶⁹

In the largest brain imaging/air pollution study done so far, including over 10,000 9-10 year old US children from across the country, median PM_{2.5} exposures ranged from 5.1 to 10.4 µg/m³. Increased PM_{2.5} exposure was associated with changes in brain morphology. A 5 µg/m³ increase in PM_{2.5} was associated with hemispheric-specific differences in gray matter across cortical regions of the frontal, parietal, temporal, and occipital lobes as well as subcortical and cerebellum brain regions. The authors said, “an increase of 5-µg/m³ was associated with differences in cortical thickness on the magnitude ranging from 0.01 to 0.04 mm, suggesting that continual exposure to PM_{2.5} during childhood and adolescence could substantially impact an individual’s brain-growth trajectories with potentially lifelong consequences.”³⁴⁴

In a cohort of people over 60 years old without a history of stroke or dementia, a 2 µg/m³ increase in PM_{2.5} was associated with a with -0.32% smaller total cerebral brain volume, (a marker of age-associated brain atrophy) and a 46% increased risk of covert brain infarcts.¹²⁷ Older women chronically exposed to PM_{2.5} of just 3.49µg/m³ had an average loss of total brain volume of 6.23cm³, equivalent to 1 to 2 years of brain aging.¹²⁸

The hippocampus is an important area of the brain involved in memory processing. Researchers found that long-term exposure to PM_{2.5} below 10 µg/m³ correlated with reduced volume of the hippocampus.¹²⁹

The prefrontal cortex is a key area of the brain involved in neurodegenerative and neuropsychiatric diseases. In a study of over 18,000 adults that had brain MRI scans, who were chronically exposed to an average PM_{2.5} of less than 10 µg/m³, there was an inverse association between PM_{2.5} exposure and prefrontal brain volume.¹³⁰

F5. PM_{2.5} and reproductive toxicity, fetal development/chromosomal integrity:

The numerous studies that show PM’s strong connection to genetic and epigenetic damage (suggesting adverse transgenerational effects), toxicity at multiple points in human reproduction, and to fetal development, together makes the case even stronger for acting more aggressively than EPA proposal on both the annual and 24 hr standard.

PM can adversely affect virtually all phases of human reproduction and early life development, causing sperm DNA damage, decreases in sperm count³²⁷ and motility,³¹⁵ decreased rates of fecundability, increases in the rates of male and female infertility,^{269,280} decreased fertilization and menstruation, and increases in miscarriages and other adverse reproductive outcomes.

F5(a). Preconception toxicity impairs fertility and organogenesis: Infertility is becoming a global public health problem, affecting at least 10% of all reproductive-aged couples worldwide. The World Health Organization estimates that pure male factors, mainly poor semen quality, could account for 50% of infertility cases. Stark changes in sperm concentration, count, and motility over a relatively short period suggest that the global trend of deteriorating semen quality is more likely to be related to environmental factors than genetics. While there are

undoubtedly multiple environmental contributors, air pollution is certainly among the most important.

The risk of PM to fetal and child organ development can begin preconception. Preconception PM2.5 exposure of parents, especially during the first 18 years of life, is associated with increased risk of early onset respiratory diseases in their offspring.³⁷⁵ Preconception PM2.5 exposure of the mother increases the risk of congenital heart malformations.³⁷⁴

Babies are essentially born pre-polluted by the air breathed by the mother during pregnancy. Particulate matter and the chemicals attached to it can cross the placenta and contaminate and interfere with fetal organ development. Air pollution breathed by a pregnant mother at critical stages in the development of the human embryo or during early infancy can cause genetic and epigenetic changes, increase the risk of birth defects like neural tube defects, and cause the baby, as an adult, to experience an increased likelihood of multiple chronic diseases, including those of the heart, lungs, immune system, brain, and even obesity, diabetes, cancer, rheumatoid arthritis,²⁹⁸ and shortened life expectancy.

Pregnant women exposed to more particulate pollution give birth to babies with significantly more chromosomal aberrations, including shorter telomeres and epigenetic changes, which can be passed on to multiple subsequent generations.

Below are numerous studies that specifically relate quantitatively to dose/response relationships relevant to setting the PM2.5 NAAQS.

F5(b). Quantitative consequences of preconception exposure: Short-term PM2.5 increases are associated with decreased fecundability. An increase in PM2.5 of 10 µg/m³ prior to attempted conception is associated with a 22% decrease in fecundability.²⁶⁶

In a highly exposed maternal population, **each 10 µg/m³ increase in periconception PM2.5 exposure was associated with a 2% increase in the rate of congenital heart disease.**³⁷⁴ One study determined the monthly average values of PM2.5 for each birth for five different monthly time periods: one and two months before/after conception, and the month of conception. Births with any congenital anomaly had a higher mean PM2.5 exposure level compared to non-anomalous births across all periconception months. **Per 10 µg/m³ increase in PM2.5 during the month before conception, the month of conception, or the month after, the risk of congenital malformation increased 13 to 39%. Increasing PM2.5 exposure levels occurring one month prior to conception consistently demonstrated the highest risk, i.e., a 17% increased risk per 4.9 µg/m³ increase in PM2.5.**¹⁴⁶

F5(c). Prenatal exposure to PM2.5 increases the risk of birth defects: Numerous studies have shown an effect of maternal PM2.5 exposure on the risk of birth defects. For example, in Taiwan, PM2.5 exposure of the pregnant mother measured during the first three months after conception revealed a 29% increased risk of hypospadias for each 15.6 µg/m³ increase in PM2.5.¹⁴⁹ While this threshold is greater than the current or proposed annual PM2.5 standard,

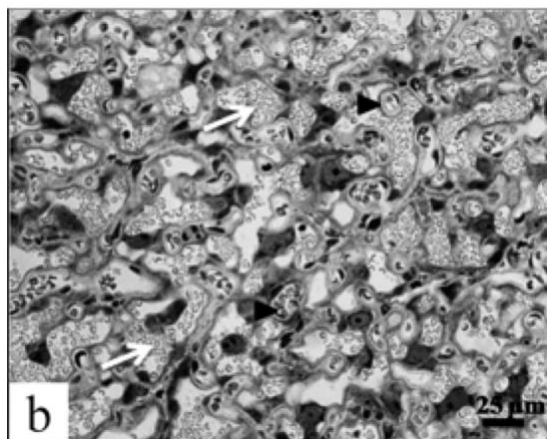
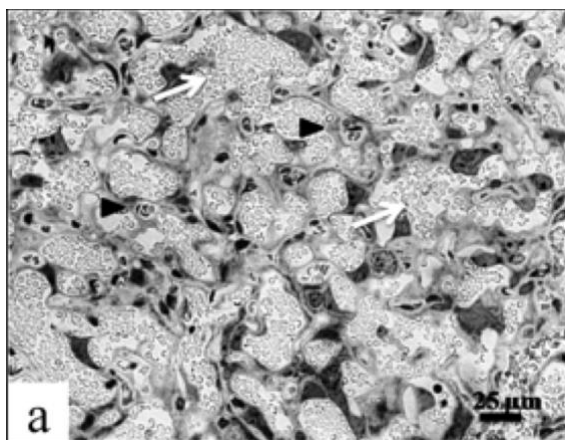
extrapolation to lower thresholds suggests that a significant reduction in birth defects would be expected by lowering the PM2.5 annual standard to 8 rather than 10 $\mu\text{g}/\text{m}^3$. A 10 $\mu\text{g}/\text{m}^3$ increase in PM2.5 at the time of birth is associated with several different types of congenital cardiac malformations.¹⁵⁰

F5(d). The effect of exposure to PM2.5 on telomeres: Telomere length is a marker of biological aging that may provide a cellular memory of exposures to oxidative stress and inflammation. Telomere length at birth has been related to life expectancy. In 641 mother/newborn pairs, a 5- $\mu\text{g}/\text{m}^3$ increment in PM2.5 exposure during the entire pregnancy was associated with 8.8% shorter cord blood leukocyte telomeres and 13.2% shorter placental telomere length.¹⁴⁷ This means nothing less than that **PM2.5 programs a person by the time of birth to a shorter life span.**

Among a group of elderly adults exposed to annual PM2.5 in a range between 15 and 23 $\mu\text{g}/\text{m}^3$, increases of 5 $\mu\text{g}/\text{m}^3$ were associated with decreases in telomere length of 16.8% and decreases in mitochondrial DNA content of 25.7%.¹⁴⁸ An increase in annual average PM2.5 exposure of just 1 $\mu\text{g}/\text{m}^3$ in African-American youth was associated with a decrease in absolute telomere length.¹⁹⁸ In a review of 7 observational studies correlating PM2.5 with telomere length, most found shorter telomeres with PM exposure.²⁷¹

F6. PM2.5 and Pregnancy and Birth Outcomes: Virtually every type of poor pregnancy outcome or complication is associated with particulate pollution, from still births and birth defects to premature births and placental rupture. This is understandable, given that one of PM2.5's most significant impacts is vascular inflammation, and the placenta can be regarded as the vascular of all human organs.

The pathologic effect on placental vasculature was illustrated by a study on mice.¹⁵¹ The microscopic photo of a near-term placental section on the left (a) is from a mouse that breathed filtered air, PM2.5 6.5 $\mu\text{g}/\text{m}^3$, during the pregnancy. On the right (b) is the same from the placenta of a mouse that breathed unfiltered Los Angeles air, with PM2.5 27.5 $\mu\text{g}/\text{m}^3$. The vascular congestion, reduction of volume, and narrowed capillaries, is obvious. On the fetal side of the placenta, vascular dilatation occurred in an apparent attempt to compensate for the vascular narrowing on the maternal side, resulting in an increase in surface area. Similar, but slightly less dramatic results were found when the exposure was preconception rather than during the pregnancy. Both periods of exposure led to significantly smaller fetal weights.



The placental vascular compromise from maternal PM2.5 exposure illustrates a likely mechanism by which PM causes impaired fetal development and poor pregnancy outcomes, as many other studies have demonstrated.

Other studies provide more detail on PM2.5's pathologic changes in the placenta, such as a significant increase of blood mononuclear cells (PBMC); platelets; the inflammatory marker, interleukin-6; vascular thrombi; and chorioamnionitis.¹⁵²

Below are some of the studies that provide dose/response information relevant to setting the NAAQS.

F6(a). PM2.5 impairs fetal growth: Examining placentas from 361 mothers, methylation of the fetal growth hormone, leptin, in the placenta was reduced with daily PM2.5 exposures during the pregnancy, 1.4% lower for each 7.5 µg/m³ PM2.5.¹⁵³

Fetal growth restriction is not only a major determinant of perinatal morbidity and mortality but also leads to adverse health effects in later life. Each 10 µg/m³ increase in maternal PM2.5 exposure increases the risk of fetal growth restriction.¹⁵⁴

Numerous studies have found an association between particulate pollution and various parameters of fetal growth. For example, a study of 3 million births across Canada found that a 10-µg/m³ increase in PM2.5 over the entire pregnancy was associated with a 4% increased risk of small-for-gestational-age (SGA) and reduced-term birthweight of 20.5 g.¹⁵⁵ Similar results were found in a US population.¹⁵⁶

F6(b). PM2.5 is associated with premature birth. "Evidence has consistently shown that adult survivors of preterm birth have increased risks of chronic disorders involving various organ systems, including cardiovascular, endocrine/metabolic, respiratory, renal, neurodevelopmental, and psychiatric disorders, which either persist from childhood into adulthood or sometimes first manifest in adulthood. These disorders also lead to moderately (30% to 50%) increased mortality risks during early to mid-adulthood among persons born

preterm compared with full-term, and even higher risks among those born at the earliest gestational ages.”³⁷⁶

Numerous studies found significant associations between PM2.5 exposure and low birth weight (LBW) and premature birth (PMB). For example, this meta-analysis of 18 studies found the risk of premature birth increased 13% per 10 µg/m³ increase in PM2.5 during the entire pregnancy.¹⁵⁷

Another meta-analysis of 25 studies found a 10 µg/m³ increase in PM2.5 was associated with a 5% increased risk of LBW, a 10% increased risk of PMB, and a 15% increased risk of SGA based on entire pregnancy exposure. The pooled estimate of decrease in birth weight was 14.58 g.¹⁵⁸ Another meta-analysis showed similar results.¹⁵⁹

Another study showed not only an association between PMB and PM2.5, a 9.6% increased risk for each 6.45 µg/m³, but also that the association existed for both primary and secondary PM.¹⁶⁰

Intrauterine inflammation (IUI) is a known contributor to poor birth outcomes, including LBW and PMB. IUI is highly associated with PM2.5 exposure. Estimates of the prevalence of IUI range from 25% to 50% of preterm births. For all exposure periods (each trimester), including the three months prior to conception, PM2.5 is associated with risk of IUI. In this study, for example, per interquartile increase in PM2.5 over the entire pregnancy (3.31 µg/m³), the risk of IUI increased 38%.¹⁶¹ Estimated exposures to PM2.5 during the period of the entire pregnancy were below the federal annual standard of 12 µg/m³ for nearly 70% of the participants. There was no threshold below which an association was not seen.

Even short-term PM2.5 is associated with PMB. This study found a 6% increased risk for an increase of 10 µg/m³ on the day prior to birth.¹⁶²

A meta-analysis of 84 studies of acute and long-term PM2.5 exposure during pregnancy found that per 10 µg/m³ long-term increase during the pregnancy, PMB risk increased 8.4%. For short-term exposure, pre-term birth risk of .3% was associated with a 10 µg/m³ increase in PM2.5 on lag day 2 and 3.¹⁶³ Globally, PM2.5 has been estimated to account for 18% of premature births. This is a tremendous liability to public health in general.¹⁶⁴

Assessing gestational age at birth offers another metric of gestational health. Each 5 µg/m³ increase in PM2.5 in the third trimester was associated with a reduction of gestational age at birth of 4.2 days.¹⁶⁵

F6(c). PM2.5 and other pregnancy, birth complications: Particulate pollution increases the risk of stillbirth. In one study, for each 4 µg/m³ increase in PM2.5, stillbirths increased over 2%.¹⁶⁶ In another study, the risk of stillbirth increased 18% for each 10 µg/m³ increase in PM2.5.¹⁶⁷

Gestational hypertension is strongly associated with PM2.5. In a US study, there was a 10% increased risk for hypertensive disorders with each increase of 5 µg/m³ in PM2.5. An effect threshold was found at 9 µg/m³, and the authors calculated that 8.1% of cases were attributable to PM2.5.¹⁶⁸ A meta-analysis of studies of hypertension in pregnancy found that a 10 µg/m³ increase in PM2.5 was associated with an increased risk of hypertension of 52% and an increased risk of pre-eclampsia of 31%.¹⁶⁹

Gestational glucose intolerance and diabetes is another pregnancy complication associated with particulate pollution. A study of Boston pregnant mothers with a mean PM2.5 exposure of 10.9 µg/m³ in the second trimester found that a 2.6 µg/m³ increase in PM2.5 was associated with a 82% increased risk of glucose intolerance.²⁴⁰ A meta-analysis of 11 studies found that an increase of 10 µg/m³ PM2.5 was associated with a 4% increase in the risk of gestational diabetes.¹⁷⁰

Premature rupture of membranes (POM) is associated with PM2.5 exposure. Per 10 µg/m³ increase, the risk of POM increased 35% for the whole pregnancy. Preterm POM was even more strongly associated with an increased risk of 53% for each increase in PM2.5 of 10 µg/m³ for the whole pregnancy, and with further positive trends for the last week and day of pregnancy.¹⁷¹

A position that the 24-hour PM2.5 standard does not need to be tightened ignores research that shows a significant correlation between acute spikes and spontaneous abortion. A 20 µg/m³ spike in PM2.5 three days prior was associated with an 18% increase in the risk of pregnancy loss.¹⁷²

F7. PM2.5 and the lung: Prenatal and childhood exposure to PM can restrict lung growth and permanently reduce size, capacity, and function, including replacing the number of alveoli (air sacs) in the lungs with essentially scar tissue. Even one weekend of severe pollution during prenatal life or infancy can increase the risk of asthma many decades later in adulthood.¹⁸⁹

PM triggers oxidative stress in the lung, inducing lung injury and scarring. PM causes, complicates, or exacerbates virtually all pulmonary diseases, from mild reactive airways disease to fatal pulmonary fibrosis. PM is associated with increased rates of serious lower respiratory infections, hospitalization, and death from most respiratory diseases, from neonates to the elderly.

Brief exposure to PM can temporarily reduce lung function even in young, healthy adults, and the reduction can last for a week after the pollution exposure is over. PM causes DNA damage, oxidative stress, and multiple avenues of cell death to lung epithelial cells.¹⁷⁴ Wildfire smoke may be ten times more toxic to the lung than other sources of particulate pollution.³⁷⁷

We cite the research below for its specific applicability to establishing the PM2.5 NAAQS.

F7(a). PM2.5 and parameters of lung function: All fractions of PM are associated with increases in the rate of respiratory and cardiovascular hospitalizations. Short-term increases in PM 2.5 of 10 µg/m³ (lag 0-5 days) were associated with a 36% increase in respiratory hospitalizations.¹⁷⁵

There are few things that correlate more closely with ultimate longevity than lung function.³⁷⁸ Multiple studies have found reduced lung function in the general population with minimal long-term and short-term PM2.5 exposure. Below are just a few of those studies.

Measuring subchronic PM2.5 exposure, i.e., over 2 months, in children ages 6 to 15, researchers found that a 12 µg/m³ increase was associated with a loss of lung function and lung capacity, as measured by forced expiratory volume (FEV1), forced vital capacity (FVC), and the ratios FEV1/FVC and maximal mid-expiratory flow (MMEF)/FVC.¹⁸¹

In over 6,000 adults in the Northeastern US, the association between long-term PM2.5 exposure and lung function and age-related lung function decline found that each 2 µg/m³ increase in average of PM2.5 was associated with a 13.5 millimeter (ml) lower FEV1 and a 2.1 ml/year faster decline in FEV1. There were similar declines in FVC.¹⁸²

A 5-µg/m³ increase in PM2.5 concentration in 1-day average before lung function testing was associated with 7.9 cubic centimeter (cc) lower FEV1 (a measure of lung air flow over time).¹⁷⁶ Researchers also found linear relationships between 1- and 2-day averages of PM2.5 and FEV1 and FVC (lung capacity measurement) but not for longer-moving averages of exposure, suggesting that adverse effects on lung function occur acutely within 24 to 48 hours.

The authors stated, “Our study suggests that the general population, not just ‘unusually sensitive’ people, may experience respiratory effects from PM2.5, NO₂, and ozone [O₃] exposure in the ‘moderate’ range. However, these values represent the average effect estimate for a distribution of effects within the study population. Acute inflammatory responses to air pollution resulting in reduced lung function may be part of the triggering mechanism for the reported association between short-term air pollution exposure and respiratory hospitalization and mortality. The magnitude of the associations we found between short-term pollutant exposure and lung function is comparable to those reported by studies that included pollution levels above current EPA standards.” A similar result was found in a study of nearly 6,000 6-8-year-old children in Europe.¹⁷⁷

The original Gauderman studies that established the loss of lung function in children exposed to air pollution were followed up 13 years later with studies that showed improved air quality was associated with improved lung function. In children followed for 4 years for lung function growth, the mean growth in FEV1 increased by 65.5 ml per decrease of 12.6 µg/m³ in long-term PM2.5 exposure.¹⁸³ In a similar study in Stockholm, a decrease in median PM2.5 from 8.24 to 5.21 over 15 years was associated with an improved lung function growth rate of 4.63 ml/yr for FEV1 and 9.38 ml/yr for FVC.³⁷⁹

Deterioration of lung function and vulnerability to disease was well illustrated by a UK study of over 265,000 people without lung disease who were followed for 12 years. Per 5 µg/m³ increase in long-term PM_{2.5} exposure, HR was 1.31 and 1.27 for progression from healthy to incident chronic lung disease and from incident chronic lung disease to chronic lung multimorbidity. The HR was 1.32, 1.24 and 1.91 for mortality risk from healthy, incident chronic lung disease, and chronic lung multimorbidity, respectively.³⁶⁰

An increase of 13.4 µg/m³ PM_{2.5} in the day prior to testing was associated with an oxygen saturation decrease of .18% in elderly subjects.¹⁸⁰

F7(b). PM_{2.5}'s effect on COPD and asthma: COPD is associated with city-level PM_{2.5}. One study found COPD prevalence increases 52% per 5 µg/m³ increase in chronic PM_{2.5}.¹⁹⁹ The risks of hospitalization for COPD increased 9%, for an increase of 10 µg/m³ PM_{2.5} measured as a moving average over 60 months.²⁰² Evaluating the relationship between short-term exposure to PM_{2.5} and COPD hospitalizations and mortality, a statistical summary of 12 studies, a 10 µg/m³ increase in daily PM_{2.5} (lag days 0-7) was associated with a 3.1% increase in COPD hospitalization and a 2.5% increase in COPD mortality.¹⁸⁵

In a study of 51,000 women in the US, self-reported wheeze, chronic cough, and doctor-diagnosed asthma were correlated with annual average PM_{2.5} estimated at their home address. An increase of 3.6 µg/m³ increased the risk of asthma 20% and of wheezing 14%.¹⁷⁸

Assessing the relationship between bronchitic symptoms (daily cough for three consecutive months) and improvements in PM_{2.5} in Southern California, researchers found that for a reduction of 6.8 µg/m³ average PM_{2.5}, symptoms decreased 32%.¹⁸⁷

Multiple studies show an association between PM_{2.5} and various metrics of asthma. Annual average concentrations at the home address were associated with an increase in the incidence of an asthma diagnosis of 4% per exposure increase of 5 µg/m³.¹⁸⁴

Among adults with active asthma, measuring PM_{2.5} for a 14-day average, PM_{2.5} ≥ 7.07 µg/m³ was associated with a 4-5% higher asthma symptom prevalence. Even in the very low range of 4.00-7.06 µg/m³ PM_{2.5}, each 1-µg/m³ increase was associated with a 3.4% increase in symptom prevalence.¹⁸⁸

A meta-analysis of 87 studies found that with short-term PM_{2.5} exposure, an increase of 10 µg/m³ was associated with a 2.3% increased risk of an asthma emergency room (ER) visit or hospitalization.¹⁸⁶ Other studies showed generally similar results for all types of respiratory hospitalizations.^{190,200,201,203} A nationwide study of respiratory admissions in Italy over 3 years found that with daily increases of 10 µg/m³ in PM_{2.5} (lag 0-5 days), hospitalizations for multiple types of respiratory illness increased 22%. The most at risk were the elderly, and strong effects were found even in non-urbanized areas.²⁰⁴

In a study of the association between PM2.5 at very low levels and asthma morbidity, children of low birthweight and an increase of 5.9 µg/m³ in daily-measured PM2.5, experienced an 8% increased risk for an ER visit, hospitalization, or observational visit for wheezing or shortness of breath. The median PM2.5 concentration was only 7.8 µg/m³.¹⁹⁵

F7(c). PM2.5 and respiratory infections: In a study of children in Atlanta, Georgia, PM2.5 was correlated to ER visits for pneumonia and upper respiratory infections in children less than five years old. A three-day moving average PM2.5 increase of 8.8 µg/m³ prior to the hospital visit increased the risk of an ER visit of about 2%.¹⁷⁹

A study of 146,000 Utah children, most younger than 2 years old, found that the risk of an acute lower respiratory infection increased within one week of an elevation in PM2.5 and peaked after 3 weeks with a cumulative 28-day odds ratio of 1.15 per 10 µg/m³ increase in PM2.5.¹⁹⁶

In a case-crossover study including 20,017 medical visits for infant bronchiolitis and 42,336 for otitis media, infant bronchiolitis risk was elevated for PM2.5 exposure on same day by 7% and 4 days prior to clinical encounter by 4%, per 10 µg/m³ increase in PM2.5. Risks for pre-term infants were substantially increased.¹⁹³

In a Utah study of patients admitted through ERs for pneumonia, researchers found PM2.5 increases of 10 µg/m³ within the 6 days prior to presentation of pneumonia, increased risk of pneumonia 35%, and pneumonia-related mortality 50%, for levels above 12 µg/m³.¹⁹⁴

A 10 µg/m³ increase in daily PM2.5 concentrations was associated with a 6% increase in the risk of infant mortality from all causes, including pneumonia and congenital heart disease, and a 10% increase in the risk for post-neonatal mortality.¹⁹⁷

Analyzing a total of 8,023,590 hospital admissions from 2011, researchers investigated the relationship between air pollution and outcomes from hospitalization and mechanical ventilation for acute respiratory distress syndrome. They found that for each 10 µg/m³ increase in PM2.5 exposure, the mortality risk was increased 8%.¹⁹¹

F7(c). PM2.5 and idiopathic pulmonary fibrosis: Idiopathic pulmonary fibrosis is a devastating, invariably fatal pulmonary disease of mostly unknown origin. Investigating the relationship between air pollution and the natural progression of the disease, researchers found that mortality was significantly associated with long-term PM2.5. An increase of 10 µg/m³ was associated with a nearly 800% increased risk of earlier mortality.¹⁹²

F8. PM2.5 and cancer: Environmental contaminants are responsible for 70-90% of cancers,^{226,227} and particulate pollution is one of the primary toxins with carcinogenic potential. Particulate pollution is associated with higher rates of breast, lung, prostate, cervical, brain, nasal, pharyngeal, esophageal, liver, pancreatic, and stomach cancer and with adult and childhood leukemia. Prenatal pollution exposure is associated with increased rates of multiple

childhood cancers. World health experts now believe that as much as 30% of lung cancer is due to air pollution.^{206,225}

The WHO has declared air pollution a leading environmental cause of cancer,²⁰⁷ more important than second-hand cigarette smoke. The WHO placed it in the same category as asbestos and ionizing radiation.

Researchers recently discovered at least one mechanism for air pollution's role in causing lung cancer.²⁰⁵ A combination of PM2.5 exposure and common mutations in the epidermal growth factor receptor (EGFR) and Kirsten rat sarcoma virus (KRAS) genes, likely a consequence of aging, are seen in about half of people with lung cancer who have never smoked. PM2.5 exposure promoted rapid changes in airway cells that had the mutations, driving them toward a cancer stem cell-like state. Particulate pollution triggers an influx of macrophages that release the inflammatory mediator, interleukin-1 β , promoting the expansion of cells with the mutations.

The studies cited below are directly relevant to the discussion of how far to strengthen the PM2.5 NAAQS.

F8(a). PM2.5 and increased risk of cancer: A recent study found reducing air pollution in 257 metropolitan areas would have as much of a reductive effect on the incidence of 12 difference smoking-related cancers as completely eliminating smoking in the population.³³ Those cancers included lung cancer, stomach cancer, kidney cancer, bladder cancer, pancreatic cancer, liver cancer, cervical cancer, oral cancer, colon cancer, esophageal cancer, cancer of the larynx, and acute myeloid leukemia.

In a Canadian study, each long-term 10 $\mu\text{g}/\text{m}^3$ increase in PM2.5 concentrations over a 20-year exposure period was associated with an increase in lung cancer incidence of 29% per 10 $\mu\text{g}/\text{m}^3$ increase in mean PM2.5.²⁰⁸

Analyzing 1,510,027 person-years in the Nurses Health Study, estimating average PM2.5 exposure for 72 months, a 10 $\mu\text{g}/\text{m}^3$ increase was associated with a 6% increased risk for lung cancer.²¹¹

A meta-analysis of 18 studies found that a 10 $\mu\text{g}/\text{m}^3$ increase in chronic PM2.5 exposure was associated with a 9% increased risk of lung cancer.²¹² Another systematic review and meta-analysis of prospective studies found similar results,²¹⁴ but others have found much stronger associations.²¹⁸ In a Canadian study with a median PM2.5 exposure of just 9.1 $\mu\text{g}/\text{m}^3$, a prospective study of 90,000 women found that an increase of 10 $\mu\text{g}/\text{m}^3$ was associated with an increased risk of lung cancer of 34%.²²⁰

The liver is another organ plausibly affected by PM due to its role in detoxifying xenobiotics embedded in PM. Rates of liver cancer are increased with long-term exposure to PM2.5. An increase of 10 $\mu\text{g}/\text{m}^3$ was associated with an increased risk of 34%.²²¹ Survival from liver cancer

is also associated with long-term PM2.5 exposure. In a study of over 22,000 patients with liver cancer in California, for every 5.0 µg/m³ increase in long-term PM2.5, all-cause mortality in these patients increased 18%.²²²

In a study of 11 European cohorts, a long-term increase in PM2.5 of 5 µg/m³ over 14 years was associated with a 38% increased risk of gastric cancer and a 5% increased risk of upper digestive tract cancers.²²⁴

In an 18-year follow-up, bladder cancer was associated with long-term PM2.5. Per 5 µg/m³ increase, the risk of cancer increased 9%.²³⁵ Death from kidney and bladder cancer is associated with long-term PM2.5 exposure—an increase of 4.4 µg/m³ was associated with an increased risk of both of about 14%.²²³

Several childhood cancers are associated with various types of air pollution. An increase of 7.84% in PM2.5 during the pregnancy was associated with an increased risk of leukemia, ependymoma, embryonal tumors, medulloblastomas, retinoblastomas, and Wilms tumors.²¹³

F8(b). Decreased rate of cancer survival: Exposure to PM2.5 after diagnosis is associated with a significant increase in the risk for mortality among adult patients with lung, breast, kidney, bladder, and liver cancer, even after controlling for multiple confounders such as socioeconomic status, race, and stage at diagnosis.^{222,223, 231,233} Proposed mechanisms for PM2.5's enhancing cancer mortality are similar to those that induce or promote the original cancer, "including genotoxic and epigenetic alterations, inflammation, xenogeneic effects or hormone dysregulation, or by reducing the immune system's ability to fight the cancer."²²⁶ These biologic pathways may also reduce the malignancy's response to cancer treatment. PM2.5 may be associated with overall recurrence, with more aggressive recurrent cancers, and mortality from these recurrent cancers.²³²

Air pollution is associated with decreased survival in patients with all types of cancer, especially breast cancer, including those treated for cancer. Air pollution decreases the efficacy of chemotherapy. Lung and cardiovascular diseases are important non-cancer causes of death among cancer patients and survivors, both of which are enhanced by air pollution. Childhood cancer survivors treated with chemotherapy have significantly higher risk for a respiratory hospitalization after exposure to PM2.5 than the general public does.²³⁴

In an analysis of 21 cohort studies from around the globe, the risk of lung cancer morbidity or mortality increased 7.23% for every 10 µg/m³ increase in chronic PM2.5.²¹⁷

Lung cancer mortality was assessed among 188,699 lifelong never-smokers drawn from the nearly 1.2 million Cancer Prevention Study-II participants enrolled by the American Cancer Society in 1982 and followed prospectively through 2008. Each 10 µg/m³ increase in mean PM2.5 was associated with a 15-27% increase in lung cancer mortality.²⁰⁹

In a whole-population Chinese cohort study, long-term exposure to PM_{2.5} reduced survival rates of lung cancer patients. An increase of 10 µg/m³ was associated with an increased mortality rate of 6.5%.³³⁴

In a California study of over 255,000 cases of breast cancer, long-term PM_{2.5} exposure was significantly associated with breast cancer survival rate. Per 5 µg/m³ long-term exposure, there was an 86% higher likelihood of early mortality, controlling for numerous other variables.²¹⁰

In a broader study of cancer mortality's association with annual average PM_{2.5}, 67,000 patients were followed for 10 years. The study found that an increase of 10 µg/m³ PM_{2.5} was associated with an increased risk of mortality of 22% for multiple types of cancer.²¹⁹

F9. PM_{2.5} and metabolic, endocrine, and kidney disease: PM_{2.5} promotes the development of inflammation in lungs, gut, and hypothalamus, and in turn, alters adipose tissue homeostasis.³³¹ More exposure to PM, even short term, decreases insulin sensitivity and glucose tolerance, increases rates of Type I³⁵⁷ and Type II diabetes, promotes obesity,³⁵⁹ and increases lipid deposition and risk of metabolic syndrome.³¹⁷

The biological pathways linking particulate pollution to diabetes include “endothelial dysfunction, dysregulation of the visceral adipose tissue through inflammation, hepatic insulin resistance, elevated hemoglobin A1c level, elevated blood pressure, alterations in autonomic tone,”²⁴⁴ and vascular insulin resistance by inducing pulmonary oxidative stress.²⁴⁶

Prenatal exposure to PM has a particularly strong association with childhood obesity. Metabolic function can be evaluated by measuring leptin and adiponectin; both are adipocyte-secreted hormones important in energy, glucose, and lipids homeostasis. Elevated levels in cord blood are considered potential predictors of the early development of obesity.

Lipid metabolism is impaired, good cholesterol (HDL) is decreased, and bad cholesterol (LDL) is increased with more air pollution.³⁴⁵ Air pollution impairs thyroid function in pregnant mothers, thyroid development in the fetus, and thyroid function in newborns. Impaired thyroid function is a likely mechanism for air pollution's causing LBW and can impair fetal brain development. Diesel exhaust impairs liver function.

A few studies have now associated maternal PM exposure with abnormal thyroid hormone levels.²⁵⁴ The clinical significance of that is not clear yet, but given the critical role that the thyroid plays in fetal development, especially of the brain, it only adds to the reasons for tighter EPA regulations.²⁵⁹

PM impairs kidney function,²⁹⁶ and kidney disease is one of the top 10 causes of death worldwide. It is also an important risk factor for cardiovascular disease. Early evidence shows PM_{2.5} impairs kidney function at the microscopic level through direct particle accumulation, inflammation, oxidative stress, apoptosis, DNA damage, autophagy, and endothelial dysfunction. It impairs the renin-angiotensin system, and immune complex deposition.

The studies cited below have quantitative relevance to tightening the PM2.5 NAAQS.

F9(a). PM2.5 and the risk of type II diabetes and glucose intolerance: An average increase in PM2.5 during pregnancy of 3.2 $\mu\text{g}/\text{m}^3$ was associated with an 11% increase in umbilical cord adiponectin levels.²⁴⁷ Umbilical cord plasma insulin levels are increased with maternal exposure to PM2.5. Following nearly 600 mother/infant pairs, cord plasma insulin levels increased 15.8% for each 2.4 $\mu\text{g}/\text{m}^3$ increase in PM2.5, corresponding to a pre-pregnancy 9 kg/m^2 higher BMI. The average PM2.5 exposure was 13.7 $\mu\text{g}/\text{m}^3$.²⁵⁰

In a study of Los Angeles, California, Latino children, ages 8 to 15 years, that were at increased risk of diabetes because of obesity, the children were followed for 3.4 years. During that time, a 4 $\mu\text{g}/\text{m}^3$ higher long-term PM2.5 was associated with a 3.3% faster decline in insulin sensitivity and a 28.5% higher acute insulin response to glucose at age 18.²⁴⁹

In more than 4,200 Chinese children ages 6-13, fasting blood glucose was 2.3% higher per 10 $\mu\text{g}/\text{m}^3$ increase in PM2.5, measured 186 days prior to the blood draw.²⁵³ In a study of over 38,000 adults in rural China and three-year-averaged PM2.5 exposures, a 1 $\mu\text{g}/\text{m}^3$ increase in PM2.5 was associated with an OR for type II diabetes of 1.02, and the black carbon component of PM2.5 was the most responsible constituent.³⁴¹

In a study of glucose metabolism in over 7,000 non-diabetic adults, increases of 5.7 $\mu\text{g}/\text{m}^3$ in 28 day mean averages of PM2.5 were associated with higher blood glucose levels, i.e., 0.91 mg/dL , and a 4.0 $\mu\text{g}/\text{m}^3$ increase over 91 days was associated with an increase in HbA1c of .07 pp.²⁵¹

In a 2010 US study, diabetes prevalence increased with increasing PM2.5 concentrations. A 1% increase in diabetes prevalence was seen with a 10 $\mu\text{g}/\text{m}^3$ increase in PM2.5 exposure, even for counties with air quality within the annual PM2.5 NAAQS (15 $\mu\text{g}/\text{m}^3$ at that time). Those counties with the highest exposure showed a > 20% increase in diabetes prevalence compared with that for those with the lowest levels of PM2.5, an association that persisted after controlling for diabetes risk factors.²³⁷ Stronger associations have been found since.

In a study of over 24,000 nurses and a 5-year annual mean of PM2.5 exposure, a 3.1 $\mu\text{g}/\text{m}^3$ increase in PM2.5 was associated with an 11% increase risk of type II diabetes.²⁴⁵

Tracking six years of PM2.5 exposure to 62,000 non-diabetic adults, a Canadian study found that an increase in PM2.5 of 10 $\mu\text{g}/\text{m}^3$ was associated with an increased risk of an eventual diagnosis of type II diabetes of 11%.²³⁸ Two other meta-analyses found nearly identical results.^{241,256} Another meta-analysis of 10 cohort studies found an increased risk for type II diabetes of 39% per 10 $\mu\text{g}/\text{m}^3$ increment in PM2.5,²⁴³ and another meta-analysis of 11 cohort studies found that a 10- $\mu\text{g}/\text{m}^3$ increase in PM2.5 in long-term exposure increased the risk of type II diabetes by 25%.²⁴⁸

In a Canadian study of 2.1 million adults with a long-term mean PM_{2.5} exposure level of only 8.7 µg/m³, a 10 µg/m³ increase was associated with an increased risk of diabetic-related mortality of 49%. The monotonic change in risk persisted to PM_{2.5} concentration < 5 µg/m³.²³⁹ A meta-analysis of 12 studies found that an increase of 10 µg/m³ long-term PM_{2.5} was associated with a 12% increased risk of diabetic mortality.²⁴²

F9(b). Obesity, metabolic syndrome, and thyroid dysfunction: Obesity is associated with PM_{2.5}. In a study population followed for eight years, annual PM_{2.5} increases of 4.5 µg/m³ were associated with a 4.53% higher fat mass.³²⁸

Metabolic syndrome (defined as central obesity plus two out of four additional risk factors, i.e., elevated triglycerides, reduced high-density lipoprotein cholesterol, elevated blood pressure, or elevated plasma glucose) is associated with PM_{2.5}. Comparing metabolic syndrome at baseline and again 5 years later, researchers found a mean annual PM_{2.5} increase of 1.5 µg/m³ was associated with an 19% increased risk of developing metabolic syndrome.²⁵²

Metabolic dysfunction–associated fatty liver disease is associated with every size fraction of PM. For long-term PM_{2.5}, increases of 10 µg/m³, the risk increased 29% among 90,000 people in China.²⁵⁷

In over 2,000 California newborns, prenatal monthly averages of PM_{2.5} were associated with total thyroid hormone TT4 levels. An increase of 16.3 µg/m³ PM_{2.5} was associated with a 1.2-µg/dL increase in TT4.²⁵⁴ Increases of 5 µg/m³ in PM_{2.5} short-term exposure during the first trimester of pregnancy were associated with a 21% increased risk of hypothyroxinemia in pregnant women.²⁵⁵

F9(c). PM_{2.5} and chronic kidney disease: Globally, nearly 7 million people are estimated to have chronic kidney disease attributable to PM_{2.5}.²⁹⁵ In a Chinese population of 47,000 with a 2-year mean PM_{2.5} exposure of 57.4 µg/m³, an increase of 10 µg/m³ in PM_{2.5} was associated with a 28% increased risk of chronic kidney disease.²⁵⁸ In a US Medicare population of 1.1 million, county-measured PM_{2.5} showed an association of 4 µg/m³, with an increased risk for chronic kidney disease of 3%.²⁶⁰ In an observational cohort study of nearly 2.5 million veterans, chronic PM_{2.5} exposure was linked to multiple metrics of diminished kidney function and kidney disease. The median baseline exposure was 11.8 µg/m³, and a 10 µg/m³ increase in PM_{2.5} over nearly 9 years of follow-up was associated with a 21-26% increased risk of diminished glomerular filtration rate, diagnosis of chronic kidney disease, and kidney failure.²⁸⁴ In a Chinese cohort of over 2,000 followed for 5 years, each 10 µg/m³ of long-term PM_{2.5} exposure was associated with an 84% increased risk of chronic kidney disease.³³³

Chronic PM_{2.5} exposure is also associated with increased mortality in patients with chronic kidney disease. The mortality HR per PM_{2.5} increase of 4.0 µg/m³ was 1.97 for ischemic heart disease and 1.42 for kidney disease among those patients concomitantly with hypertension.³³⁸

PM2.5 is also associated with mortality rates of patients on dialysis. Short-term increases of PM2.5 of 10 µg/m³ are associated with a mortality increase of 7%.³²⁵ There was no evidence of a threshold in the exposure-response relationship.

F10. Miscellaneous health impacts of PM2.5: Air pollution exposure rapidly increases reactive oxygen species production, causes systemic oxidative stress,^{262,273} triggers an inflammatory chemical cascade,²⁸³ increases in serum concentrations of the stress chemicals cortisol, cortisone, epinephrine, and norepinephrine,²⁸² endothelial cell death, cytotoxicity,²⁶⁷ macrophage infiltration, and triggers the release of damaging extracellular vesicles.³¹⁶ PM penetrates intracellular structures, including the nucleus of the cell, interfering with chromosomal and mitochondrial function²⁶⁴ and causing DNA damage, changes in DNA methylation,^{265, 317} and epigenetic damage.^{283,318} The consequences are widespread.

In addition to what has been addressed so far, PM has been associated with delayed maturation of the fetal immune system and immune suppression,³⁷³ alteration of the gut microbiome beginning in infancy,³⁷⁰ inflammatory bowel disease,^{288,314} childhood obesity,³⁰⁴ numerous types of bacterial and viral infections,^{272,274,278,292,320} lupus, juvenile and adult arthritis,^{263,300} endocrine-disrupting effects on developmental puberty,²⁷⁷ osteoporosis,^{286,303,311} and sleep apnea.³⁷⁸ Air pollution can induce liver toxicity²⁶⁸ and accelerate liver inflammation²⁸¹ and steatosis. Pollution exposure in utero or in infancy increases the likelihood of osteoarthritis and rheumatoid arthritis decades later in adulthood.²⁹⁸ PM is able to penetrate the skin, cause damage to the skin and corneas,^{307,313} and increase rates of autoimmune skin disorders;³⁴⁶ it is associated with age-related eye diseases like glaucoma.³²² PM accelerates the aging process²⁷¹ and decreases life expectancy.²⁹⁷

Studying over 95 million Medicare inpatient claims for 13 years, short-term PM2.5 exposure was associated with increased risk of hospitalization for multiple diseases, including those not frequently studied, such as septicemia, fluid and electrolyte disorders, urinary tract and skin and subcutaneous infections, acute and unspecified renal failure, and intestinal obstruction without hernia, phlebitis, thrombophlebitis, and thromboembolism.³⁰¹ For each 1µg/m³ increase in PM2.5, lag 0-1, the absolute increase in risk of hospital admissions for all these disease groups ranged from 0.02 to 0.68 per 10 million people at risk per day, and the relative percentage increase in risk of these hospital admissions ranged from 0.05% to 0.40%. **When restricting the analysis to days with daily PM2.5 concentrations of 25 µg/m³ or less, absolute and relative percentage increases in risk of hospital admission remained consistent with the main analysis for most disease groups.**

Furthermore, each unit increase in lag 0-1 PM2.5 was associated with an annual increase of 5,692 hospital admissions, 32,314 days in hospital, and 634 deaths at discharge. It was also associated with \$100 million annual inpatient and post-acute care costs, and \$6.6 billion in the value of statistical life due to the lives lost at discharge.

C-reactive protein is a marker of systemic inflammation and is associated with numerous chronic diseases. A 3- to 7-day moving average of PM2.5 is positively associated with C-reactive

protein concentrations. A 5 µg/m³ higher 5-day moving average of PM_{2.5} was associated with 4.2% higher circulating C-reactive protein.²⁷⁹

In a study of multimorbidity status based on 41 physical and mental conditions, over 364,000 people with a mean age of 52 were assessed and correlated to their PM_{2.5} exposure. A 1.71 µg/m³ increase in PM_{2.5} was associated with an OR of 1.21. It is notable that the threshold between the third and fourth exposure quartiles was only 10.56 µg/m³.³⁶⁶

In preschool-age children, short-term spikes in PM_{2.5} were associated with symptom onset of juvenile arthritis. Per 10 µg/m³ increase in 3-day lag moving average, the risk increased 76%.²⁷⁵

PM aggravates inflammatory autoimmune disorders like lupus erythematosus (LE).²⁸⁷ In a group of 237 patients with LE, a 10 µg/m³ increase in PM_{2.5} averaged over 48 hours prior to a clinic visit, there was a 34% higher risk of serum-specific autoantibodies and a 28% increased number of renal tubular cellular casts, i.e., markers of LE disease activity.²⁶¹

Sleep apnea is a steadily increasing public health problem, now affecting over 25% of American adults. The incidence of sleep apnea correlates with long-term PM_{2.5}. A 5 µg/m³ increase in annual PM_{2.5} was associated with 60% greater odds of being diagnosed with sleep apnea.²⁹³

Uterine fibroids may afflict as many as 60% of women; they are a common reason for hysterectomies. The incidence of uterine fibroids correlates with PM_{2.5}. In a cohort-based, case control study over 10 years in Taiwan, an increase in long-term PM_{2.5} of 10 µg/m³ was associated with a 10.5% increase in the risk of being diagnosed with uterine fibroids.²⁹⁴

In six low- and middle-income countries, frailty (defined by the frailty index) in older adults correlates to long-term PM_{2.5} exposure. Each 10 µg/m³ increase in PM_{2.5} was associated with a 30% increase in frailty.³⁰⁶

Numerous studies have been published showing not just mortality risks quantifiable to PM_{2.5} exposure, but shortened life expectancy. In a nationwide study of Taiwan over 7 years, 10 µg/m³ long-term exposure was associated with a shortened life expectancy of .3 years.²⁹⁷

F11. Environmental justice: Populations of color and the economically disadvantaged bear a disproportionate burden of health impacts associated with PM_{2.5} exposure.^{24,25,26} While this is not likely to be based on different physiologic response to environmental toxins, it nonetheless mitigates for stricter standards than what would otherwise be indicated by studies of large heterogeneous populations. Not only are these groups disproportionately impacted by similar concentrations of PM_{2.5} and other pollutants, but these same groups are invariably exposed to higher concentrations, adding to the need for stricter standards.²⁷ They are particularly exposed to higher short-term PM_{2.5}.³²¹

A recent study by the Center for Air, Climate, and Energy Solutions found that the disparity in soot exposure between White, Black, Latino, and Asian Americans was consistent throughout

the country, in both rural and urban settings, and at all income levels. Seventy-five percent of Black Americans are exposed to PM_{2.5} concentrations greater than 8 µg/m³ each year, compared to 59% of white Americans. “Low-income populations currently have 49% higher likelihood of living in areas that exceed 12 µg/m³ in comparison with wealthier populations. This difference drops to low-income populations having a 5% higher likelihood of living in areas that exceed 8 µg/m³.”²³

Low-income populations have a 49% higher likelihood of being chronically exposed to the current annual standard 12 µg/m³ or greater, compared with wealthier populations. This difference drops to low-income populations’ having a 5% higher likelihood of living in areas that exceed 8 µg/m³. Furthermore, Black populations over 65 years old have three times as many PM_{2.5}-attributable deaths per capita compared to all other races. ER visits for asthma show an even starker contrast for risk based on race, with a 600% higher asthma ER visit rate for non-white and white Hispanic populations compared to Caucasians.²⁸

In a review of 124 articles that explored race and air pollution as risk factors for poor pregnancy outcome, 13% specifically compared pregnancy outcomes among two or more racial groups. “Findings across all reviewed articles showed more adverse pregnancy outcomes (pre-term birth, SGA, LBW, and stillbirths) related to exposure to air pollution among Blacks and Hispanics than among non-Hispanic Whites.”³⁶⁵

Even within areas of similar economic, minority, and ethnic composition, there are large discrepancies in the spacial distribution of pollution, such that people can experience dramatically different levels within the same monitoring district. Severe hot spots of pollution can be completely missed by state monitoring networks. For example, a household downwind of a neighbor burning wood for heat during the winter can experience Beijing, China, levels of pollution, while an upwind neighbor can enjoy clean air. Studies from California show that within a single square kilometer of a residential area, concentrations of wood smoke can vary as much as 2,500 times. The highest measured concentrations were up to 100 times higher than the community average.²⁹ Similar distribution discrepancies are in play within neighborhoods adjacent to freeways or near industrial facilities.

There is a difference between genders in air pollution risks. Women are not thought of as a disadvantaged demographic, but statistically they are more likely to have cardiovascular complications related to air pollution. For example, several studies show women, especially post-menopausal women, have higher risk of cardiovascular disease from air pollution compared to men,^{41,42,380} Women have smaller coronary arteries and are more likely to develop disease in the coronary microvasculature.³⁸²

A meta-analysis of 25 studies found the women-to-men RRR of ischemia heart disease (IHD) was 1.05 per 10 µg/m³ increment in PM_{2.5} exposure, indicating significant excess risk of IHD in women.³⁸¹ This should be factored into the NAAQS.

G. ECONOMIC CONSIDERATIONS

THE ECONOMIC BENEFIT OF TIGHTENING THE ANNUAL PM2.5 STANDARD IS OVERWHELMINGLY POSITIVE, NATIONALLY, AND IN UTAH

Prior to the COVID pandemic, the World Health Organization concluded that air pollution is the leading avoidable cause of death worldwide, including tobacco smoking, alcohol use, road accidents and transmissible diseases such as AIDS, malaria, and tuberculosis.³⁸⁴ This health hazard associated with air pollution has prompted the adoption of increasingly stringent environmental regulations, but disagreement remains over how stringent those regulations should be.

In the United States, even though the Clean Air Act forbids it, the EPA still sees air quality standards as requiring a difficult tradeoff between their benefits to health and the costs that they impose on the economy, as investment capital is diverted from productive activities towards pollution control. The tradeoff is conventionally framed as one of jobs versus the environment. Recent research, however, shows that it is more accurate to first analyze the tradeoff between the direct economic or “market” benefits of reducing pollution exposure and its economic or “market” costs, before adding avoided healthcare costs and “welfare” benefits to the equation. Doing so reveals that the balance tilts heavily toward tighter air pollution controls, especially when it involves PM2.5.

G1(a). There are four channels through which PM2.5 pollution can reduce aggregate economic activity:

- Reducing the number of workers (through deaths and migration).
- Reducing the number workhours per worker, if they are too sick to work or have to miss work to care for a sick relative.
- Reducing the productivity of workers during workhours
- Reducing the quality of natural capital, which is an input into production in particular in the agriculture sector.

Recent advances in econometric modelling and available data show that the effect of changes in PM2.5 concentrations on the first three channels is much greater than previously estimated. Typically, in cost-benefit analyses supporting air pollution control policies, the estimated “market” benefits (e.g., reduced absenteeism at work), are minor compared to estimates of non-market impacts such as avoided deaths. For example, the US Environmental Protection Agency estimated that total benefits of the Clean Air Act Amendments between 1990 and 2020 amounted to \$12 trillion (2006 dollars). It attributed 85% of these benefits to reduced premature mortality.³⁸⁵ Similarly, recent analysis by the OECD estimates that the total annual market costs of outdoor air pollution (including reduced agricultural yields, absenteeism at

work and health expenditures) amount to 0.3% of global GDP in 2015 while the costs from non-market impacts represent 6% of total income.³⁸⁶

A series of micro studies, however, shows that PM2.5 exposure can cause very substantial direct reductions in labor productivity by impairing cognitive or physical ability. (For a summary of these studies see Graff Zivin and Neidell, 2018).³⁸⁷ These studies primarily observe the changes in individual worker productivity caused by concurrent exposure to high concentrations of PM2.5. For example, air pollution has been shown to decrease workers' productivity at a large farm in California,³⁸⁸ at a garment manufacturing facility in India,³⁸⁹ or at a Chinese call center.³⁹⁰ There is also evidence that pollution affects productivity in high-skill tasks, such as student performance in standardized high-school examinations³⁹¹ or investors' performance at the New York Stock Exchange.³⁹² Most recently, a large-scale study using data taken from the near-universe of manufacturing plants in China found evidence that a 1 $\mu\text{g}/\text{m}^3$ increase in average annual PM2.5 concentration (up from a mean of 53 $\mu\text{g}/\text{m}^3$) reduces value added per worker (worker productivity) by 1.1%.³⁹³

For the most part, these studies evaluate impacts of PM2.5 on specific workforces in developed countries (e.g. box packers, stock traders) or in less developed countries with high pollution levels (China, India). A 2020 study entitled "The Economic Cost Of Air Pollution: Evidence From Europe," (OECD Study)³⁹⁴ conducted by the economic research staff of the Organization of Economic Co-operation and Development, avoids the heterogeneity of the earlier studies by estimating the impact of variations in PM2.5 exposure on general levels of economic activity in a developed country context, using regional data from Europe.

The OECD Study finds that changes in annual PM2.5 concentrations cause changes in GDP levels per worker, and per capita, for the European Union member countries. By analyzing the response of aggregate economic output, this approach avoids the difficulties of modelling idiosyncratic populations as well as potential productivity displacement effects within a year, and factor reallocation across firms. This high resolution study uses data from European NUTS3 regions (analogous to counties in the United States), between 2000 and 2015. It thereby reflects the effects of PM2.5 on developed economies in a contemporaneous period. It also uses a hybrid of weather satellite and on-ground observations to estimate PM2.5 concentrations.

The OECD Study employs a two-stage regression model. A set of two instrumental (proxy) variables are used as explanatory variables in the first stage. One is the number of days in a given "county," in a given year. The other is shifts in wind direction. These data on inversion event frequency and shifts in wind direction were regressed on PM2.5 concentrations. The response of PM2.5 concentrations to changes in inversion-event frequency and to changes in wind direction each was highly statistically significant, and robust to changes in weather control variable specification, and fixed geographic and time effects.

Inferred PM2.5 concentration is the explanatory variable used for the second stage regression. The dependent variable is per capita GDP. As noted above, PM2.5 pollution can affect aggregate economic activity through its impact on three labor-related quantities-- population

size, presence at work, and productivity at work. Table 4 of the OECD Study shows that increasing PM_{2.5} concentration by 1 µg/m³ (approximately a 10% increase) decreases output per capita by 1.1%. It can be inferred from the table's point estimates that 96% of the effect on output per capita is due to reduced labor productivity, while the remainder is due to a decrease in the population available to work. This inference is consistent with the medical literature that finds that PM_{2.5} pollution primarily affects the mortality of old people and young children (neither of which contribute significantly to economic activity in developed economies), but rarely affects mortality among working-age individuals.

The response of GDP for the EU countries to annual changes in PM_{2.5} concentrations was highly statistically significant, and robust to geographic subsampling, to the removal of geographic fixed effects, and to the presence of a control variable for SO₂ concentrations—the pollutant most highly correlated with PM_{2.5} concentrations

Using the OECD Study's baseline GDP-weighted estimates, it found that a 1 µg/m³ decrease in PM_{2.5} concentrations increases Europe's GDP by 1.1%. While large relative to previous studies of labor productivity effects, this result is comparable to those reported in the emerging literature that focuses on the aggregate productivity effects of pollution. As of 2020, only three peer-reviewed studies estimated the effects of long-term exposure to PM_{2.5} on a general population, but their findings are consistent with the OECD Study results.

In a study that includes nearly all Chinese manufacturing plants, Fu et al. estimate that a 1 µg/m³ increase in PM_{2.5} concentrations causes a decrease in labor productivity of 1.1%.³⁹⁵ Since this increase represented only a 2.2% change from baseline PM_{2.5} concentrations, compared to the 10% change from baseline investigated by the OECD Study, it estimates a much higher labor productivity response. This suggests that air pollution has a substantial impact on productivity even at much lower concentration levels than those observed in China, and the effect is non-linear. Borgschulte et al. focus on PM_{2.5} pollution peaks in the US caused by forest fires. They estimate that spending one day exposed to a smoke plume increases PM_{2.5} concentration by 4µg/m³, which causes a reduction in income of 10% across all workers.³⁹⁶ If the effect is linear, this would imply that a 1µg/m³ increase in pollution causes a 2.5% reduction in income, which is over twice as high as the OECD Study's estimate.

As noted, the OECD Study estimates that a 1µg/m³ decrease in annual PM_{2.5} concentrations increases GDP by 1.1%. In 2022, the European Union's GDP was \$16.6 trillion (USD). Applying the OECD Study result to that GDP amount implies that a reduction in PM_{2.5} concentrations of 1µg/m³ would increase the EU's GDP by \$182.6 billion. In 2022, the GDP of the United States was roughly \$26 trillion. Applying the OECD Study result to the considerably larger GDP amount **for the United States implies that 1µg/m³ decrease in its annual PM_{2.5} concentrations would increase its annual GDP by \$286 billion.**

Whether reducing an NAAQS annual standard for PM_{2.5} by 1µg/m³ actually results in a reduction in national average annual PM_{2.5} concentrations by that amount depends on the baseline concentration of PM_{2.5} as well as the spatial and temporal distribution of PM_{2.5}

emissions—a complex modelling exercise beyond the scope of these comments. The EPA, however, has made estimates that allow the benefits and costs of tightening the annual PM_{2.5} by 1 µg/m³ (from 9 micrograms to 8 micrograms) to be inferred.

The EPA estimates that reducing the annual PM_{2.5} standard from the current 12 µg/m³ to 9 µg/m³ would require additional compliance measures in 51 counties across the nation and avoid \$43 billion in annual health-related costs. Separately, it estimates that reducing the current annual PM_{2.5} standard from 12 to 8 µg/m³ would require additional compliance measures in 141 counties and avoid \$95 billion in health-related costs. These estimates from the EPA Policy Assessment are summarized in the January 9, 2023, edition of the E&E News.³⁹⁷ Because the EPA separately estimates the benefits and costs of tightening the current standard to 9 micrograms, and then estimates the benefits and costs of tightening the current standard to 8 micrograms, it allows us to estimate the by 1 microgram by simply finding the difference between those two estimates.

G2. The arithmetic needed to find the difference in impact between the two tightened standards is as follows: The EPA estimates that the health-related benefits associated with tightening to 9 micrograms is \$43 billion. It estimates that the health-related benefits associated with tightening the standard to 8 micrograms is \$95 billion. The difference between the two is \$52 billion (\$95-\$43 = \$52). **\$52 billion is the estimated benefit from tightening the annual standard to 8 ug/m3 instead of 9, if the dose response curve is linear.**

A more complete estimate of the benefit of tightening the annual PM_{2.5} standard from 9 µg/m³ to 8 µg/m³ requires that effects on labor productivity be taken into account. As discussed above in connection with the OECD Study, **a 1 µg/m³ decrease in annual PM_{2.5} concentrations can be expected to increase national GDP by \$286 billion due to a 1.1% increase in labor productivity.** Therefore, a more complete estimate of the benefit of tightening the annual PM_{2.5} standard from 9 to 8 micrograms should take both health-related cost reductions and productivity increases into account. These benefits are separate and distinct. Summing them yields a plausible comprehensive estimate of \$338 billion (\$286 + \$52 = \$338) in annual benefits that would be realized by tightening the annual PM_{2.5} standard to 8 µg/m³ instead of 9 ug/m3. The case for tightening the annual PM_{2.5} standard to 8 µg/m³ becomes even more compelling when the benefits are compared to the EPA's estimate of the associated annual compliance costs.

THE ECONOMIC BENEFITS TO THE WASATCH FRONT OF TIGHTENING PM_{2.5} STANDARDS FAR OUTWEIGHT THEIR COMPLIANCE COSTS

With respect to air quality, the Greater Salt Lake City Metropolitan area is beleaguered. It has never met federal attainment levels for ozone or 24-hour PM_{2.5} pollution. Its severe nonattainment status has earned it consistent “F” ratings by the American Lung Association for both measures. The concurrent negative impact of exceedances by both pollutants makes it especially important that the EPA use all the tools in its toolbox—tightening both its annual and its 24-hour standard—to mitigate the harm to area residents' health and their economy from

currently excessive concentrations of PM2.5. According to the American Lung Association's 2019 State of the Air report,³⁹⁸ the Salt Lake Metro Area ranked 7th out of 217 metropolitan areas for highest 24-hour PM2.5, and 11th out of 228 metropolitan areas for highest ozone pollution. For 24-hour PM2.5, this report ranks Salt Lake next below Los Angeles.

The Salt Lake metro area now faces three sources of increases in PM2.5 going forward. As the regional climate rapidly heats up and dries out, it faces the likelihood that the adjacent Great Salt Lake will completely dry up over the next decade, exposing its vast, toxin-laced lakebed to wind erosion. This can be expected to massively increase particulate pollution in the metro area—some of it PM2.5. The hotter, drier climate also is increasing the frequency and scale of forest fires in the West, greatly increasing the Salt Lake metro area's episodic exposure to PM2.5. In addition, the Utah State government has announced plans to transform Salt Lake into an international logistics hub. If these plans succeed, it will dramatically increase the number of diesel-powered trucks and trains moving within the metro area, and their emissions of PM2.5.

Seasonal factors are central to understanding why the Salt Lake area's air is as bad as it is. Like many metropolitan areas in the Western United States, Salt Lake is situated in an atmospheric basin that is surrounded by mountains. In the winter, cold air at ground level can get trapped beneath warmer air as a result of temperature inversions. These often occur after a snowstorm, when snow cover cools ground level air, or shortly after dusk and throughout the night, when there's no direct sunlight.

In winter, Salt Lake residents often find themselves trapped in a "bottle" of cold, stagnant air. The pollutants in that air have no outlet, causing pollution to build until the weather changes. Consequently, winter months can have more than five times the PM2.5 concentration as summer months. December, January, and November are typically Salt Lake's worst months for air quality. In 2019, they had Air Quality Index ratings of 60, 57, and 39, respectively, which are clearly unhealthy under the federal guidelines. June, May, and April are Salt Lake City's best months for air quality, with AQI ratings of 10, 10, and 11, which are clearly within federal guidelines.³⁹⁹ Nevertheless, if the Salt Lake area's air quality were only evaluated and regulated from the perspective of annual averages, the Salt Lake area's air quality would appear to fall in the AQI "good" range. If averaged over all of 2019, the Salt Lake area's daily AQI would have been 25. Looked at only from the standpoint of annual averages, Salt Lake's air quality would raise no regulatory concerns, and provided no grounds for federal regulatory relief.

Annual averages conceal the intense but transient pollution events which commonly afflict the Salt Lake area, causing measurable harm to its residents on a substantial number of "unhealthy air" days each year. Between 2016 and 2018, for example, the Salt Lake area experienced a weighted average of 25.7 days of unhealthy ozone and 11.5 days of unhealthy PM2.5. NAAQS targets a weighted average of no more than 3.2 days of unhealthy pollution a year.⁴⁰⁰

Such frequent violations of the NAAQS target, and the harm that flows from them, would be overlooked, unregulated, and unmitigated if only the annual PM2.5 standard were applied to the Salt Lake area. Interactive graphs published by the Utah Department of Environmental Quality,⁴⁰¹ show that the Salt Lake area (as indicated by the data points (labelled "Near Road,"

“Rose Park,” and “Hawthorn”) is safely within attainment of the current $12 \mu\text{g}/\text{m}^3$ annual NAAQS standard for PM_{2.5} and likely would remain in attainment if that standard were tightened to $10 \mu\text{g}/\text{m}^3$ or $9 \mu\text{g}/\text{m}^3$. They also show that historically, Salt Lake has been in nonattainment for the 24-hour PM_{2.5} standard of $35 \mu\text{g}/\text{m}^3$, but has been trending steadily toward attainment of that standard. In this docket, the EPA proposes not to tighten its obsolete 24-hour PM_{2.5} standard to reflect the overwhelming weight of recent epidemiological research. If it adheres to that approach, the Salt Lake area may soon have no help from the EPA in mitigating the serious harm to public health and the local economy that it continues to suffer from intense, transient spikes of PM_{2.5} pollution.

Current concentrations of PM_{2.5} in the Salt Lake area are particularly harmful to its children, the elderly, and those with heart and lung diseases such as COPD, asthma, and lung cancer. The Salt Lake area has over 600,000 residents that are categorized as especially susceptible to harm from its unhealthy PM_{2.5} levels.⁴⁰² That harm comes from both long term and short term exposure.

If the EPA were to tighten the annual PM_{2.5} standard to $8 \mu\text{g}/\text{m}^3$, it would place the Salt Lake Metro Area in non-attainment status on that ground alone, as can be seen from the Interactive graphs published by the Utah Department of Environmental Quality,⁴⁰³ Salt Lake and adjacent Wasatch Front counties would still have an obligation to adopt an SIP that would, at the least, require it to avoid further deterioration of its annual PM_{2.5} concentrations. If the EPA were to tighten the annual PM_{2.5} standard only to 10 or $9 \mu\text{g}/\text{m}^3$, the Utah DEQ’s interactive graphs demonstrate that it is doubtful that the Wasatch Front counties would violate that annual standard or a 24-hour standard, going forward. This is likely to deprive the Wasatch Front of any federal assistance in improving its frequently unhealthy air quality.

The intermittent, transitory spikes in PM_{2.5} concentrations that plague Wasatch Front communities also harm the economy of the Wasatch Front.

The discussion above of the OECD Study and other research that focuses on the impact that PM_{2.5} has on aggregate economic activity concludes that if the EPA were to tighten the 24-hour PM_{2.5} standard from $9 \mu\text{g}/\text{m}^3$ to $8 \mu\text{g}/\text{m}^3$ it would likely result in an increase of \$52 billion in healthcare-related benefits nationally, and an increase in the nation’s GDP of another \$286 billion, largely through an increase in labor productivity. That line of research also emphasizes that both the healthcare costs associated with PM_{2.5} pollution and the harm that they do to labor productivity are disproportionately large for economic sub-regions (such as the Wasatch Front) whose PM_{2.5} concentrations are above the economy-wide mean.

A simplistic estimate of the net benefit to the economy of the Wasatch Front of tightening the annual PM_{2.5} standard by roughly 10% (from $9 \mu\text{g}/\text{m}^3$ to $8 \mu\text{g}/\text{m}^3$) can be obtained by assuming that the economic costs and benefits of reductions in PM_{2.5} for the Wasatch Front will reflect the national average. As noted above, EPA estimates imply that, at the national level, health-related costs of \$52 billion could be avoided each year by tightening the annual PM_{2.5} standard from $9 \mu\text{g}/\text{m}^3$ to $8 \mu\text{g}/\text{m}^3$. As calculated above, tightening the annual PM_{2.5} standard from 9

$\mu\text{g}/\text{m}^3$ to $8 \mu\text{g}/\text{m}^3$ would also increase national GDP by \$286 billion annually. Nationally, the sum of these distinct benefits is \$338 billion, while the additional compliance cost associated with a 10% tightening is several orders of magnitude smaller.

The estimated increase in national GDP caused by each $1 \mu\text{g}/\text{m}^3$ decrease in annual PM_{2.5} is closely analogous to the one measured for the EU because Utah and the EU have roughly the same annual average PM_{2.5} concentration baseline. Substantial proportions of both populations are subject to seasonal temperature inversions and, therefore, are subject to wide transitory variations in PM_{2.5} exposure. Both the United States and the European Union have similar demographic profiles, and both are at roughly the same advanced stage of economic development. For example, all of the 28 EU member states but Bulgaria have a very high Human Development Index according to the United Nations Development Program.⁴⁰⁴

It is reasonable to apply the same elasticity of GDP with respect to PM_{2.5} exposure estimated by the OECD model (1.1%) to the GDP of the United States generally, and to the Wasatch Front's GDP in particular. Doing so results in an estimated labor productivity increase from each $1 \mu\text{g}/\text{m}^3$ decrease in annual PM_{2.5} along the Wasatch Front of \$2.475 billion. The calculations are presented below.

The Wasatch Front has 75% of Utah's population.⁴⁰⁵ It is reasonable to presume that the Wasatch Front also produces 75% of Utah's GDP. Utah's GDP for 2021 was \$225 Billion.⁴⁰⁶ The response of that GDP to a 1 microgram reduction in annual PM_{2.5} exposure is found by multiplying it by the 1.1% elasticity estimated by the OECD Study. The arithmetic is as follows:

$$\begin{aligned} & [0.011 \text{ GDP increase from a } 1 \mu\text{g}/\text{m}^3 \text{ decrease in PM}_{2.5}] \\ & \times [\text{Utah GDP of } \$225 \text{ billion}] \times [\text{WF share of Utah GDP of} \\ & .75] = \$2.475 \text{ billion increase in Wasatch Front GDP} \\ & \text{each year from increased labor productivity alone.} \end{aligned}$$

As noted above, the EPA estimates (by implication) that the healthcare-related cost avoided annually at the national level by tightening the annual PM_{2.5} standard from $9 \mu\text{g}/\text{m}^3$ to $8 \mu\text{g}/\text{m}^3$ would be \$52 billion. It is reasonable to assume that the Wasatch Front counties would receive at least a proportional share of this benefit, based on its share of the national population. As of the 2020 census, the population of the Wasatch Front counties (Cache, Weber, Davis, Salt Lake, and Utah Counties) was 2,602,693 million, the population of the United States was 331.4 million, and the Wasatch Front's share of the national population total was 0.785%. Therefore, the Wasatch Front's proportional share of the annual healthcare-related savings associated with a tightening of the annual PM_{2.5} standard from $9 \mu\text{g}/\text{m}^3$ to $8 \mu\text{g}/\text{m}^3$ would be \$408 million ($\$52 \text{ billion} \times 0.00785 = \408.2 million). Adding \$408.2 million in avoided health care costs to \$2.475 billion in increased labor productivity yields a total annual net benefit of \$2.883 billion to the Wasatch Front economy of tightening the annual PM_{2.5} standard from 9 micrograms to 8 micrograms. Since the EPA's estimate of the additional national compliance cost of this tightening was several orders of magnitude smaller than its benefits, the same can be presumed to be true for the local Wasatch Front economy.

An alternative calculation of the economic costs of PM_{2.5} pollution to the Wasatch Front community is provided in a study mentioned earlier in this report, published in 2020 in the journal *Atmosphere*. Entitled “Human Health and Economic Costs of Air Pollution in Utah: An Expert Assessment “ (BYU Study),⁴⁰⁷ the study has 23 co-authors. It employed an approach called expert assessment, which analyzes all available research and experience from published and unpublished scientific studies. Combining expertise from public health, atmospheric science, and economics, the researchers identified the types of disease and economic damage arising from Utah’s air pollution and then quantified their impact.

The BYU Study focuses on the total burden of PM_{2.5} exposure on Wasatch Front residents, rather than the burden of an incremental tightening of the annual standard from 9 µg/m³ to 8 µg/m³. The study found that economic losses ranged between \$750 million and \$3.3 billion, including health care expenses, crop damage and lost earning potential, in addition to indirect costs such as loss of tourism, decreased growth and regulatory burdens. The mean of its estimates of the annual direct costs of this exposure is \$1 billion. The mean of its estimates of the indirect costs of this exposure is \$0.9 billion. The studies’ mean estimate of PM_{2.5}’s share of these costs is 55%. Fifty five percent of the \$1.9 billion estimate of annual direct and indirect air pollution costs to the Wasatch Front counties comes to \$1.045 billion that is attributable to PM_{2.5}.

Section 4.1 of the BYU Study offers a second approach to calculating the cost burden of exposure to air pollution along the Wasatch Front. It says that the market cost of air pollution scaled down from national to local levels of population and GDP are about \$2 billion, while this total swells to about \$7 billion when scaled down welfare costs are included. Fifty five percent of \$7 billion yields a rough estimate of the annual burden of exposure to PM_{2.5} along the Wasatch Front of \$3.85 billion. It should be borne in mind, however, that this estimates a total annual burden of PM_{2.5} exposure rather than the 1 µg/m³ increment analyzed above, nor does it account for the dominant component of PM_{2.5} exposure’s market costs, which is its effect on aggregate labor productivity. The analysis of the net economic benefit from tightening the annual PM_{2.5} standard from 9 to 8 micrograms provided above, therefore, provides a more relevant guide to the EPA when considering how stringent PM_{2.5} NAAQS standards should be.

H. CONCLUSION

Like with justice, “public health protection delayed is public health protection denied.” The United States federal government has a long history of ignoring science and allowing businesses to manufacture products and create emissions that endanger the public long after the science has convincingly shown the associated health hazards. Lead, mercury, ionizing radiation, asbestos, and tobacco are just some of the toxins that were not banned or regulated until decades after their hazards were well established. Creation of the EPA was supposed to change that paradigm. But the fact that EPA has only banned eight substances in its history while the

public is exposed to 140,000 industrial chemicals tells a disturbing story in and of itself. “Many of the most dangerous substances which faced bans in other countries, remained on the market for decades.”³⁸³ That pesticides kill plants and insects means they are poisonous to the same biologic world that humans inhabit and depend on. EPA now “manages” over 16,800 pesticides, including 1,200 active ingredients. In their entire history EPA has canceled the registration of only 37 pesticides, and in the last decade have only forced one pesticide off the market. Meanwhile the European Union has banned or restricted over 1,000 chemicals just since 2007.

Numerous books and investigative journalism articles by ProPublica, the Intercept, the Center for Public Integrity, Le Monde, and many others, have detailed why EPA has failed to protect the public from these poisons. EPA’s default assumption is chemicals are innocent and treated as such, until or unless proven--virtually without doubt--that they are guilty. And in the rare instance that happens, it is invariably after public health has seen prolonged harm on a mass scale. Just like with hazardous chemicals, EPA’s long running modus operandi is to assume current NAAQS are safe unless there is near absolute proof that they are not.

Having closely followed the medical research on air pollution for the last 16 years, there is little doubt in our minds that the medical research will only continue to expand and become more convincing that current NAAQS PM2.5 standards and the EPA proposals are both too weak. We reiterate that EPA has not changed the PM2.5 24 hr. standard since 2006 and the annual standard since 2012. Consistent with both the science and EPA’s legal mandate, we urge EPA to adopt a 24-hour PM2.5 standard of 20µg/m³ and an annual standard of 8 µg/m³.

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References

1. <https://www.epa.gov/clean-air-act-overview/benefits-and-costs-clean-air-act-1990-2020-second-prospective-study>
2. <https://www.nejm.org/doi/full/10.1056/NEJMs2011009>

3. <https://www.cfr.org/in-brief/us-life-expectancy-decline-why-arent-other-countries-suffering-same-problem>
4. <https://assets.prb.org/pdf11/aging-in-america.pdf>
5. Ugai, T., Sasamoto, N., Lee, HY. et al. Is early-onset cancer an emerging global epidemic? Current evidence and future implications. *Nat Rev Clin Oncol* 19, 656–673 (2022).
<https://doi.org/10.1038/s41571-022-00672-8>
6. Turner M, et al. Outdoor air pollution and cancer: An overview of the current evidence and public health recommendations. *CA: A Cancer Journal for Clinicians*. Volume 70, Issue 6 November/December 2020. Pages 460-479
7. T. Benmarhnia, Linkages between air pollution and the health burden from COVID-19: Methodological challenges and opportunities. *Am. J. Epidemiol.*, kwaa148 (2020).
8. E. Conticini, B. Frediani, D. Caro, Can atmospheric pollution be considered a co-factor in extremely high level of SARS-CoV-2 lethality in Northern Italy? *Environ. Pollut.* 261, 114465 (2020).
9. M. A. Cole, C. Ozgen, E. Strobl, Air pollution exposure and COVID-19 in Dutch municipalities. *Environ. Resour. Econ.* (Dordr), 1–30 (2020).
10. Wu X, et al. Air pollution and COVID-19 mortality in the United States: Strengths and limitations of an ecological regression analysis. *Science Advances*. 4 Nov 2020, VOL. 6, NO. 45
11. <https://www.mdpi.com/2073-4433/11/11/1238>
12. <https://www.scientificamerican.com/article/californias-2020-wildfires-negated-years-of-emission-cuts/>
13. World Health Organization. WHO Global Air Quality Guidelines: Particulate Matter PM2.5 and PM10), Ozone, Nitrogen Dioxide, Sulfur Dioxide and Carbon Monoxide. Geneva: World Health Organization; 2021.
<https://apps.who.int/iris/bitstream/handle/10665/345329/9789240034228-eng.pdf>
14. <https://www.scientificamerican.com/article/most-experimental-drugs-are-tested-offshore-raising-concerns-about-data/>
15. https://www.nrdc.org/sites/default/files/media-uploads/2020-10-01_ozone_naaqs_proposal_ngo_coalition_comments.pdf p. 33.
16. EPA, Nov. 2015, Preamble to the Integrated Science Assessments

<https://nepis.epa.gov/Exe/ZyNET.exe/P100PDP0.TXT?ZyActionD=ZyDocument&Client=EPA&Index=2011+Thru+2015&Docs=&Query=&Time=&EndTime=&SearchMethod=1&TocRestrict=n&Toc=&TocEntry=&QField=&QFieldYear=&QFieldMonth=&QFieldDay=&IntQFieldOp=0&ExtQFieldOp=0&XmlQuery=&File=D%3A%5Czyfiles%5CIndex%20Data%5C11thru15%5CTxt%5C00000021%5CP100PDP0.txt&User=ANONYMOUS&Password=anonymous&SortMethod=h%7C-&MaximumDocuments=1&FuzzyDegree=0&ImageQuality=r75g8/r75g8/x150y150g16/i425&Display=hpfr&DefSeekPage=x&SearchBack=ZyActionL&Back=ZyActionS&BackDesc=Results%20page&MaximumPages=1&ZyEntry=1&SeekPage=x&ZyPURL>

17. Miller MR. Oxidative stress and the cardiovascular effects of air pollution. *Free Radic Biol Med.* 2020 May 1;151:69-87. doi: 10.1016/j.freeradbiomed.2020.01.004. Epub 2020 Jan 7. PMID: 31923583; PMCID: PMC7322534.

18. Wolf D, Ley K. Immunity and Inflammation in Atherosclerosis. *Circulation Research.* . 2019;124:315–327, 17 Jan 2019, <https://doi.org/10.1161/CIRCRESAHA.118>.

19. https://www.euro.who.int/_data/assets/pdf_file/0006/189051/Health-effects-of-particulate-matter-final-Eng.pdf

20. H. Traboulsi, N. Guerrina, M. lu, D. Maysinger, P. Ariya, C. Baglole. Inhaled pollutants: the molecular scene behind respiratory and systemic diseases associated with ultrafine particulate matter. *Int. J. Mol. Sci.*, 18 (2017), p. 243, 10.3390/ijms18020243

21. de Jesus A, et al. Ultrafine particles and PM_{2.5} in the air of cities around the world: Are they representative of each other?, *Environment International*, Volume 129, 2019, Pages 118-135, ISSN 0160-4120

22. Jedrychowski WA, Majewska R, Spengler JD, Camann D, Roen EL, Perera FP. Prenatal exposure to fine particles and polycyclic aromatic hydrocarbons and birth outcomes: a two-pollutant approach. *Int Arch Occup Environ Health.* 2017 Apr;90(3):255-264. doi: 10.1007/s00420-016-1192-9. Epub 2017 Feb 7. PMID: 28168423; PMCID: PMC5360842.

23. Report, “Analysis of PM_{2.5}-Related Health Burdens Under Current and Alternative NAAQS” by Industrial Economics, Inc. April, 2022, commissioned by the Environmental Defense Fund

24. Erickson AC, Ostry A, Chan LH, Arbour L. The reduction of birth weight by fine particulate matter and its modification by maternal and neighbourhood-level factors: a multilevel analysis in British Columbia, Canada. *Environ Health.* 2016 Apr 14;15:51. doi: 10.1186/s12940-016-0133-0. PMID: 27079512; PMCID: PMC4831087.

25. Rosofsky, A., Levy, J. I., Zanobetti, A., Janulewicz, P., & Fabian, M. P. (2018). Temporal trends in air pollution exposure inequality in Massachusetts. *Environmental research*, 161, 76-86.

26. Tessum, C. W., Apte, J. S., Goodkind, A. L., Muller, N. Z., Mullins, K. A., Paoletta, D. A., ... & Hill, J. D. (2019). *Inequity in consumption of goods and services adds to racial–ethnic disparities in air*
27. Colmer, J., Hardman, I., Shimshack, J., & Voorheis, J. (2020). *Disparities in PM_{2.5} air pollution in the United States*. *Science*, 369(6503), 575-578.
28. Alhanti, B.A., Chang, H.H., Winkvist, A., Mulholland, J.A., Darrow, L.A. and Sarnat, S.E., 2016. *Ambient air pollution and emergency department visits for asthma: a multi-city assessment of effect modification by age*. *Journal of exposure science & environmental epidemiology*, 26(2), pp.180-188.
29. Thatcher, T. & Kirchstetter, T. (2011). *Assessing Near-Field Exposures from Distributed Residential Wood Smoke Combustion Sources*. Report prepared for the California Air Resources Board.
30. Fleming S, et al. *Normal ranges of heart rate and respiratory rate in children from birth to 18 years: a systematic review of observational studies*. *Lancet*. 2011;377:1011–8.
31. EPA’s 2019 Integrated Science Assessment for Particulate Matter.
32. Chen X, Chen S, Zhu Z, Luo J, Wang H, Wulayin M, Huang C, Zhao W, Wang Q. *Identifying the critical windows and joint effects of temperature and PM_{2.5} exposure on small for gestational age*. *Environ Int*. 2023 Feb 18;173:107832. doi: 10.1016/j.envint.2023.107832. Epub ahead of print. PMID: 36822007.
33. Myers DJ, Kriebel D. *If Smoking Were Eliminated, Which US Counties Would Still Have High Rates of Smoking-Related Cancers?* *Int J Environ Res Public Health*. 2022 Nov 19;19(22):15292. doi: 10.3390/ijerph192215292. PMID: 36430011; PMCID: PMC9690633.
34. GBD 2017 Risk Factor Collaborators. *Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017*. *Lancet*. 2018 Nov 10;392(10159):1923-1994. doi: 10.1016/S0140-6736(18)32225-6. Epub 2018 Nov 8. Erratum in: *Lancet*. 2019 Jan 12;393(10167):132. Erratum in: *Lancet*. 2019 Jun 22;393(10190):e44. PMID: 30496105; PMCID: PMC6227755.
35. Peters, A. *Air Quality and Cardiovascular Health: Smoke and Pollution Matter*. *Circulation*. 2009; 120:924-927
36. Makar M., Antonelli J., Di Q., Cutler D., Schwartz J., Dominici F. *Estimating the causal effect of fine particulate matter levels on death and hospitalization: Are levels below the safety standards harmful?* *Epidemiology*. 2017;28:627–634. doi: 10.1097/EDE.0000000000000690

37. Chen J, Hoek G. Long-term exposure to PM and all-cause and cause-specific mortality: A systematic review and meta-analysis. *Environ Int.* 2020 Oct;143:105974. doi: 10.1016/j.envint.2020.105974. Epub 2020 Jul 20. PMID: 32703584.
38. Hacksaw A, et al. Low cigarette consumption and risk of coronary heart disease and stroke: meta-analysis of 141 cohort studies in 55 study reports. *BMJ* 2018;360:j5855
39. Inoue-Choi M, Liao L, Reyes-Guzman C, Hartge P, Caporaso N, Freedman N. Association of long-term low-intensity smoking with all-cause and cause-specific mortality in the NIH-AARP Diet and Health Study. *JAMA Internal Medicine.* December 5, 2016. DOI: 10.1001/jamainternmed.2016.7511
40. Bowe B, et al. Burden of Cause-Specific Mortality Associated With PM_{2.5} Air Pollution in the United States. *JAMA Network Open.* November 20, 2019
41. Miller KA, Siscovick DS, Sheppard L, Shepherd K, Sullivan JH, Anderson GL, Kaufman JD. Long-term exposure to air pollution and incidence of cardiovascular events in women. *N Engl J Med.* 2007 Feb 1;356(5):447-58. Doi: 10.1056/NEJMoa054409. PMID: 17267905.
42. Zhang J, Wang X, Yan M, Shan A, Wang C, Yang X, Tang N. Sex Differences in Cardiovascular Risk Associated With Long-Term PM_{2.5} Exposure: A Systematic Review and Meta-Analysis of Cohort Studies. *Front Public Health.* 2022 Feb 2;10:802167. doi: 10.3389/fpubh.2022.802167. PMID: 35186842; PMCID: PMC8847390.
43. Pope, CA III, Ezzate, M., Dockery, D. Fine-Particulate Air Pollution and Life Expectancy in the United States. *NEJM.* Vol. 360:376-386 Jan. 22, 2009 Num. 4.
44. Pilz et al. (2018), Lane et al. (2016), Strak et al. (2012), Chung et al 2015, Franck et al. (2011), Atkinson et al. (2010)
45. Meng X, Ma Y, Chen R, Zhou Z, Chen B, Kan H. Size-fractionated particle number concentrations and daily mortality in a Chinese city. *Environ Health Perspect.* 2013 Oct;121(10):1174-8. doi: 10.1289/ehp.1206398. Epub 2013 Aug 13. PMID: 23942310; PMCID: PMC3801202.
46. Krall JR, GB Anderson, F Dominici, ML Bel, RD Peng. Short-term exposure to particulate matter constituents and mortality in a national study of U.S. urban communities. 2013. <http://ehp.niehs.nih.gov/1206185/>. *Environmental Health Perspectives*; <http://dx.doi.org/10.1289/ehp.1206185>.
47. Wang, Y, et al. Long-term Exposure to PM_{2.5} and Mortality Among Older Adults in the Southeastern US. *Epidemiology* 28(2):p 207-214, March 2017.

48. Di Q, et al. Air Pollution and Mortality in the Medicare Population. *New England Journal of Medicine*, 2017; 376 (26): 2513 DOI: 10.1056/NEJMoa1702747
49. Qian D, et al. Association of Short-term Exposure to Air Pollution With Mortality in Older Adults. *JAMA*. 2017;318(24):2446-2456. doi: 10.1001/jama.2017.17923
50. Renard J-P, et al. Relation between PM2.5 pollution and Covid-19 mortality in Western Europe for the 2020–2022 period, *Science of The Total Environment*. Volume 848, 2022, 157579, ISSN 0048-9697
51. Mustafic H, Jabre P, Caussin C, Murad MH, Escolano S, Tafflet M, Périer MC, Marijon E, Vernerey D, Empana JP, Jouven X. Main air pollutants and myocardial infarction: a systematic review and meta-analysis. *JAMA*. 2012 Feb 15;307(7):713-21. doi: 10.1001/jama.2012.126. PMID: 22337682.
52. Miller M, et al. Inhaled Nanoparticles Accumulate at Sites of Vascular Disease. *ACS Nano*. 2017 May 23; 11(5): 4542–4552.
53. Lepeule J, Laden F, Dockery D, Schwartz J. Chronic Exposure to Fine Particles and Mortality: An Extended Follow-Up of the Harvard Six Cities Study from 1974 to 2009. *Environ Health Perspect*. 2012 Mar 28.
54. Dai L, Zanobetti A, Koutrakis P, Schwartz JD. Associations of fine particulate matter species with mortality in the United States: a multicity time-series analysis. *Environ Health Perspect*. 2014 Aug;122(8):837-42. doi: 10.1289/ehp.1307568. Epub 2014 May 6. Erratum in: *Environ Health Perspect*. 2016 Jun 1;124(6):A104. PMID: 24800826; PMCID: PMC4123030.
55. Crouse DL, Peters PA, van Donkelaar A, Goldberg MS, Villeneuve PJ, Brion O, et al. 2012. Risk of Nonaccidental and Cardiovascular Mortality in Relation to Long-term Exposure to Low Concentrations of Fine Particulate Matter: A Canadian National-Level Cohort Study. *Environ Health Perspect* 120:708-714. <http://dx.doi.org/10.1289/ehp.1104049>
56. Shi L, Zanobetti A, Kloog I, Coull BA, Koutrakis P, Melly SJ, Schwartz JD. Low-Concentration PM2.5 and Mortality: Estimating Acute and Chronic Effects in a Population-Based Study. *Environ Health Perspect*. 2016 Jan;124(1):46-52. doi: 10.1289/ehp.1409111. Epub 2015 Jun 3. PMID: 26038801; PMCID: PMC4710600.
57. Schwartz J, Austin E, Bind MA, Zanobetti A, Koutrakis P. Estimating Causal Associations of Fine Particles With Daily Deaths in Boston. *Am J Epidemiol*. 2015 Oct 1;182(7):644-50. doi: 10.1093/aje/kwv101. Epub 2015 Sep 6. PMID: 26346544; PMCID: PMC4692977.
58. Lee M, Koutrakis P, Coull B, Kloog I, Schwartz J. Acute effect of fine particulate matter on mortality in three Southeastern states from 2007-2011. *J Expo Sci Environ Epidemiol*. 2016 Mar-

Apr;26(2):173-9. doi: 10.1038/jes.2015.47. Epub 2015 Aug 26. PMID: 26306925; PMCID: PMC4758853.

59. Schwartz J. et al. Estimating Causal Effects of Local Air Pollution on Daily Deaths: Effect of Low Levels. *Environ Health Perspect*; DOI: 10.1289/EHP232

60. Kim H, Kim J, Kim S, Kang SH, Kim HJ, Kim H, Heo J, Yi SM, Kim K, Youn TJ, Chae IH. Cardiovascular Effects of Long-Term Exposure to Air Pollution: A Population-Based Study With 900 845 Person-Years of Follow-up. *J Am Heart Assoc*. 2017 Nov 8;6(11):e007170. doi: 10.1161/JAHA.117.007170. PMID: 29118034; PMCID: PMC5721790.

61. Corrigan AE, Becker MM, Neas LM, Cascio WE, Rappold AG. Fine particulate matters: The impact of air quality standards on cardiovascular mortality. *Environ Res*. 2018 Feb;161:364-369. doi: 10.1016/j.envres.2017.11.025. Epub 2017 Dec 1. PMID: 29195185; PMCID: PMC6372949.

62. Adar SD, Klein R, Klein BE, Szpiro AA, Cotch MF, Wong TY, O'Neill MS, Shrager S, Barr RG, Siscovick DS, Davignus ML, Sampson PD, Kaufman JD. Air Pollution and the microvasculature: a cross-sectional assessment of in vivo retinal images in the population-based multi-ethnic study of atherosclerosis (MESA). *PLoS Med*. 2010 Nov 30;7(11):e1000372. doi: 10.1371/journal.pmed.1000372. PMID: 21152417; PMCID: PMC2994677.

63. Madrigano J, Kloog I, Goldberg R, Coull BA, Mittleman MA, Schwartz J. Long-term exposure to PM_{2.5} and incidence of acute myocardial infarction. *Environ Health Perspect*. 2013 Feb;121(2):192-6. doi: 10.1289/ehp.1205284. Epub 2012 Nov 29. PMID: 23204289; PMCID: PMC3569684.

64. Alexeeff S, et al. Association of Long-term Exposure to Particulate Air Pollution With Cardiovascular Events in California. *JAMA Netw Open*. 2023;6(2):e230561. doi:10.1001/jamanetworkopen.2023.0561

65. Pope CA, Muhlestein JB, Anderson JL, Cannon JB, Hales NM, Meredith KG, Le V, Horne BD. Short-Term Exposure to Fine Particulate Matter Air Pollution Is Preferentially Associated With the Risk of ST-Segment Elevation Acute Coronary Events. *J Am Heart Assoc*. 2015 Dec 8;4(12):e002506. doi: 10.1161/JAHA.115.002506. PMID: 26645834; PMCID: PMC4845284.

66. Cesaroni G, et al. Long term exposure to ambient air pollution and incidence of acute coronary events: prospective cohort study and meta- analysis in 11 European cohorts from the ESCAPE Project. *BMJ* 2014;348:f7412

67. Cramer J, et al. Long-Term Exposure to Air Pollution and Incidence of Myocardial Infarction: A Danish Nurse Cohort Study. *Environ Health Perspect*. 2020 May;128(5):57003. doi: 10.1289/EHP5818. Epub 2020 May 6.

68. Chen R, Jiang Y, Hu J, Chen H, Li H, Meng X, Ji JS, Gao Y, Wang W, Liu C, Fang W, Yan H, Chen J, Wang W, Xiang D, Su X, Yu B, Wang Y, Xu Y, Wang L, Li C, Chen Y, Bell ML, Cohen AJ, Ge J, Huo Y, Kan H. Hourly Air Pollutants and Acute Coronary Syndrome Onset In 1.29 Million Patients. *Circulation*. 2022 Apr 22. doi: 10.1161/CIRCULATIONAHA.121.057179. Epub ahead of print. PMID: 35450432.
69. Cowell WJ, et al. Prenatal Exposure to PM2.5 and Cardiac Vagal Tone during Infancy: Findings from a Multiethnic Birth Cohort. *Environmental Health Perspectives*, 2019; 127 (10): 107007 DOI: 10.1289/EHP4434
70. Buccelletti E, Gilardi E, Scaini E, Galiuto L, Persiani R, Biondi A, et al. 2009. Heart rate variability and myocardial infarction: systematic literature review and metanalysis. *Eur Rev Med Pharmacol Sci* 13(4):299–307, PMID: 19694345
71. Licht CMM, Vreeburg SA, van Reedt Dortland AK, Giltay EJ, Hoogendijk WJ, DeRijk RH, et al. 2010. Increased sympathetic and decreased parasympathetic activity rather than changes in hypothalamic-pituitary-adrenal axis activity is associated with metabolic abnormalities. *J Clin Endocrinol Metab* 95(5):2458–2466, PMID: 20237163, 10.1210/jc.2009-2801.
72. Thayer JF, Yamamoto SS, Brosschot JF. 2010. The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. *Int J Cardiol* 141(2):122–131, PMID: 19910061, 10.1016/j.ijcard.2009.09.543.
73. Jung EM, et al. Association between prenatal exposure to PM2.5 and the increased risk of specified infant mortality in South Korea. *Environment International*, Volume 144, 2020, 105997.
74. Van Hee VC, Szpiro AA, Prineas R, Neyer J, Watson K, Siscovick D, Kyun Park S, Kaufman JD. Association of long-term air pollution with ventricular conduction and repolarization abnormalities. *Epidemiology*. 2011 Nov;22(6):773-80. doi: 10.1097/EDE.0b013e31823061a9. PMID: 21918454; PMCID: PMC3197855.75.
75. Silverman RA, Ito K, Freese J, Kaufman BJ, De Claro D, Braun J, Prezant DJ. Association of ambient fine particles with out-of-hospital cardiac arrests in New York City. *Am J Epidemiol*. 2010 Oct 15;172(8):917-23. doi: 10.1093/aje/kwq217. Epub 2010 Aug 20. PMID: 20729350; PMCID: PMC2984245.
76. Kang SH, Heo J, Oh IY, Kim J, Lim WH, Cho Y, Choi EK, Yi SM, Do Shin S, Kim H, Oh S. Ambient air pollution and out-of-hospital cardiac arrest. *Int J Cardiol*. 2016 Jan 15;203:1086-92. doi: 10.1016/j.ijcard.2015.11.100. Epub 2015 Nov 18. PMID: 26646382.
77. Madhloum N. et al. Neonatal blood pressure in association with prenatal air pollution exposure, traffic, and land use indicators: An ENVIRONAGE birth cohort study. *Environ Int*. 2019 Jun 18;130:104853. doi: 10.1016/j.envint.2019.05.047. [Epub ahead of print]

78. Zhang M, Mueller NT, Wang H, Hong X, Appel LJ, Wang X. Maternal Exposure to Ambient Particulate Matter $\leq 2.5 \mu\text{m}$ During Pregnancy and the Risk for High Blood Pressure in Childhood Hypertension. 2018 Jul;72(1):194-201. doi: 10.1161/HYPERTENSIONAHA.117.10944. Epub 2018 May 14. PMID: 29760154; PMCID: PMC6002908.
79. Mehta AJ, Zanobetti A, Koutrakis P, Mittleman MA, Sparrow D, Vokonas P, Schwartz J. Associations between short-term changes in air pollution and correlates of arterial stiffness: The Veterans Affairs Normative Aging Study, 2007-2011. *Am J Epidemiol.* 2014 Jan 15;179(2):192-9. doi: 10.1093/aje/kwt271. Epub 2013 Nov 13. PMID: 24227017; PMCID: PMC3873113.
80. Mehta AJ, Zanobetti A, Koutrakis P, Mittleman MA, Sparrow D, Vokonas P, Schwartz J. Associations between short-term changes in air pollution and correlates of arterial stiffness: The Veterans Affairs Normative Aging Study, 2007-2011. *Am J Epidemiol.* 2014 Jan 15;179(2):192-9. doi: 10.1093/aje/kwt271. Epub 2013 Nov 13. PMID: 24227017; PMCID: PMC3873113.
81. Zhang Z, Guo C, Lau AKH, Chan TC, Chuang YC, Lin C, Jiang WK, Yeoh EK, Tam T, Woo KS, Yan BP, Chang LY, Wong MCS, Lao XQ. Long-Term Exposure to Fine Particulate Matter, Blood Pressure, and Incident Hypertension in Taiwanese Adults. *Environ Health Perspect.* 2018 Jan 18;126(1):017008. doi: 10.1289/EHP2466. PMID: 29351544; PMCID: PMC6014706.
82. Kubesch N, et al. Arterial blood pressure responses to short-term exposure to low and high traffic-related air pollution with and without moderate physical activity. *European Journal of Preventive Cardiology.* October 17, 2014, Volume 22, Issue 5.
83. Sofianopoulou E, et al. Traffic exposures, air pollution and outcomes in pulmonary arterial hypertension: A United Kingdom cohort study analysis. *Eur Respir J.* 2019 Mar 28. pii: 1801429. doi: 10.1183/13993003.01429-2018. [Epub ahead of print]
84. Adar SD, Sheppard L, Vedal S, Polak JF, Sampson PD, Diez Roux AV, Budoff M, Jacobs DR Jr, Barr RG, Watson K, Kaufman JD. Fine particulate air pollution and the progression of carotid intima-medial thickness: a prospective cohort study from the multi-ethnic study of atherosclerosis and air pollution. *PLoS Med.* 2013;10(4):e1001430. doi:
85. Shah ASV, Langrish JP, Nair H, et al. Global association of air pollution and heart failure: a systematic review and meta-analysis. *The Lancet.* Published online July 10 2013
86. Kloog I, Zanobetti A, Nordio F, Coull BA, Baccarelli AA, Schwartz J. Effects of airborne fine particles (PM_{2.5}) on deep vein thrombosis admissions in the northeastern United States. *J Thromb Haemost.* 2015 May;13(5):768-74. doi: 10.1111/jth.12873. Epub 2015 Mar 28. PMID: 25678264; PMCID: PMC4424156
87. Miller MR, et al. Inhaled Nanoparticles Accumulate at Sites of Vascular Disease. *ACS Nano.* 2017 Apr 26. doi: 10.1021/acsnano. 6b08551. [Epub ahead of print]

88. Aung N, et al. Association Between Ambient Air Pollution and Cardiac Morpho-Functional Phenotypes, insights From the UK Biobank Population Imaging Study. Originally published 3 Aug 2018 *Circulation*. 2018;0:CIRCULATIONAHA.118.034856
89. Makar M, Antonelli J, Di Q, Cutler D, Schwartz J, Dominici F. Estimating the Causal Effect of Low Levels of Fine Particulate Matter on Hospitalization. *Epidemiology*. 2017 Sep;28(5):627-634. doi: 10.1097/EDE.0000000000000690. PMID: 28768298; PMCID: PMC5624531
90. Varatharaj A, Galea I. The blood-brain barrier in systemic inflammation *Brain Behav. Immun.*, 60 (2017), pp. 1-12, 10.1016/j.bbi.2016.03.010
91. Béjot Y, et al. A review of epidemiological research on stroke and dementia and exposure to air pollution. *Int J Stroke*. 2018 Jan 1:1747493018772800. doi: 10.1177/1747493018772800. [Epub ahead of print]
92. Mateen F, Brook R. Air Pollution as an Emerging Global Risk Factor for Stroke *JAMA* 2011;305(12):1240-1241. doi:10.1001/jama.2011.352
93. Wellenius GA, Burger MR, Coull BA, Schwartz J, Suh HH, Koutrakis P, Schlaug G, Gold DR, Mittleman MA. Ambient air pollution and the risk of acute ischemic stroke. *Arch Intern Med*. 2012 Feb 13;172(3):229-34. doi: 10.1001/archinternmed.2011.732. PMID: 22332153; PMCID: PMC3639313.
94. Mullen C, et al. Effects of PM2.5 on Third Grade Students' Proficiency in Math and English Language Arts. *Int. J. Environ. Res. Public Health* 2020, 17(18), 6931; <https://doi.org/10.3390/ijerph17186931>
95. Laurent JGC, MacNaughton P, Jones E, Young AS, Bliss M, Flanigan S, Vallarino J, Chen LJ, Cao X, Allen JG. Associations between Acute Exposures to PM2.5 and Carbon Dioxide Indoors and Cognitive Function in Office Workers: A Multicountry Longitudinal Prospective Observational Study. *Environ Res Lett*. 2021 Sep;16(9):094047. doi: 10.1088/1748-9326/ac1bd8. Epub 2021 Sep 9. PMID: 35330988; PMCID: PMC8942432.
96. Weuve J, Puett R, Schwartz J, Yanosky J, Laden F, Grodstein F. Exposure to Particulate Air Pollution and Cognitive Decline in Older Women *Arch Intern Med*. 2012;172(3):219-227. doi:10.1001/archinternmed.2011.683
97. Petkus AJ, et al. Exposure to fine particulate matter and temporal dynamics of episodic memory and depressive symptoms in older women. *Environ Int*. 2019 Dec 24;135:105196. doi: 10.1016/j.envint. 2019.105196. [Epub ahead of print]
98. Yu X, et al. Exposure to air pollution and cognitive impairment risk: a meta-analysis of longitudinal cohort studies with dose-response analysis. *J Glob Health*. 2020 Jun;10(1):010417. doi: 10.7189/jogh. 10.010417.

99. Grande G, et al. Association Between Cardiovascular Disease and Long-term Exposure to Air Pollution With the Risk of Dementia. *JAMA Neurology*, 2020; DOI: 10.1001/jamaneurol.2019.4914
100. Shaffer RM, Blanco MN, Li G, Adar SD, Carone M, Szpiro AA, Kaufman JD, Larson TV, Larson EB, Crane PK, Sheppard L. Fine Particulate Matter and Dementia Incidence in the Adult Changes in Thought Study. *Environ Health Perspect*. 2021 Aug;129(8):87001. doi: 10.1289/EHP9018. Epub 2021 Aug 4. PMID: 34347531; PMCID: PMC8336685
101. Wang X, et al. Association of improved air quality with lower dementia risk in older women. *Proceedings of the National Academy of Sciences* Jan 2022, 119 (2) e2107833119; DOI: 10.1073/pnas. 2107833119
102. Younan D, Wang X, Millstein J, Petkus AJ, Beavers DP, Espeland MA, Chui HC, Resnick SM, Gatz M, Kaufman JD, Wellenius GA, Whitsel EA, Manson JE, Rapp SR, Chen JC. Air quality improvement and cognitive decline in community-dwelling older women in the United States: A longitudinal cohort study. *PLoS Med*. 2022 Feb 3;19(2):e1003893. doi: 10.1371/journal.pmed.1003893. PMID: 35113870; PMCID: PMC8812844.
103. Letellier N, et al. Air quality improvement and incident dementia: Effects of observed and hypothetical reductions in air pollutant using parametric g-computation. *Alzheimers Dement*. 2022 Feb 9. doi: 10.1002/alz.12606
104. Fu P, Yung KKL. Air Pollution and Alzheimer's Disease: A Systematic Review and Meta-Analysis. *J Alzheimers Dis*. 2020;77(2):701-714. doi: 10.3233/JAD-200483. PMID: 32741830.
105. Jung CR, Lin YT, Hwang BF. Ozone, particulate matter, and newly diagnosed Alzheimer's disease: a population-based cohort study in Taiwan. *J Alzheimers Dis*. 2015;44(2):573-84. doi: 10.3233/JAD-140855.
106. Younan D, et al. Particulate matter and episodic memory decline mediated by early neuroanatomic biomarkers of Alzheimer's disease. *Brain*, awz348, <https://doi.org/10.1093/brain/awz348>. Published: 20 November 2019
107. Iaccarino L, et al. Association Between Ambient Air Pollution and Amyloid Positron Emission Tomography Positivity in Older Adults With Cognitive Impairment. *JAMA Neurol*. Published online November 30, 2020. doi:10.1001/jamaneurol.2020.3962
108. Rhew SH, Kravchenko J, Lysterly HK. Exposure to low-dose ambient fine particulate matter PM_{2.5} and Alzheimer's disease, non-Alzheimer's dementia, and Parkinson's disease in North Carolina. *PLoS One*. 2021;16(7):e0253253. Published 2021 Jul 9. doi:10.1371/journal.pone.0253253

109. Kioumourtzoglou MA, Schwartz JD, Weisskopf MG, Melly SJ, Wang Y, Dominici F, Zanobetti A. 2016. Long-term PM_{2.5} exposure and neurological hospital admissions in the northeastern United States. *Environ Health Perspect* 124:23-29; <http://dx.doi.org/10.1289/ehp.1408973>.
110. Zanobetti A, et al. A national case-crossover analysis of the short-term effect of PM_{2.5} on hospitalizations and mortality in subjects with diabetes and neurological disorders. *Environmental Health* 2014, 13:38 doi:10.1186/1476-069X-13-38
111. Lee H, Myung W, Kim DK, Kim SE, Kim CT, Kim H. Short-term air pollution exposure aggravates Parkinson's disease in a population-based cohort. *Sci Rep*. 2017 Mar 16;7:44741. doi: 10.1038/srep44741. PMID: 28300224; PMCID: PMC5353743
112. Chen H, et al. Exposure to ambient air pollution and the incidence of dementia: A population-based cohort study. *Environment International*. Volume 108, November 2017, Pages 271-277
113. Morgan, Z.E.M., Bailey, M.J., Trifonova, D.I. et al. Prenatal exposure to ambient air pollution is associated with neurodevelopmental outcomes at 2 years of age. *Environ Health* 22, 11 (2023). <https://doi.org/10.1186/s12940-022-00951-y>
114. Wang P, et al. (2017) Socioeconomic disparities and sexual dimorphism in neurotoxic effects of ambient fine particles on youth IQ: A longitudinal analysis. *PLoS ONE* 12(12): e0188731. <https://doi.org/10.1371/journal.pone.0188731>
115. Liu H, et al. Particulate matter exposure during pregnancy and infancy and risks of autism spectrum disorder in children: A systematic review and meta-analysis. *Science of The Total Environment*, Volume 855, 2023, 158830.
116. Becerra TA, Wilhelm M, Olsen J, Cockburn M, Ritz B. Ambient air pollution and autism in Los Angeles county, California. *Environ Health Perspect*. 2013 Mar;121(3):380-6. doi: 10.1289/ehp.1205827. Epub 2012 Dec 18. PMID: 23249813; PMCID: PMC3621187.
117. Flores-Pajot MC, Ofner M, Do MT, Lavigne E, Villeneuve PJ. Childhood autism spectrum disorders and exposure to nitrogen dioxide, and particulate matter air pollution: A review and meta-analysis. *Environ Res*. 2016 Aug 25. pii: S0013-9351(16)30317-6. doi: 10.1016/j.envres.2016.07.030. [Epub ahead of print]
118. Raz R, Roberts AL, Lyall K, Hart JE, Just AC, Laden F, Weisskopf MG. Autism spectrum disorder and particulate matter air pollution before, during, and after pregnancy: a nested case-control analysis within the Nurses' Health Study II Cohort. *Environ Health Perspect*. 2015 Mar;123(3):264-70. doi: 10.1289/ehp.1408133. Epub 2014 Dec 18. PMID: 25522338; PMCID: PMC4348742.

119. Lam J, Sutton P, Kalkbrenner A, Windham G, Halladay A, Koustas E, Lawler C, Davidson L, Daniels N, Newschaffer C, Woodruff T. A Systematic Review and Meta-Analysis of Multiple Airborne Pollutants and Autism Spectrum Disorder. *PLoS One*. 2016 Sep 21;11(9):e0161851. doi: 10.1371/journal.pone.0161851.
120. Jo H, et al. Sex-specific associations of autism spectrum disorder with residential air pollution exposure in a large Southern California pregnancy cohort. *Environ Pollut*. 2019 Nov;254(Pt A):113010. doi: 10.1016/j.envpol.2019.113010. Epub 2019 Aug 5.
121. Saenen N, et al. In Utero Fine Particle Air Pollution and Placental Expression of Genes in the Brain-Derived Neurotrophic Factor Signaling Pathway: An ENVIRONAGE Birth Cohort Study *Environ Health Perspect*; DOI:10.1289/ehp.1408549
122. Ailshire J, Clarke P. Fine Particulate Matter Air Pollution and Cognitive Function Among U.S. Older Adults. *Gerontol B Psychol Sci Soc Sci* (2014) doi: 10.1093/geronb/ gbu064. First published online: June 6, 2014
123. Tonne C, Elbaz A, Beevers S, Singh-Manoux A. Traffic-related Air Pollution in Relation to Cognitive Function in Older Adults. *Epidemiology*. 2014 Jul 16. [Epub ahead of print]
124. Guxens M, Lubczyńska MJ, Muetzel RL, Dalmau-Bueno A, Jaddoe VWV, Hoek G, van der Lugt A, Verhulst FC, White T, Brunekreef B, Tiemeier H, El Marroun H. Air Pollution Exposure During Fetal Life, Brain Morphology, and Cognitive Function in School-Age Children. *Biol Psychiatry*. 2018 Aug 15;84(4):295-303. doi:
125. Mortamais M, et al. Effects of prenatal exposure to particulate matter air pollution on corpus callosum and behavioral problems in children. *Environ Res*. 2019 Sep 7;178:108734. doi: 10.1016/j.envres. 2019.108734. [Epub ahead of print]
126. Peterson BS, Bansal R, Sawardekar S, Nati C, Elgablawy ER, Hoepner LA, Garcia W, Hao X, Margolis A, Perera F, Rauh V. Prenatal exposure to air pollution is associated with altered brain structure, function, and metabolism in childhood. *J Child Psychol Psychiatry*. 2022 Nov;63(11):1316-1331. doi: 10.1111/jcpp.13578. Epub 2022 Feb 14. PMID: 35165899.
127. Wilker E, et al. Long-Term Exposure to Fine Particulate Matter, Residential Proximity to Major Roads and Measures of Brain Structure. doi: 10.1161/ STROKEAHA.114.008348. Published online before print April 23, 2015
128. Chen JC, et al. Ambient Air Pollution and Neurotoxicity on Brain Structure: Evidence From Women's Health Initiative Memory Study. *ANN NEUROL* 2015;78:466–476
129. Hedges DW, et al. Association between Exposure to Air Pollution and Hippocampal Volume in Adults in the UK Biobank. *Neurotoxicology*. 2019 Jun 17. pii: S0161-813X(19)30053-1. doi: 10.1016/j.neuro.2019.06.005. [Epub ahead of print]

130. Gale S, et al. Association between exposure to air pollution and prefrontal cortical volume in adults: A cross-sectional study from the UK biobank, *Environmental Research*, Volume 185, 2020, 109365.
131. Kim KN, Lim YH, Bae HJ, Kim M, Jung K, Hong YC. 2016. Long-term fine particulate matter exposure and major depressive disorder in a community-based urban cohort. *Environ Health Perspect* 124:1547-1553; <http://dx.doi.org/10.1289/EHP192>.
132. Brokamp C, et al. Psychiatric Emergency Department Utilization and Fine Particulate Matter: A Case-Crossover Study. *Environ Health Perspect*. 2019 Sep;127(9):97006. doi: 10.1289/EHP4815. Epub 2019 Sep 25. PMID: 31553231
133. Burkhardt J, et al. The effect of pollution on crime: Evidence from data on particulate matter and ozone. *Journal of Environmental Economics and Management*, 2019; 102267 DOI: 10.1016/j.jeem. 2019.102267
134. Anenberg, S.C., Haines, S., Wang, E. et al. Synergistic health effects of air pollution, temperature, and pollen exposure: a systematic review of epidemiological evidence. *Environ Health* 19, 130 (2020). <https://doi.org/10.1186/s12940-020-00681-z>
135. https://www.firescience.gov/projects/16-1-08-1/project/16-1-08-1_2020GL088988.pdf
136. Mauderly J, Samet J. Is There Evidence for Synergy Among Air Pollutants in Causing Health Effects? *EHP*, Vol. 117, No. 1, 2009. <https://doi.org/10.1289/ehp.11654>
137. Maher B, et al. Magnetite pollution nanoparticles in the human brain *PNAS* September 27, 2016 113 (39) 10797-10801; first published September 6, 2016
138. Calderón-Garcidueñas L, et al. Combustion- and friction-derived magnetic air pollution nanoparticles in human hearts. *Environmental Research*. Volume 176, September 2019, 108567
139. Bové, H., Bongaerts, E., Slenders, E. et al. Ambient black carbon particles reach the fetal side of human placenta. *Nat Commun* 10, 3866 (2019). <https://doi.org/10.1038/s41467-019-11654-3>
140. Bongaerts E, et al. Maternal exposure to ambient black carbon particles and their presence in maternal and fetal circulation and organs: an analysis of two independent population-based observational studies. *The Lancet, Planetary Health*. Published:October, 2022 DOI:[https://doi.org/10.1016/S2542-5196\(22\)00200-5](https://doi.org/10.1016/S2542-5196(22)00200-5)
141. Amato-Lourenço LF, Dos Santos Galvão L, de Weger LA, Hiemstra PS, Vijver MG, Mauad T. An emerging class of air pollutants: Potential effects of microplastics to respiratory human

health? *Sci Total Environ.* 2020 Dec 20;749:141676. doi: 10.1016/j.scitotenv.2020.141676. Epub 2020 Aug 13. PMID: 32827829; PMCID: PMC7424328.

142. Wright S.L., Kelly F.J. Plastic and human health: a micro issue? *Environ. Sci. Technol.* 2017;51(12):6634–6647. (Jun 20)

143. Foulon V., Le Roux F., Lambert C., Huvet A., Soudant P., Paul-Pont I. Colonization of polystyrene microparticles by *Vibrio crassostreae*: light and electron microscopic investigation. *Environ. Sci. Technol.* 2016;50(20):10988–10996.

144. Leslie H, et al. Discovery and quantification of plastic particle pollution in human blood, *Environment International*, Volume 163, 2022, 107199, ISSN 0160-412.

145. Horvatits T, Tamminga M, Liu B, et al. Microplastics detected in cirrhotic liver tissue. *eBioMedicine.* 2022 doi: 10.1016/j.ebiom.2022.104147

146. Ren S, Haynes E, Hall E, Hossain M, Chen A, Muglia L, Lu L, DeFranco E. Periconception Exposure to Air Pollution and Risk of Congenital Malformations. *J Pediatr.* 2018 Feb;193:76-84.e6. doi: 10.1016/j.jpeds.2017.09.076. Epub 2017 Dec 11. PMID: 29237538; PMCID: PMC5794608.

147. Martens DS, Cox B, Janssen BG, Clemente DBP, Gasparini A, Vanpoucke C, Lefebvre W, Roels HA, Plusquin M, Nawrot TS. Prenatal Air Pollution and Newborns' Predisposition to Accelerated Biological Aging. *JAMA Pediatr.* 2017 Dec 1;171(12):1160-1167. doi: 10.1001/jamapediatrics.2017.3024. PMID: 29049509; PMCID: PMC6233867.

148. Pieters N, Janssen BG, Dewitte H, et al. Biomolecular Markers Within the Core Axis of Aging and Particulate Air Pollution Exposure in the Elderly: A Cross-Sectional Study. *Environ Health Perspect* 2016;124:943-50.

149. Huang CC, Pan SC, Chen BY, Guo YL. Periconceptional exposure to air pollution and congenital hypospadias among full-term infants. *Environ Res.* 2020 Apr;183:109151. doi: 10.1016/j.envres.2020.109151. Epub 2020 Jan 17. PMID: 32000002.

150. Girguis MS, Strickland MJ, Hu X, Liu Y, Bartell SM, Vieira VM. Maternal exposure to traffic-related air pollution and birth defects in Massachusetts. *Environ Res.* 2016 Apr;146:1-9. doi: 10.1016/j.envres.2015.12.010. Epub 2015 Dec 17. PMID: 26705853; PMCID: PMC4761511.

151. Veras, M., Damaceno-Rodrigues, N., Caldini, E. et al. Particulate Urban Air Pollution Affects the Functional Morphology of Mouse Placenta. *Biology of Reproduction* September 1, 2008 vol. 79 no. 3 578-584

152. Liu Y, Wang L, Wang F, Li C. Effect of Fine Particulate Matter (PM_{2.5}) on Rat Placenta Pathology and Perinatal Outcomes. *Med Sci Monit*. 2016 Sep 15;22:3274-80. doi: 10.12659/msm.897808. PMID: 27629830; PMCID: PMC5036383.
153. Saenen ND, Vrijens K, Janssen BG, Roels HA, Neven KY, Vanden Berghe W, Gyselaers W, Vanpoucke C, Lefebvre W, De Boever P, Nawrot TS. Lower Placental Leptin Promoter Methylation in Association with Fine Particulate Matter Air Pollution during Pregnancy and Placental Nitrosative Stress at Birth in the ENVIRONAGE Cohort. *Environ Health Perspect*. 2017 Feb;125(2):262-268. doi: 10.1289/EHP38. Epub 2016 Sep 13. PMID: 27623604; PMCID: PMC5289914.
154. Cao Z, et al. Maternal exposure to ambient fine particulate matter and fetal growth in Shanghai, China. *Environ Health*. 2019 May 16;18(1): 49. doi: 10.1186/s12940-019-0485-3.
155. Stieb DM, Chen L, Beckerman BS, Jerrett M, Crouse DL, Omariba DW, Peters PA, van Donkelaar A, Martin RV, Burnett RT, Gilbert NL, Tjepkema M, Liu S, Dugandzic RM. 2016. Associations of pregnancy outcomes and PM_{2.5} in a National Canadian Study. *Environ Health Perspect* 124:243–249; <http://dx.doi.org/10.1289/ehp.1408995>
156. Lamichhane DK, Leem JH, Lee JY, Kim HC. A meta-analysis of exposure to particulate matter and adverse birth outcomes. *Environ Health Toxicol*. 2015 Nov 3;30:e2015011. doi: 10.5620/ehp.e2015011. PMID: 26796890; PMCID: PMC4722965
157. Sun X, Luo X, Zhao C, Chung Ng RW, Lim CE, Zhang B, Liu T. The association between fine particulate matter exposure during pregnancy and preterm birth: a meta-analysis. *BMC Pregnancy Childbirth*. 2015 Nov 18;15:300. doi: 10.1186/s12884-015-0738-2. PMID: 26581753; PMCID: PMC4650291.
158. Zhu X, Liu Y, Chen Y, Yao C, Che Z, Cao J. Maternal exposure to fine particulate matter (PM_{2.5}) and pregnancy outcomes: a meta-analysis. *Environ Sci Pollut Res Int*. 2015 Mar;22(5):3383-96. doi: 10.1007/s11356-014-3458-7. Epub 2014 Aug 28. Erratum in: *Environ Sci Pollut Res Int*. 2015 Mar;22(5):3397-9. PMID: 25163563.
159. Sun X, Luo X, Zhao C, Zhang B, Tao J, Yang Z, Ma W, Liu T. The associations between birth weight and exposure to fine particulate matter (PM_{2.5}) and its chemical constituents during pregnancy: A meta-analysis. *Environ Pollut*. 2016 Apr;211:38-47. doi: 10.1016/j.envpol.2015.12.022. Epub 2015 Dec 29. PMID: 26736054.
160. Laurent O, Hu J, Li L, Kleeman MJ, Bartell SM, Cockburn M, Escobedo L, Wu J. 2016. A statewide nested case-control study of preterm birth and air pollution by source and composition: California, 2001–2008. *Environ Health Perspect* 124:1479–1486; <http://dx.doi.org/10.1289/ehp.1510133>

161. Nachman RM, Mao G, Zhang X, Hong X, Chen Z, Soria CS, He H, Wang G, Caruso D, Pearson C, Biswal S, Zuckerman B, Wills-Karp M, Wang X. 2016. Intrauterine inflammation and maternal exposure to ambient PM_{2.5} during preconception and specific periods of pregnancy: the Boston Birth Cohort. *Environ Health Perspect* 124:1608–1615; <http://dx.doi.org/10.1289/EHP243>
162. Li X, Liu Y, Liu F, Wang Y, Yang X, Yu J, Xue X, Jiao A, Lu Y, Tian L, Deng S, Xiang H. Analysis of short-term and sub-chronic effects of ambient air pollution on preterm birth in central China. *Environ Sci Pollut Res Int*. 2018 Jul;25(19):19028-19039. doi: 10.1007/s11356-018-2061-8. Epub 2018 May 2. PMID: 29721794.
163. Yu Z, Zhang X, Zhang J, Feng Y, Zhang H, Wan Z, Xiao C, Zhang H, Wang Q, Huang C. Gestational exposure to ambient particulate matter and preterm birth: An updated systematic review and meta-analysis. *Environ Res*. 2022 Sep;212(Pt C):113381. doi: 10.1016/j.envres.2022.113381. Epub 2022 May 4. PMID: 35523275.
164. Malley CS, Kuynlenstierna JC, Vallack HW, Henze DK, Blencowe H, Ashmore MR. Preterm birth associated with maternal fine particulate matter exposure: A global, regional and national assessment. *Environ Int*. 2017 Apr;101:173-182. doi: 10.1016/j.envint.2017.01.023. Epub 2017 Feb 10. PMID: 28196630.
165. Qiu X, Fong KC, Shi L, Papatheodorou S, Di Q, Just A, Kosheleva A, Messerlian C, Schwartz JD. Prenatal exposure to particulate air pollution and gestational age at delivery in Massachusetts neonates 2001-2015: A perspective of causal modeling and health disparities. *Environ Epidemiol*. 2020 Sep 14;4(5):e113. doi: 10.1097/EE9.0000000000000113. PMID: 33154990; PMCID: PMC7595249.
166. Siddika N, Balogun HA, Amegah AK, Jaakkola JJ. Prenatal ambient air pollution exposure and the risk of stillbirth: systematic review and meta-analysis of the empirical evidence. *Occup Environ Med*. 2016 Sep;73(9):573-81. doi: 10.1136/oemed-2015-103086. Epub 2016 May 24. PMID: 27221104.
167. Yang S, Tan Y, Mei H, Wang F, Li N, Zhao J, Zhang Y, Qian Z, Chang JJ, Syberg KM, Peng A, Mei H, Zhang D, Zhang Y, Xu S, Li Y, Zheng T, Zhang B. Ambient air pollution the risk of stillbirth: A prospective birth cohort study in Wuhan, China. *Int J Hyg Environ Health*. 2018 Feb 5. pii: S1438-4639(17)30531-X. doi: 10.1016/j.ijheh. 2018.01.014. [Epub ahead of print] PMID: 29422441 [PubMed - as supplied by publisher]
168. Xue T, Zhu T, Lin W, Talbott EO. Association Between Hypertensive Disorders in Pregnancy and Particulate Matter in the Contiguous United States, 1999-2004. *Hypertension*. 2018 Jul;72(1):77-84. doi: 10.1161/HYPERTENSIONAHA.118.11080. Epub 2018 May 21. PMID: 29785958.

169. Sun M, Yan W, Fang K, Chen D, Liu J, Chen Y, Duan J, Chen R, Sun Z, Wang X, Xia Y. The correlation between PM_{2.5} exposure and hypertensive disorders in pregnancy: A Meta-analysis. *Sci Total Environ*. 2020 Feb 10;703:134985. doi: 10.1016/j.scitotenv.2019.134985. Epub 2019 Nov 2. PMID: 31731170.
170. Hu CY, Gao X, Fang Y, Jiang W, Huang K, Hua XG, Yang XJ, Chen HB, Jiang ZX, Zhang XJ. Human epidemiological evidence about the association between air pollution exposure and gestational diabetes mellitus: Systematic review and meta-analysis. *Environ Res*. 2020 Jan;180:108843. doi: 10.1016/j.envres.2019.108843. Epub 2019 Oct 21. PMID: 31670082.
Copy
171. Wang K, Tian Y, Zheng H, Shan S, Zhao X, Liu C. Maternal exposure to ambient fine particulate matter and risk of premature rupture of membranes in Wuhan, Central China: a cohort study. *Environ Health*. 2019 Nov 14;18(1):96. doi: 10.1186/s12940-019-0534-y. PMID: 31727105; PMCID: PMC6857323.
172. Zhou W, Ming X, Chen Q, Liu X, Yin P. The acute effect and lag effect analysis between exposures to ambient air pollutants and spontaneous abortion: a case-crossover study in China, 2017-2019. *Environ Sci Pollut Res Int*. 2022 Sep;29(44):67380-67389. doi: 10.1007/s11356-022-20379-8. Epub 2022 May 6. PMID: 35522417; PMCID: PMC9492619.
173. Son JY, et al. Survival Analysis of Long-Term Exposure to Different Sizes of Airborne Particulate Matter and Risk of Infant Mortality Using a Birth Cohort in Seoul, Korea. Vol. 119, Published:1 May 2011, <https://doi.org/10.1289/ehp.1002364>
174. Deng X, Zhang F, Wang L, Rui W, Long F, Zhao Y, Chen D, Ding W. Airborne fine particulate matter induces multiple cell death pathways in human lung epithelial cells. *Apoptosis*. 2014 Jul;19(7):1099-112. doi: 10.1007/s10495-014-0980-5. PMID: 24722831.
175. Stafoggia M, Samoli E, Alessandrini E, Cadum E, Ostro B, Berti G, Faustini A, Jacquemin B, Linares C, Pascal M, Randi G, Ranzi A, Stivanello E, Forastiere F; MED-PARTICLES Study Group. Short-term associations between fine and coarse particulate matter and hospitalizations in Southern Europe: results from the MED-PARTICLES project. *Environ Health Perspect*. 2013 Sep;121(9):1026-33. doi: 10.1289/ehp.1206151. Epub 2013 Jun 18. PMID: 23777832; PMCID: PMC3764077.
176. Rice MB, Ljungman PL, Wilker EH, Gold DR, Schwartz JD, Koutrakis P, Washko GR, O'Connor GT, Mittleman MA. Short-term exposure to air pollution and lung function in the Framingham Heart Study. *Am J Respir Crit Care Med*. 2013 Dec 1;188(11):1351-7. doi: 10.1164/rccm.201308-1414OC. PMID: 24200465; PMCID: PMC3919078.
177. Gehring U, Gruzieva O, Agius RM, Beelen R, Custovic A, Cyrys J, Eeftens M, Flexeder C, Fuertes E, Heinrich J, Hoffmann B, de Jongste JC, Kerkhof M, Klümper C, Korek M, Mölter A, Schultz ES, Simpson A, Sugiri D, Svartengren M, von Berg A, Wijga AH, Pershagen G, Brunekreef

B. Air pollution exposure and lung function in children: the ESCAPE project. *Environ Health Perspect.* 2013 Nov-Dec;121(11-12):1357-64. doi: 10.1289/ehp.1306770. Epub 2013 Sep 27. PMID: 24076757; PMCID: PMC3855518.

178. Young MT, Sandler DP, DeRoo LA, Vedal S, Kaufman JD, London SJ. Ambient air pollution exposure and incident adult asthma in a nationwide cohort of U.S. women. *Am J Respir Crit Care Med.* 2014 Oct 15;190(8):914-21. doi: 10.1164/rccm.201403-0525OC. PMID: 25172226; PMCID: PMC4299575.

179. Darrow LA, Klein M, Flanders WD, Mulholland JA, Tolbert PE, Strickland MJ. Air pollution and acute respiratory infections among children 0-4 years of age: an 18-year time-series study. *Am J Epidemiol.* 2014 Nov 15;180(10):968-77. doi: 10.1093/aje/kwu234. Epub 2014 Oct 16. PMID: 25324558; PMCID: PMC4224364.

180. Luttmann-Gibson H, Sarnat SE, Suh HH, Coull BA, Schwartz J, Zanobetti A, Gold DR. Short-term effects of air pollution on oxygen saturation in a cohort of senior adults in Steubenville, Ohio. *J Occup Environ Med.* 2014 Feb;56(2):149-54. doi: 10.1097/JOM.0000000000000089. PMID: 24451609; PMCID: PMC3987810.

181. Chen CH, Chan CC, Chen BY, Cheng TJ, Leon Guo Y. Effects of particulate air pollution and ozone on lung function in non-asthmatic children. *Environ Res.* 2015 Feb;137:40-8. doi: 10.1016/j.envres.2014.11.021. Epub 2014 Dec 6. PMID: 25486544.

182. Rice MB, Ljungman PL, Wilker EH, Dorans KS, Gold DR, Schwartz J, Koutrakis P, Washko GR, O'Connor GT, Mittleman MA. Long-term exposure to traffic emissions and fine particulate matter and lung function decline in the Framingham heart study. *Am J Respir Crit Care Med.* 2015 Mar 15;191(6):656-64. doi: 10.1164/rccm.201410-1875OC. PMID: 25590631; PMCID: PMC4384780.

183. Gauderman WJ, Urman R, Avol E, Berhane K, McConnell R, Rappaport E, Chang R, Lurmann F, Gilliland F. Association of improved air quality with lung development in children. *N Engl J Med.* 2015 Mar 5;372(10):905-13. doi: 10.1056/NEJMoa1414123. PMID: 25738666; PMCID: PMC4430551.

184. Jacquemin B, Siroux V, Sanchez M, Carsin AE, Schikowski T, Adam M, Bellisario V, Buschka A, Bono R, Brunekreef B, Cai Y, Cirach M, Clavel-Chapelon F, Declercq C, de Marco R, de Nazelle A, Ducret-Stich RE, Ferretti VV, Gerbase MW, Hardy R, Heinrich J, Janson C, Jarvis D, Al Kanaani Z, Keidel D, Kuh D, Le Moual N, Nieuwenhuijsen MJ, Marcon A, Modig L, Pin I, Rochat T, Schindler C, Sugiri D, Stempfelet M, Temam S, Tsai MY, Varraso R, Vienneau D, Vierkötter A, Hansell AL, Krämer U, Probst-Hensch NM, Sunyer J, Künzli N, Kauffmann F. Ambient air pollution and adult asthma incidence in six European cohorts (ESCAPE). *Environ Health Perspect.* 2015 Jun;123(6):613-21. doi: 10.1289/ehp.1408206. Epub 2015 Feb 24. PMID: 25712593; PMCID: PMC4455584.

185. Li MH, Fan LC, Mao B, Yang JW, Choi AMK, Cao WJ, Xu JF. Short-term Exposure to Ambient Fine Particulate Matter Increases Hospitalizations and Mortality in COPD: A Systematic Review and Meta-analysis. *Chest*. 2016 Feb;149(2):447-458. doi: 10.1378/chest.15-0513. Epub 2016 Jan 12. PMID: 26111257.
186. Zheng XY, Ding H, Jiang LN, Chen SW, Zheng JP, Qiu M, Zhou YX, Chen Q, Guan WJ. Association between Air Pollutants and Asthma Emergency Room Visits and Hospital Admissions in Time Series Studies: A Systematic Review and Meta-Analysis. *PLoS One*. 2015 Sep 18;10(9):e0138146. doi: 10.1371/journal.pone.0138146. PMID: 26382947; PMCID: PMC4575194.
187. Berhane K, Chang CC, McConnell R, Gauderman WJ, Avol E, Rapaport E, Urman R, Lurmann F, Gilliland F. Association of Changes in Air Quality With Bronchitic Symptoms in Children in California, 1993-2012. *JAMA*. 2016 Apr 12;315(14):1491-501. doi: 10.1001/jama.2016.3444. Erratum in: *JAMA*. 2018 Apr 24;319(16):1728. PMID: 27115265; PMCID: PMC5679287.
188. Mirabelli MC, Vaidyanathan A, Flanders WD, Qin X, Garbe P. 2016. Outdoor PM_{2.5}, ambient air temperature, and asthma symptoms in the past 14 days among adults with active asthma. *Environ Health Perspect* 124:1882-1890; <http://dx.doi.org/10.1289/EHP92>.
189. Bharadwaj P, Zivin JG, Mullins JT, Neidell M. Early-Life Exposure to the Great Smog of 1952 and the Development of Asthma. *Am J Respir Crit Care Med*. 2016 Dec 15;194(12):1475-1482. doi: 10.1164/rccm.201603-0451OC. PMID: 27392261; PMCID: PMC5440984.
190. Strickland M, et al. Pediatric Emergency Visits and Short-Term Changes in PM_{2.5} Concentrations in the U.S. State of Georgia. *Environ Health Perspect*; DOI:10.1289/ehp.1509856
191. Rush B, McDermid RC, Celi LA, Walley KR, Russell JA, Boyd JH. Association between chronic exposure to air pollution and mortality in the acute respiratory distress syndrome. *Environ Pollut*. 2017 May;224:352-356. doi: 10.1016/j.envpol.2017.02.014. Epub 2017 Feb 13. PMID: 28202265; PMCID: PMC5683074.
192. Sesé L, et al. Role of atmospheric pollution on the natural history of idiopathic pulmonary fibrosis. *Thorax*. 2017 Aug 10. pii: thoraxjnl-2017-209967. doi: 10.1136/thoraxjnl-2017-209967. [Epub ahead of print]
193. Girguis MS, Strickland MJ, Hu X, Liu Y, Chang HH, Kloog I, Belanoff C, Bartell SM, Vieira VM. Exposure to acute air pollution and risk of bronchiolitis and otitis media for preterm and term infants. *J Expo Sci Environ Epidemiol*. 2018 Jun;28(4):348-357. doi: 10.1038/s41370-017-0006-9. Epub 2017 Dec 21. PMID: 29269754; PMCID: PMC6013343.

194. Pirozzi CS, Jones BE, VanDerslice JA, Zhang Y, Paine R 3rd, Dean NC. Short-Term Air Pollution and Incident Pneumonia. A Case-Crossover Study. *Ann Am Thorac Soc*. 2018 Apr;15(4):449-459. doi: 10.1513/AnnalsATS.201706-495OC. PMID: 29283681.
195. Khalili R, Bartell SM, Hu X, Liu Y, Chang HH, Belanoff C, Strickland MJ, Vieira VM. Early-life exposure to PM_{2.5} and risk of acute asthma clinical encounters among children in Massachusetts: a case-crossover analysis. *Environ Health*. 2018 Feb 21;17(1):20. doi: 10.1186/s12940-018-0361-6. Erratum in: *Environ Health*. 2018 Mar 6;17(1):25. PMID: 29466982; PMCID: PMC5822480.
196. Horne BD, Joy EA, Hofmann MG, Gesteland PH, Cannon JB, Lefler JS, Blagev DP, Korgenski EK, Torosyan N, Hansen GI, Kartchner D, Pope CA 3rd. Short-Term Elevation of Fine Particulate Matter Air Pollution and Acute Lower Respiratory Infection. *Am J Respir Crit Care Med*. 2018 Sep 15;198(6):759-766. doi: 10.1164/rccm.201709-1883OC. PMID: 29652174.
197. Wang J, Cao H, Sun D, Qi Z, Guo C, Peng W, Sun Y, Xie Y, Liu X, Li B, Luo Y, Pan Y, Li Y, Zhang L. Associations between ambient air pollution and mortality from all causes, pneumonia, and congenital heart diseases among children aged under 5 years in Beijing, China: A population-based time series study. *Environ Res*. 2019 Sep;176:108531. doi: 10.1016/j.envres.2019.108531. Epub 2019 Jun 11. PMID: 31226628.
198. Lee EY, et al. Ambient Air Pollution, Asthma Drug Response and Telomere Length in African American Youth. *J Allergy Clin Immunol*. 2019 Jun 24. pii: S0091-6749(19)30820-6. doi: 10.1016/j.jaci. 2019.06.009. [Epub ahead of print]
199. Doiron D, de Hoogh K, Probst-Hensch N, Fortier I, Cai Y, De Matteis S, Hansell AL. Air pollution, lung function and COPD: results from the population-based UK Biobank study. *Eur Respir J*. 2019 Jul 25;54(1):1802140. doi: 10.1183/13993003.02140-2018. PMID: 31285306.
200. Slama A, Śliwczyński A, Woźnica-Pyzikiewicz J, Zdrolik M, Wiśnicki B, Kubajek J, Turzańska-Wieczorek O, Studnicki M, Wierzba W, Franek E. The short-term effects of air pollution on respiratory disease hospitalizations in 5 cities in Poland: comparison of time-series and case-crossover analyses. *Environ Sci Pollut Res Int*. 2020 Jul;27(19):24582-24590. doi: 10.1007/s11356-020-08542-5. Epub 2020 Apr 30. PMID: 32356054; PMCID: PMC7326830.
201. Wang Z, Zhou Y, Zhang Y, Huang X, Duan X, Ou Y, Liu S, Hu W, Liao C, Zheng Y, Wang L, Xie M, Yang H, Xiao S, Luo M, Tang L, Zheng J, Liu S, Wu F, Deng Z, Tian H, Peng J, Wang X, Zhong N, Ran P. Association of hospital admission for bronchiectasis with air pollution: A province-wide time-series study in southern China. *Int J Hyg Environ Health*. 2021 Jan;231:113654. doi: 10.1016/j.ijheh.2020.113654. Epub 2020 Nov 3. PMID: 33157415.
202. Han C, Oh J, Lim YH, Kim S, Hong YC. Long-term exposure to fine particulate matter and development of chronic obstructive pulmonary disease in the elderly. *Environ Int*. 2020 Oct;143:105895. doi: 10.1016/j.envint.2020.105895. Epub 2020 Jun 30. PMID: 32615346.

213. Heck JE, Wu J, Lombardi C, Qiu J, Meyers TJ, Wilhelm M, Cockburn M, Ritz B. Childhood cancer and traffic-related air pollution exposure in pregnancy and early life. *Environ Health Perspect.* 2013 Nov-Dec;121(11-12):1385-91. doi: 10.1289/ehp.1306761. Epub 2013 Sep 10. PMID: 24021746; PMCID: PMC3855517.
214. Cui P, Huang Y, Han J, Song F, Chen K. Ambient particulate matter and lung cancer incidence and mortality: a meta-analysis of prospective studies. *Eur J Public Health.* 2014 Sep 8. pii: cku145. [Epub ahead of print]
215. <https://www.popsci.com/environment/air-quality-world-population/>
216. Yu W, et al. Global estimates of daily ambient fine particulate matter concentrations and unequal spatiotemporal distribution of population exposure: a machine learning modelling study. *VOLUME 7, ISSUE 3, E209-E218, March 2023.* DOI:[https://doi.org/10.1016/S2542-5196\(23\)00008-6](https://doi.org/10.1016/S2542-5196(23)00008-6)
217. Yang WS, Zhao H, Wang X, Deng Q, Fan WY, Wang L. An evidence-based assessment for the association between long-term exposure to outdoor air pollution and the risk of lung cancer. *Eur J Cancer Prev.* 2016 May;25(3):163-72. doi: 10.1097/CEJ.0000000000000158. PMID: 25757194.
218. Raaschou-Nielsen O, Andersen ZJ, Beelen R, Samoli E, Stafoggia M, Weinmayr G, Hoffmann B, Fischer P, Nieuwenhuijsen MJ, Brunekreef B, Xun WW, Katsouyanni K, Dimakopoulou K, Sommar J, Forsberg B, Modig L, Oudin A, Oftedal B, Schwarze PE, Nafstad P, De Faire U, Pedersen NL, Ostenson CG, Fratiglioni L, Penell J, Korek M, Pershagen G, Eriksen KT, Sørensen M, Tjønneland A, Ellermann T, Eeftens M, Peeters PH, Meliefste K, Wang M, Bueno-de-Mesquita B, Key TJ, de Hoogh K, Concin H, Nagel G, Vilier A, Grioni S, Krogh V, Tsai MY, Ricceri F, Sacerdote C, Galassi C, Migliore E, Ranzi A, Cesaroni G, Badaloni C, Forastiere F, Tamayo I, Amiano P, Dorronsoro M, Trichopoulou A, Bamia C, Vineis P, Hoek G. Air pollution and lung cancer incidence in 17 European cohorts: prospective analyses from the European Study of Cohorts for Air Pollution Effects (ESCAPE). *Lancet Oncol.* 2013 Aug;14(9):813-22. doi: 10.1016/S1470-2045(13)70279-1. Epub 2013 Jul 10. PMID: 23849838.
219. Wong CM, Tsang H, Lai HK, Thomas GN, Lam KB, Chan KP, Zheng Q, Ayres JG, Lee SY, Lam TH, Thach TQ. Cancer Mortality Risks from Long-term Exposure to Ambient Fine Particle. *Cancer Epidemiol Biomarkers Prev.* 2016 May;25(5):839-45. doi: 10.1158/1055-9965.EPI-15-0626. PMID: 27197138; PMCID: PMC5505442.
220. Tomczak A, Miller AB, Weichenthal SA, To T, Wall C, van Donkelaar A, Martin RV, Crouse DL, Villeneuve PJ. Long-term exposure to fine particulate matter air pollution and the risk of lung cancer among participants of the Canadian National Breast Screening Study. *Int J Cancer.* 2016 Nov 1;139(9):1958-66. doi: 10.1002/ijc.30255. Epub 2016 Aug 4. PMID: 27380650.

221. Pedersen M, Andersen ZJ, Stafoggia M, Weinmayr G, Galassi C, Sørensen M, Eriksen KT, Tjønneland A, Loft S, Jaensch A, Nagel G, Concin H, Tsai MY, Grioni S, Marcon A, Krogh V, Ricceri F, Sacerdote C, Ranzi A, Sokhi R, Vermeulen R, Hoogh K, Wang M, Beelen R, Vineis P, Brunekreef B, Hoek G, Raaschou-Nielsen O. Ambient air pollution and primary liver cancer incidence in four European cohorts within the ESCAPE project. *Environ Res.* 2017 Apr;154:226-233. doi: 10.1016/j.envres.2017.01.006. Epub 2017 Jan 17. PMID: 28107740.
222. Deng H, Eckel SP, Liu L, Lurmann FW, Cockburn MG, Gilliland FD. Particulate matter air pollution and liver cancer survival. *Int J Cancer.* 2017 Aug 15;141(4):744-749. doi: 10.1002/ijc.30779. Epub 2017 Jun 7. PMID: 28589567; PMCID: PMC5505313.
223. Turner MC, Krewski D, Diver WR, Pope CA 3rd, Burnett RT, Jerrett M, Marshall JD, Gapstur SM. Ambient Air Pollution and Cancer Mortality in the Cancer Prevention Study II. *Environ Health Perspect.* 2017 Aug 21;125(8):087013. doi: 10.1289/EHP1249. PMID: 28886601; PMCID: PMC5783657.
224. Nagel G, Stafoggia M, Pedersen M, Andersen ZJ, Galassi C, Munkenast J, Jaensch A, Sommar J, Forsberg B, Olsson D, Oftedal B, Krog NH, Aamodt G, Pyko A, Pershagen G, Korek M, De Faire U, Pedersen NL, Östenson CG, Fratiglioni L, Sørensen M, Tjønneland A, Peeters PH, Bueno-de-Mesquita B, Vermeulen R, Eeftens M, Plusquin M, Key TJ, Concin H, Lang A, Wang M, Tsai MY, Grioni S, Marcon A, Krogh V, Ricceri F, Sacerdote C, Ranzi A, Cesaroni G, Forastiere F, Tamayo-Uria I, Amiano P, Dorronsoro M, de Hoogh K, Beelen R, Vineis P, Brunekreef B, Hoek G, Raaschou-Nielsen O, Weinmayr G. Air pollution and incidence of cancers of the stomach and the upper aerodigestive tract in the European Study of Cohorts for Air Pollution Effects (ESCAPE). *Int J Cancer.* 2018 Oct 1;143(7):1632-1643. doi: 10.1002/ijc.31564. Epub 2018 Jul 3. PMID: 29696642.
225. Santibáñez-Andrade M, Chirino YI, González-Ramírez I, Sánchez-Pérez Y, García-Cuellar CM. Deciphering the Code between Air Pollution and Disease: The Effect of Particulate Matter on Cancer Hallmarks. *Int J Mol Sci.* 2019 Dec 24;21(1):136. doi: 10.3390/ijms21010136. PMID: 31878205; PMCID: PMC6982149.
226. Ou JY, Kirchhoff AC, Hanson HA. Air Pollution across the Cancer Continuum: Extending Our Understanding of the Relationship between Environmental Exposures and Cancer. *Cancer Epidemiol Biomarkers Prev.* 2020 Oct;29(10):1876-1879. doi: 10.1158/1055-9965.EPI-19-1588. PMID: 33004409
227. Wu S, Powers S, Zhu W, Hannun YA. Substantial contribution of extrinsic risk factors to cancer development. *Nature* 2016;529:43–7.
228. Hu H, Dailey AB, Kan H, Xu X. The effect of atmospheric particulate matter on survival of breast cancer among US females. *Breast Cancer Res Treat* 2013;139:217–26.
Google ScholarCrossref PubMed

229. Huo Q, Zhang N, Wang X, Jiang L, Ma T, Yang Q. Effects of ambient particulate matter on human breast cancer: is xenogenesis responsible? *PLoS One* 2013;8:e76609. Google ScholarCrossref PubMed
230. Tagliabue G, Borgini A, Tittarelli A, van Donkelaar A, Martin RV, Bertoldi M, et al Atmospheric fine particulate matter and breast cancer mortality: a population-based cohort study. *BMJ Open* 2016;6:e012580. Google ScholarCrossref PubMed
231. Eckel SP, Cockburn M, Shu YH, Deng H, Lurmann FW, Liu L, et al Air pollution affects lung cancer survival. *Thorax* 2016;71:891–8. Google ScholarCrossref PubMed
232. DuPre NC, Hart JE, Holmes MD, Poole EM, James P, Kraft P, et al Particulate matter and traffic-related exposures in relation to breast cancer survival. *Cancer Epidemiol Biomarkers Prev* 2019;28:751–9. Google ScholarCrossref PubMed
233. Kim HB, Shim JY, Park B, Lee YJ. Long-term exposure to air pollutants and cancer mortality: a meta-analysis of cohort studies. *Int J Environ Res Public Health* 2018;15. pii: 2608.
234. Ou JY, Hanson HA, Ramsay JM, Leiser CL, Zhang Y, VanDerslice JA, et al Fine particulate matter and respiratory healthcare encounters among survivors of childhood cancers. *Int J Environ Res Public Health* 2019;16. pii: E1081.
235. Chen J, Rodopoulou S, Strak M, de Hoogh K, Taj T, Poulsen AH, Andersen ZJ, Bellander T, Brandt J, Zitt E, Fecht D, Forastiere F, Gulliver J, Hertel O, Hoffmann B, Hvidtfeldt UA, Verschuren WMM, Jørgensen JT, Katsouyanni K, Ketzel M, Lager A, Leander K, Liu S, Ljungman P, Severi G, Boutron-Ruault MC, Magnusson PKE, Nagel G, Pershagen G, Peters A, Rizzuto D, van der Schouw YT, Samoli E, Sørensen M, Stafoggia M, Tjønneland A, Weinmayr G, Wolf K, Brunekreef B, Raaschou-Nielsen O, Hoek G. Long-term exposure to ambient air pollution and bladder cancer incidence in a pooled European cohort: the ELAPSE project. *Br J Cancer*. 2022 Jun;126(10):1499-1507. doi: 10.1038/s41416-022-01735-4. Epub 2022 Feb 16. PMID: 35173304; PMCID: PMC9090745.
236. Gomez J, et al The projected future degradation in air quality is caused by more abundant natural aerosols in a warmer world. *Communications Earth & Environment*, 2023; 4 (1) DOI: 10.1038/s43247-023-00688-7
237. Pearson JF, Bachireddy C, Shyamprasad S, Goldfine AB, Brownstein JS. Association between fine particulate matter and diabetes prevalence in the U.S. *Diabetes Care*. 2010 Oct;33(10):2196-201. doi: 10.2337/dc10-0698. Epub 2010 Jul 13. PMID: 20628090; PMCID: PMC2945160.
238. Chen H, Burnett RT, Kwong JC, Villeneuve PJ, Goldberg MS, Brook RD, van Donkelaar A, Jerrett M, Martin RV, Brook JR, Copes R. Risk of incident diabetes in relation to long-term

exposure to fine particulate matter in Ontario, Canada. *Environ Health Perspect.* 2013 Jul;121(7):804-10. doi: 10.1289/ehp.1205958. Epub 2013 Apr 26. PMID: 23632126; PMCID: PMC3701997.

239. Brook RD, Cakmak S, Turner MC, Brook JR, Crouse DL, Peters PA, van Donkelaar A, Villeneuve PJ, Brion O, Jerrett M, Martin RV, Rajagopalan S, Goldberg MS, Pope CA 3rd, Burnett RT. Long-term fine particulate matter exposure and mortality from diabetes in Canada. *Diabetes Care.* 2013 Oct;36(10):3313-20. doi: 10.2337/dc12-2189. Epub 2013 Jun 18. PMID: 23780947; PMCID: PMC3781571.

240. Fleisch AF, Gold DR, Rifas-Shiman SL, Koutrakis P, Schwartz JD, Kloog I, Melly S, Coull BA, Zanobetti A, Gillman MW, Oken E. Air pollution exposure and abnormal glucose tolerance during pregnancy: the project Viva cohort. *Environ Health Perspect.* 2014 Apr;122(4):378-83. doi: 10.1289/ehp.1307065. Epub 2014 Feb 7. PMID: 24508979; PMCID: PMC3984217.

241. Park SK, Wang W. Ambient Air Pollution and Type 2 Diabetes: A Systematic Review of Epidemiologic Research. *Curr Environ Health Rep.* 2014 Sep 1;1(3):275-286. doi: 10.1007/s40572-014-0017-9. PMID: 25170433; PMCID: PMC4142518.

242. Li C, Fang D, Xu D, Wang B, Zhao S, Yan S, Wang Y. Main air pollutants and diabetes-associated mortality: a systematic review and meta-analysis. *Eur J Endocrinol.* 2014 Nov;171(5):R183-90. doi: 10.1530/EJE-14-0287. PMID: 25298377.

243. Wang B, Xu D, Jing Z, Liu D, Yan S, Wang Y. Effect of long-term exposure to air pollution on type 2 diabetes mellitus risk: a systemic review and meta-analysis of cohort studies. *Eur J Endocrinol.* 2014 Nov;171(5):R173-82. doi: 10.1530/EJE-14-0365. PMID: 25298376.

244. Esposito K, Petrizzo M, Maiorino MI, Bellastella G, Giugliano D. Particulate matter pollutants and risk of type 2 diabetes: a time for concern? *Endocrine.* 2016 Jan;51(1):32-7. doi: 10.1007/s12020-015-0638-2. Epub 2015 May 30. PMID: 26024974.

245. Hansen AB, Ravnskjaer L, Loft S, Andersen KK, Brauner EV, Baastrup R, Yao C, Ketzel M, Becker T, Brandt J, Hertel O, Andersen ZJ. Long-term exposure to fine particulate matter and incidence of diabetes in the Danish Nurse Cohort. *Environ Int.* 2016 May;91:243-50. doi: 10.1016/j.envint.2016.02.036. Epub 2016 Mar 16. PMID: 26989812.

246. Haberzettl P, O'Toole TE, Bhatnagar A, Conklin DJ. Exposure to Fine Particulate Air Pollution Causes Vascular Insulin Resistance by Inducing Pulmonary Oxidative Stress. *Environ Health Perspect.* 2016 Dec;124(12):1830-1839. doi: 10.1289/EHP212. Epub 2016 Apr 29. PMID: 27128347; PMCID: PMC5132639.

247. Lavigne E, Ashley-Martin J, Dodds L, Arbuckle TE, Hystad P, Johnson M, Crouse DL, Ettinger AS, Shapiro GD, Fisher M, Morisset AS, Taback S, Bouchard MF, Sun L, Monnier P, Dallaire R, Fraser WD. Air Pollution Exposure During Pregnancy and Fetal Markers of Metabolic function:

The MIREC Study. Am J Epidemiol. 2016 May 1;183(9):842-51. doi: 10.1093/aje/kwv256. Epub 2016 Mar 29. PMID: 27026336; PMCID: PMC4851989.

248. He D, Wu S, Zhao H, Qiu H, Fu Y, Li X, He Y. Association between particulate matter 2.5 and diabetes mellitus: A meta-analysis of cohort studies. *J Diabetes Investig.* 2017 Sep;8(5):687-696. doi: 10.1111/jdi.12631. Epub 2017 May 3. PMID: 28122165; PMCID: PMC5583950.

249. Alderete TL, Habre R, Toledo-Corral CM, Berhane K, Chen Z, Lurmann FW, Weigensberg MJ, Goran MI, Gilliland FD. Longitudinal Associations Between Ambient Air Pollution With Insulin Sensitivity, β -Cell Function, and Adiposity in Los Angeles Latino Children. *Diabetes.* 2017 Jul;66(7):1789-1796. doi: 10.2337/db16-1416. Epub 2017 Jan 30. PMID: 28137791; PMCID: PMC5482082.

250. Madhloum N, Janssen BG, Martens DS, Saenen ND, Bijmens E, Gyselaers W, Penders J, Vanpoucke C, Lefebvre W, Plusquin M, Nawrot TS. Cord plasma insulin and in utero exposure to ambient air pollution. *Environ Int.* 2017 Aug;105:126-132. doi: 10.1016/j.envint.2017.05.012. Epub 2017 May 22. PMID: 28545656.

251. Lucht SA, Hennig F, Matthiessen C, Ohlwein S, Icks A, Moebus S, Jöckel KH, Jakobs H, Hoffmann B. Air Pollution and Glucose Metabolism: An Analysis in Non-Diabetic Participants of the Heinz Nixdorf Recall Study. *Environ Health Perspect.* 2018 Apr 3;126(4):047001. doi: 10.1289/EHP2561. PMID: 29616776; PMCID: PMC6071794.

252. Matthiessen C, Lucht S, Hennig F, Ohlwein S, Jakobs H, Jöckel KH, Moebus S, Hoffmann B; Heinz Nixdorf Recall Study Investigative Group. Long-term exposure to airborne particulate matter and NO₂ and prevalent and incident metabolic syndrome - Results from the Heinz Nixdorf Recall Study. *Environ Int.* 2018 Jul;116:74-82. doi: 10.1016/j.envint.2018.02.035. Epub 2018 Jun 14. PMID: 30000000; PMCID: PMC6071794.

253. Cai L, Wang S, Gao P, Shen X, Jalaludin B, Bloom MS, Wang Q, Bao J, Zeng X, Gui Z, Chen Y, Huang C. Effects of ambient particulate matter on fasting blood glucose among primary school children in Guangzhou, China. *Environ Res.* 2019 Sep;176:108541. doi: 10.1016/j.envres.2019.108541. Epub 2019 Jun 18. PMID: 31271922.

254. Howe CG, Eckel SP, Habre R, Girguis MS, Gao L, Lurmann FW, Gilliland FD, Breton CV. Association of Prenatal Exposure to Ambient and Traffic-Related Air Pollution With Newborn Thyroid Function: Findings From the Children's Health Study. *JAMA Netw Open.* 2018 Sep 7;1(5):e182172. doi: 10.1001/jamanetworkopen.2018.2172. PMID: 30646156; PMCID: PMC6324507.

255. Ghassabian A, Pierotti L, Basterrechea M, Chatzi L, Estarlich M, Fernández-Somoano A, Fleisch AF, Gold DR, Julvez J, Karakosta P, Lertxundi A, Lopez-Espinosa MJ, Mulder TA, Korevaar TIM, Oken E, Peeters RP, Rifas-Shiman S, Stephanou E, Tardón A, Tiemeier H, Vrijheid M, Vrijlkotte TGM, Sunyer J, Guxens M. Association of Exposure to Ambient Air Pollution With

Thyroid Function During Pregnancy. *JAMA Netw Open*. 2019 Oct 2;2(10):e1912902. doi: 10.1001/jamanetworkopen.2019.12902. PMID: 31617922; PMCID: PMC6806433.

256. Yang BY, Fan S, Thiering E, Seissler J, Nowak D, Dong GH, Heinrich J. Ambient air pollution and diabetes: A systematic review and meta-analysis. *Environ Res*. 2020 Jan;180:108817. doi: 10.1016/j.envres.2019.108817. Epub 2019 Oct 12. PMID: 31627156.

257. Guo B, Guo Y, Nima Q, Feng Y, Wang Z, Lu R, Baimayangji, Ma Y, Zhou J, Xu H, Chen L, Chen G, Li S, Tong H, Ding X, Zhao X; China Multi-Ethnic Cohort (CMEC) collaborative group. Exposure to air pollution is associated with an increased risk of metabolic dysfunction-associated fatty liver disease. *J Hepatol*. 2022 Mar;76(3):518-525. doi: 10.1016/j.jhep.2021.10.016. Epub 2021 Dec 6. PMID: 34883157.

258. Li G, Huang J, Wang J, Zhao M, Liu Y, Guo X, Wu S, Zhang L. Long-Term Exposure to Ambient PM_{2.5} and Increased Risk of CKD Prevalence in China. *J Am Soc Nephrol*. 2021 Feb;32(2):448-458. doi: 10.1681/ASN.2020040517. Epub 2020 Dec 17. Erratum in: *J Am Soc Nephrol*. 2021 Aug;32(8):2101. PMID: 33334736; PMCID: PMC8054885.

259. Xu W, Wang S, Jiang L, Sun X, Wang N, Liu X, Yao X, Qiu T, Zhang C, Li J, Deng H, Yang G. The influence of PM_{2.5} exposure on kidney diseases. *Hum Exp Toxicol*. 2022 Jan-Dec;41:9603271211069982. doi: 10.1177/09603271211069982. PMID: 35174736.

260. Bragg-Gresham J, Morgenstern H, McClellan W, Saydah S, Pavkov M, Williams D, Powe N, Tuot D, Hsu R, Saran R; Centers for Disease Control and Prevention CKD Surveillance System. County-level air quality and the prevalence of diagnosed chronic kidney disease in the US Medicare population. *PLoS One*. 2018 Jul 31;13(7):e0200612. doi: 10.1371/journal.pone.0200612. PMID: 30063741; PMCID: PMC6067706.

261. Bernatsky S, Fournier M, Pineau CA, Clarke AE, Vinet E, Smargiassi A. Associations between ambient fine particulate levels and disease activity in patients with systemic lupus erythematosus (SLE). *Environ Health Perspect*. 2011 Jan;119(1):45-9. doi: 10.1289/ehp.1002123. Epub 2010 Sep 22. PMID: 20870568; PMCID: PMC3018498.

262. Bae S, Pan XC, Kim SY, Park K, Kim YH, Kim H, Hong YC. Exposures to particulate matter and polycyclic aromatic hydrocarbons and oxidative stress in schoolchildren. *Environ Health Perspect*. 2010 Apr;118(4):579-83. doi: 10.1289/ehp.0901077. PMID: 20368125; PMCID: PMC2854738.

263. Zeff AS, Prahalad S, Lefevre S, Clifford B, McNally B, Bohnsack JF, Pope CA 3rd. Juvenile idiopathic arthritis and exposure to fine particulate air pollution. *Clin Exp Rheumatol*. 2009 Sep-Oct;27(5):877-84. PMID: 19917177.

264. Xu Z, Xu X, Zhong M, Hotchkiss IP, Lewandowski RP, Wagner JG, Bramble LA, Yang Y, Wang A, Harkema JR, Lippmann M, Rajagopalan S, Chen LC, Sun Q. Ambient particulate air pollution

induces oxidative stress and alterations of mitochondria and gene expression in brown and white adipose tissues. Part Fibre Toxicol. 2011 Jul 11;8:20. doi: 10.1186/1743-8977-8-20. PMID: 21745393; PMCID: PMC3152885.

265. Risom L, Møller P, Loft S. Oxidative stress-induced DNA damage by particulate air pollution. *Mutat Res.* 2005 Dec 30;592(1-2):119-37. doi: 10.1016/j.mrfmmm.2005.06.012. Epub 2005 Aug 8. PMID: 16085126.

266. Slama R, Bottagisi S, Solansky I, Lepeule J, Giorgis-Allemand L, Sram R. Short-term impact of atmospheric pollution on fecundability. *Epidemiology.* 2013 Nov;24(6):871-9. doi: 10.1097/EDE.0b013e3182a702c5. PMID: 24051894.

267. Cimino F, Speciale A, Siracusa L, Naccari C, Saija A, Mancari F, Raciti R, Cristani M, Trombetta D. Cytotoxic effects induced in vitro by organic extracts from urban air particulate matter in human leukocytes. *Drug Chem Toxicol.* 2014 Jan;37(1):32-9. doi: 10.3109/01480545.2013.806529. Epub 2013 Nov 6. PMID: 24195653.

268. Kim JW, Park S, Lim CW, Lee K, Kim B. The role of air pollutants in initiating liver disease. *Toxicol Res.* 2014 Jun;30(2):65-70. doi: 10.5487/TR.2014.30.2.065. PMID: 25071914; PMCID: PMC4112066.

269. Frutos V, González-Comadrán M, Solà I, Jacquemin B, Carreras R, Checa Vizcaíno MA. Impact of air pollution on fertility: a systematic review. *Gynecol Endocrinol.* 2015 Jan;31(1):7-13. doi: 10.3109/09513590.2014.958992. Epub 2014 Sep 12. PMID: 25212280.

270. Bakian AV, Huber RS, Coon H, Gray D, Wilson P, McMahon WM, Renshaw PF. Acute air pollution exposure and risk of suicide completion. *Am J Epidemiol.* 2015 Mar 1;181(5):295-303. doi: 10.1093/aje/kwu341. Epub 2015 Feb 10. PMID: 25673816; PMCID: PMC4339389.

271. Zhao B, Vo HQ, Johnston FH, Negishi K. Air pollution and telomere length: a systematic review of 12,058 subjects. *Cardiovasc Diagn Ther* 2018;8(4):480-492. doi: 10.21037/cdt.2018.06.05

272. Feng C, Li J, Sun W, Zhang Y, Wang Q. Impact of ambient fine particulate matter (PM_{2.5}) exposure on the risk of influenza-like-illness: a time-series analysis in Beijing, China. *Environ Health.* 2016 Feb 11;15:17. doi: 10.1186/s12940-016-0115-2. PMID: 26864833; PMCID: PMC4750357.

273. Li W, Wilker EH, Dorans KS, Rice MB, Schwartz J, Coull BA, Koutrakis P, Gold DR, Keaney JF Jr, Lin H, Vasan RS, Benjamin EJ, Mittleman MA. Short-Term Exposure to Air Pollution and Biomarkers of Oxidative Stress: The Framingham Heart Study. *J Am Heart Assoc.* 2016 Apr 28;5(5):e002742. doi: 10.1161/JAHA.115.002742. PMID: 27126478; PMCID: PMC4889166.

274. Nucci P, Sacchi M, Pichi F, Allegri P, Serafino M, Dello Strologo M, De Cillà S, Villani E. *Pediatric Conjunctivitis and Air Pollution Exposure: A Prospective Observational Study*. *Semin Ophthalmol*. 2017;32(4):407-411. doi: 10.3109/08820538.2015.1115088. Epub 2016 Apr 15. PMID: 27082495.
275. Zeft AS, Prahalad S, Schneider R, Dedeoglu F, Weiss PF, Grom AA, Mix C, Pope Rd CA. *Systemic onset juvenile idiopathic arthritis and exposure to fine particulate air pollution*. *Clin Exp Rheumatol*. 2016 Sep-Oct;34(5):946-952. Epub 2016 Sep 1. PMID: 27607024.
276. <https://aanfiles.blob.core.windows.net/aanfiles/46bd5456-4ce2-43fa-a2ea-1ccdedf39703/EMBARGOED%202023%20AAN%20AM%20Abstract%20%234319%20-%20Fine%20Particulate%20Matter%20and%20Parkinson%20Disease%20Risk%20in%20Medicare%20Beneficiaries.pdf>
277. Huang JV, Leung GM, Schooling CM. *The Association of Air Pollution With Pubertal Development: Evidence From Hong Kong's "Children of 1997" Birth Cohort*. *Am J Epidemiol*. 2017 May 15;185(10):914-923. doi: 10.1093/aje/kww200. PMID: 28444106.
278. Psoter KJ, De Roos AJ, Wakefield J, Mayer JD, Rosenfeld M. *Air pollution exposure is associated with MRSA acquisition in young U.S. children with cystic fibrosis*. *BMC Pulm Med*. 2017 Jul 27;17(1):106. doi: 10.1186/s12890-017-0449-8. PMID: 28750627; PMCID: PMC5530959.
279. Li W, Dorans KS, Wilker EH, Rice MB, Ljungman PL, Schwartz JD, Coull BA, Koutrakis P, Gold DR, Keaney JF Jr, Vasan RS, Benjamin EJ, Mittleman MA. *Short-Term Exposure to Ambient Air Pollution and Biomarkers of Systemic Inflammation: The Framingham Heart Study*. *Arterioscler Thromb Vasc Biol*. 2017 Sep;37(9):1793-1800. doi: 10.1161/ATVBAHA.117.309799. Epub 2017 Jul 27. PMID: 28751572; PMCID: PMC5570664.
280. Merklinger-Gruchala A, et al. *Effect of Air Pollution on Menstrual Cycle Length-A Prognostic Factor of Women's Reproductive Health*. *Int J Environ Res Public Health*. 2017 Jul 20;14(7). pii: E816. doi: 10.3390/ijerph14070816.
281. Hsieh S, Leaderer BP, Feldstein AE, Santoro N, McKay LA, Caprio S, McConnell R. *Traffic-related air pollution associations with cytokeratin-18, a marker of hepatocellular apoptosis, in an overweight and obese paediatric population*. *Pediatr Obes*. 2018 Jun;13(6):342-347. doi: 10.1111/ijpo.12228. Epub 2017 Jul 20. PMID: 28730729; PMCID: PMC5775922.
282. Li H, et al. *Particulate Matter Exposure and Stress Hormone Levels: A Randomized, Double-Blind, Crossover Trial of Air Purification* <https://doi.org/10.1161/CIRCULATIONAHA.116.026796> *Circulation*. 2017;136:618-627
283. Wang C, Chen R, Shi M, Cai J, Shi J, Yang C, Li H, Lin Z, Meng X, Liu C, Niu Y, Xia Y, Zhao Z, Kan H, Weinberg CR. *Possible Mediation by Methylation in Acute Inflammation Following*

Personal Exposure to Fine Particulate Air Pollution. Am J Epidemiol. 2018 Mar 1;187(3):484-493. doi: 10.1093/aje/kwx277. PMID: 29020142; PMCID: PMC5860518.

284. Bowe B, Xie Y, Li T, Yan Y, Xian H, Al-Aly Z. Particulate Matter Air Pollution and the Risk of Incident CKD and Progression to ESRD. *J Am Soc Nephrol.* 2018 Jan;29(1):218-230. doi: 10.1681/ASN.2017030253. Epub 2017 Sep 21. PMID: 28935655; PMCID: PMC5748906.

285. Son JY, Lee HJ, Koutrakis P, Bell ML. Pregnancy and Lifetime Exposure to Fine Particulate Matter and Infant Mortality in Massachusetts, 2001-2007. *Am J Epidemiol.* 2017 Dec 1;186(11):1268-1276. doi: 10.1093/aje/kwx015. PMID: 29121205; PMCID: PMC5860580.

286. Prada D, Zhong J, Colicino E, Zanobetti A, Schwartz J, Dagincourt N, Fang SC, Kloog I, Zmuda JM, Holick M, Herrera LA, Hou L, Dominici F, Bartali B, Baccarelli AA. Association of air particulate pollution with bone loss over time and bone fracture risk: analysis of data from two independent studies. *Lancet Planet Health.* 2017 Nov;1(8):e337-e347. doi: 10.1016/S2542-5196(17)30136-5. Epub 2017 Nov 9. PMID: 29527596; PMCID: PMC5841468.

287. Alves AGF, de Azevedo Giacomini MF, Braga ALF, Sallum AME, Pereira LAA, Farhat LC, Strufaldi FL, de Faria Coimbra Lichtenfels AJ, de Santana Carvalho T, Nakagawa NK, Silva CA, Farhat SCL. Influence of air pollution on airway inflammation and disease activity in childhood-systemic lupus erythematosus. *Clin Rheumatol.* 2018 Mar;37(3):683-690. doi: 10.1007/s10067-017-3893-1. Epub 2017 Nov 2. PMID: 29098476.

288. Mutlu EA, Comba IY, Cho T, Engen PA, Yazıcı C, Soberanes S, Hamanaka RB, Niğdelioğlu R, Meliton AY, Ghio AJ, Budinger GRS, Mutlu GM. Inhalational exposure to particulate matter air pollution alters the composition of the gut microbiome. *Environ Pollut.* 2018 Sep;240:817-830. doi: 10.1016/j.envpol.2018.04.130. Epub 2018 May 18. PMID: 29783199; PMCID: PMC6400491.

289. Yitshak-Sade M, Bobb JF, Schwartz JD, Kloog I, Zanobetti A. The association between short and long-term exposure to PM_{2.5} and temperature and hospital admissions in New England and the synergistic effect of the short-term exposures. *Sci Total Environ.* 2018 Oct 15;639:868-875. doi: 10.1016/j.scitotenv.2018.05.181. Epub 2018 May 26. PMID: 29929325; PMCID: PMC6051434.

290. Schwartz J, et al. A National Multicity Analysis of the Causal Effect of Local Pollution, NO₂ and PM_{2.5} on Mortality. *EHP*, Vol. 26, No. 8, Published:31 August 2018CID: 087004

291. Heft-Neal S, Burney J, Bendavid E, Burke M. Robust relationship between air quality and infant mortality in Africa. *Nature.* 2018 Jul;559(7713):254-258. doi: 10.1038/s41586-018-0263-3. Epub 2018 Jun 27. PMID: 29950722.

292. Chen CC, Yang CY. Effects of ambient air pollution exposure on frequency of hospital admissions for appendicitis in Taipei, Taiwan. *J Toxicol Environ Health A.* 2018;81(17):854-860. doi: 10.1080/15287394.2018.1498276. Epub 2018 Jul 26. PMID: 30047832.

293. Billings ME, Gold D, Szpiro A, Aaron CP, Jorgensen N, Gassett A, Leary PJ, Kaufman JD, Redline SR. The Association of Ambient Air Pollution with Sleep Apnea: The Multi-Ethnic Study of Atherosclerosis. *Ann Am Thorac Soc*. 2019 Mar;16(3):363-370. doi: 10.1513/AnnalsATS.201804-248OC. PMID: 30571166; PMCID: PMC6394120.
294. Lin CY, Wang CM, Chen ML, Hwang BF. The effects of exposure to air pollution on the development of uterine fibroids. *Int J Hyg Environ Health*. 2019 Apr;222(3):549-555. doi: 10.1016/j.ijheh.2019.02.004. Epub 2019 Feb 26. PMID: 30819602.
295. Bowe B, Xie Y, Li T, Yan Y, Xian H, Al-Aly Z. Estimates of the 2016 global burden of kidney disease attributable to ambient fine particulate matter air pollution. *BMJ Open*. 2019 May 9;9(5):e022450. doi: 10.1136/bmjopen-2018-022450. PMID: 31072847; PMCID: PMC6528010.
296. Wang HH, Zhang SC, Wang J, Chen X, Yin H, Huang DY. Combined toxicity of outdoor air pollution on kidney function among adult women in Mianyang City, southwest China. *Chemosphere*. 2020 Jan;238:124603. doi: 10.1016/j.chemosphere.2019.124603. Epub 2019 Aug 16. PMID: 31442773
297. Chen CC, Chen PS, Yang CY. Relationship between fine particulate air pollution exposure and human adult life expectancy in Taiwan. *J Toxicol Environ Health A*. 2019;82(14):826-832. doi: 10.1080/15287394.2019.1658386. Epub 2019 Aug 22. PMID: 31438783.
298. Shepherd A, Mullins JT. Arthritis diagnosis and early-life exposure to air pollution. *Environ Pollut*. 2019 Oct;253:1030-1037. doi: 10.1016/j.envpol.2019.07.054. Epub 2019 Jul 13. PMID: 31434180.
299. Lee W, Choi HM, Kim D, Honda Y, Leon Guo YL, Kim H. Synergic effect between high temperature and air pollution on mortality in Northeast Asia. *Environ Res*. 2019 Nov;178:108735. doi: 10.1016/j.envres.2019.108735. Epub 2019 Sep 9. PMID: 31539825.
300. Alex AM, Kunkel G, Sayles H, Flautero Arcos JD, Mikuls TR, Kerr GS. Exposure to ambient air pollution and autoantibody status in rheumatoid arthritis. *Clin Rheumatol*. 2020 Mar;39(3):761-768. doi: 10.1007/s10067-019-04813-w. Epub 2019 Nov 15. PMID: 31729679.
301. Wei Y, Wang Y, Di Q, et al. Short term exposure to fine particulate matter and hospital admission risks and costs in the Medicare population: time stratified, case crossover study. *BMJ*. 2019;367:l6258. Published 2019 Nov 27. doi:10.1136/bmj.l6258
302. Bowe B, Xie Y, Yan Y, Al-Aly Z. Burden of Cause-Specific Mortality Associated With PM2.5 Air Pollution in the United States. *JAMA Netw Open*. 2019 Nov 1;2(11):e1915834. doi: 10.1001/jamanetworkopen.2019.15834. PMID: 31747037; PMCID: PMC6902821.

303. Ranzani OT, et al. Association of Ambient and Household Air Pollution With Bone Mineral Content Among Adults in Peri-urban South India. *JAMA Netw Open*. 2020 Jan 3;3(1):e1918504. doi: 10.1001/jamanetworkopen.2019.18504.
304. Wang Z, Zhao L, Huang Q, Hong A, Yu C, Xiao Q, Zou B, Ji S, Zhang L, Zou K, Ning Y, Zhang J, Jia P. Traffic-related environmental factors and childhood obesity: A systematic review and meta-analysis. *Obes Rev*. 2021 Feb;22 Suppl 1(Suppl 1):e12995. doi: 10.1111/obr.12995. Epub 2020 Jan 30. PMID: 32003149; PMCID: PMC7988540.
305. Groves CP, Butland BK, Atkinson RW, Delaney AP, Pilcher DV. Intensive care admissions and outcomes associated with short-term exposure to ambient air pollution: a time series analysis. *Intensive Care Med*. 2020 Jun;46(6):1213-1221. doi: 10.1007/s00134-020-06052-z. Epub 2020 Apr 30. PMID: 32355989.
306. Lee WJ, Liu CY, Peng LN, Lin CH, Lin HP, Chen LK. PM2.5 air pollution contributes to the burden of frailty. *Sci Rep*. 2020 Sep 2;10(1): 14478. doi: 10.1038/s41598-020-71408-w.
307. Hyun SW, Song SJ, Park B, Lee TG, Kim CS. Toxicological effects of urban particulate matter on corneal and conjunctival epithelial cells. *Toxicol Res*. 2020 Feb 10;36(4):311-318. doi: 10.1007/s43188-019-00034-0. PMID: 33005590; PMCID: PMC7494700
308. Wu X, Braun D, Schwartz J, Kioumourtzoglou MA, Dominici F. Evaluating the impact of long-term exposure to fine particulate matter on mortality among the elderly. *Sci Adv*. 2020 Jul 17;6(29):eaba5692. doi: 10.1126/sciadv.aba5692. PMID: 32832626; PMCID: PMC7439614.
309. Danesh Yazdi M, Wang Y, Di Q, Wei Y, Requia WJ, Shi L, Sabath MB, Dominici F, Coull BA, Evans JS, Koutrakis P, Schwartz JD. Long-Term Association of Air Pollution and Hospital Admissions Among Medicare Participants Using a Doubly Robust Additive Model. *Circulation*. 2021 Apr 20;143(16):1584-1596. doi: 10.1161/CIRCULATIONAHA.120.050252. Epub 2021 Feb 22. PMID: 33611922; PMCID: PMC8055197.
310. Scheers H, Jacobs L, Casas L, Nemery B, Nawrot TS. Long-term exposure to particulate matter air pollution is a risk factor for stroke: meta-analytical evidence. *Stroke*. 2015; 46:3058–3066. doi: 10.1161/STROKEAHA.115.009913
311. Adami G, Cattani G, Rossini M, Viapiana O, Olivi P, Orsolini G, Bertoldo E, Fracassi E, Gatti D, Fassio A. Association between exposure to fine particulate matter and osteoporosis: a population-based cohort study. *Osteoporos Int*. 2022 Jan;33(1):169-176. doi: 10.1007/s00198-021-06060-9. Epub 2021 Jul 15. PMID: 34268604; PMCID: PMC8758604.
312. Bozack A, Pierre S, DeFelice N, Colicino E, Jack D, Chillrud SN, Rundle A, Astua A, Quinn JW, McGuinn L, Yang Q, Johnson K, Masci J, Lukban L, Maru D, Lee AG. Long-Term Air Pollution Exposure and COVID-19 Mortality: A Patient-Level Analysis from New York City. *Am J Respir Crit Care Med*. 2022 Mar 15;205(6):651-662. doi: 10.1164/rccm.202104-0845OC. PMID: 34881681.

313. Hyun SW, Song SJ, Park B, Lee TG, Kim CS. Toxicological effects of urban particulate matter on corneal and conjunctival epithelial cells. *Toxicol Res*. 2020 Feb 10;36(4):311-318. doi: 10.1007/s43188-019-00034-0. PMID: 33005590; PMCID: PMC7494700.
314. Ding S, Sun S, Ding R, Song S, Cao Y, Zhang L. Association between exposure to air pollutants and the risk of inflammatory bowel diseases visits. *Environ Sci Pollut Res Int*. 2022 Mar;29(12):17645-17654. doi: 10.1007/s11356-021-17009-0. Epub 2021 Oct 20. PMID: 34669131.
315. Zhao Y, Zhu Q, Lin J, Cai J. Association of Exposure to Particulate Matter Air Pollution With Semen Quality Among Men in China. *JAMA Netw Open*. 2022 Feb 1;5(2):e2148684. doi: 10.1001/jamanetworkopen.2021.48684. PMID: 35175344
316. Eckhardt CM, Baccarelli AA, Wu H. Environmental Exposures and Extracellular Vesicles: Indicators of Systemic Effects and Human Disease. *Curr Environ Health Rep*. 2022 Sep;9(3):465-476. doi: 10.1007/s40572-022-00357-5. Epub 2022 Apr 21. PMID: 35449498; PMCID: PMC9395256.
317. Poursafa P, Kamali Z, Fraszczyk E, Boezen HM, Vaez A, Snieder H. DNA methylation: a potential mediator between air pollution and metabolic syndrome. *Clin Epigenetics*. 2022 Jun 30;14(1):82. doi: 10.1186/s13148-022-01301-y. PMID: 35773726; PMCID: PMC9245491.
318. Song AY, Feinberg JI, Bakulski KM, Croen LA, Fallin MD, Newschaffer CJ, Hertz-Picciotto I, Schmidt RJ, Ladd-Acosta C, Volk HE. Prenatal Exposure to Ambient Air Pollution and Epigenetic Aging at Birth in Newborns. *Front Genet*. 2022 Jun 28;13:929416. doi: 10.3389/fgene.2022.929416. PMID: 35836579; PMCID: PMC9274082.
319. Pignon B, Borel C, Lajnef M, Richard JR, Szöke A, Hemery F, Leboyer M, Foret G, Schürhoff F. PM2.5 and PM10 air pollution peaks are associated with emergency department visits for psychotic and mood disorders. *Environ Sci Pollut Res Int*. 2022 Dec;29(59):88577-88586. doi: 10.1007/s11356-022-21964-7. Epub 2022 Jul 14. PMID: 35834080; PMCID: PMC9281271.
320. Lau C, Behlen JC, Myers A, Li Y, Zhao J, Harvey N, Wright G, Hoffmann AR, Zhang R, Johnson NM. In Utero Ultrafine Particulate Exposure Yields Sex- and Dose-Specific Responses to Neonatal Respiratory Syncytial Virus Infection. *Environ Sci Technol*. 2022 Aug 16;56(16):11527-11535. doi: 10.1021/acs.est.2c02786. Epub 2022 Aug 4. PMID: 35926851; PMCID: PMC9386899.
321. Collins TW, Grineski SE, Shaker Y, Mullen CJ. Communities of color are disproportionately exposed to long-term and short-term PM2.5 in metropolitan America. *Environ Res*. 2022 Nov;214(Pt 4):114038. doi: 10.1016/j.envres.2022.114038. Epub 2022 Aug 10. PMID: 35961542.
322. Grant A, Leung G, Freeman EE. Ambient Air Pollution and Age-Related Eye Disease: A Systematic Review and Meta-Analysis. *Invest Ophthalmol Vis Sci*. 2022 Aug 2;63(9):17. doi: 10.1167/iovs.63.9.17. PMID: 35960515; PMCID: PMC9396677.

323. Basith S, Manavalan B, Shin TH, Park CB, Lee WS, Kim J, Lee G. The Impact of Fine Particulate Matter 2.5 on the Cardiovascular System: A Review of the Invisible Killer. *Nanomaterials (Basel)*. 2022 Aug 2;12(15):2656. doi: 10.3390/nano12152656. PMID: 35957086; PMCID: PMC9370264.
324. Chaulin AM, Sergeev AK. Modern Concepts of the Role of Fine Particles (PM 2.5) in the Genesis of Atherosclerosis and Myocardial Damage: Clinical and Epidemiological Data, the Main Pathophysiological Mechanisms. *Curr Cardiol Rev*. 2023;19(2):25-39. doi: 10.2174/1573403X18666220817103105. PMID: 35980071.
325. Lou X, Zhang P, Shi N, Ding Z, Xu Z, Liu B, Hu W, Yan T, Wang J, Liu L, Zha Y, Wang J, Chen W, Xu C, Xu J, Jiang H, Ma H, Yuan W, Wang C, Liao Y, Wang D, Yao L, Chen M, Li G, Li Y, Wang P, Li X, Lu C, Tang W, Wan J, Li R, Xiao X, Zhang C, Jiao J, Zhang W, Yuan J, Lan L, Li J, Zhang P, Zheng W, Chen J. Associations between short-term exposure of ambient particulate matter and hemodialysis patients death: A nationwide, longitudinal case-control study in China. *Sci Total Environ*. 2022 Dec 15;852:158215. doi:
326. Yuan X, Yang Y, Liu C, Tian Y, Xia D, Liu Z, Pan L, Xiong M, Xiong J, Meng L, Zhang Z, Ye K, Jiang H, Zhang Z. Fine Particulate Matter Triggers α -Synuclein Fibrillization and Parkinson-like Neurodegeneration. *Mov Disord*. 2022 Sep;37(9):1817-1830. doi: 10.1002/mds.29181. Epub 2022 Aug 22. PMID: 36054165.
327. Yu X, Wang Q, Wei J, Zeng Q, Xiao L, Ni H, Xu T, Wu H, Guo P, Zhang X. Impacts of traffic-related particulate matter pollution on semen quality: A retrospective cohort study relying on the random forest model in a megacity of South China. *Sci Total Environ*. 2022 Dec 10;851(Pt 2):158387. doi: 10.1016/j.scitotenv.2022.158387. Epub 2022 Aug 29. PMID: 36049696.
328. Wang X, Karvonen-Gutierrez CA, Gold EB, Derby C, Greendale G, Wu X, Schwartz J, Park SK. Longitudinal Associations of Air Pollution With Body Size and Composition in Midlife Women: The Study of Women's Health Across the Nation. *Diabetes Care*. 2022 Nov 1;45(11):2577-2584. doi: 10.2337/dc22-0963. PMID: 36084038; PMCID: PMC9679268.
329. Guxens M, Lubczynska MJ, Perez-Crespo L, Muetzel RL, El Marroun H, Basagana X, Hoek G, Tiemeier H. Associations of Air Pollution on the Brain in Children: A Brain Imaging Study. *Res Rep Health Eff Inst*. 2022 Feb;(209):1-61. PMID: 36106707.
330. Brunekreef B, Strak M, Chen J, Andersen ZJ, Atkinson R, Bauwelinck M, Bellander T, Boutron MC, Brandt J, Carey I, Cesaroni G, Forastiere F, Fecht D, Gulliver J, Hertel O, Hoffmann B, de Hoogh K, Houthuijs D, Hvidtfeldt U, Janssen N, Jorgensen J, Katsouyanni K, Ketzel M, Klompmaker J, Hjertager Krog N, Liu S, Ljungman P, Mehta A, Nagel G, Oftedal B, Pershagen G, Peters A, Raaschou-Nielsen O, Renzi M, Rodopoulou S, Samoli E, Schwarze P, Sigsgaard T, Stafoggia M, Vienneau D, Weinmayr G, Wolf K, Hoek G. Mortality and Morbidity Effects of Long-

Term Exposure to Low-Level PM2.5, BC, NO2, and O3: An Analysis of European Cohorts in the ELAPSE Project. Res Rep Health Eff Inst. 2021 Sep;(208):1-127. PMID: 36106702.

331. Della Guardia L, Shin AC. White and brown adipose tissue functionality is impaired by fine particulate matter (PM2.5) exposure. *J Mol Med (Berl)*. 2022 May;100(5):665-676. doi: 10.1007/s00109-022-02183-6. Epub 2022 Mar 14. Erratum in: *J Mol Med (Berl)*. 2022 Apr 27;: PMID: 35286401; PMCID: PMC9110515.

332. Tian F, Cai M, Li H, Qian ZM, Chen L, Zou H, Zhang Z, Wang C, Xian H, McMillin SE, Lin H. Air Pollution Associated With Incident Stroke, Poststroke Cardiovascular Events, and Death: A Trajectory Analysis of a Prospective Cohort. *Neurology*. 2022 Nov 29;99(22):e2474-e2484. doi: 10.1212/WNL.0000000000201316. Epub 2022 Sep 28. PMID: 36171142.

333. Liu L, Tian X, Zhao Y, Zhao Z, Luo L, Luo H, Han Z, Kang X, Wang X, Liu X, Guo X, Tao L, Luo Y. Long-term exposure to PM2.5 and PM10 and chronic kidney disease: the Beijing Health Management Cohort, from 2013 to 2018. *Environ Sci Pollut Res Int*. 2023 Feb;30(7):17817-17827. doi: 10.1007/s11356-022-23251-x. Epub 2022 Oct 6. PMID: 36203044.

334. Yang L, Wang N, Liu S, Xiao Q, Geng G, Zhang X, Li H, Zheng Y, Guo F, Li Q, Li J, Ren A, Xue T, Ji J. The PM2.5 concentration reduction improves survival rate of lung cancer in Beijing. *Sci Total Environ*. 2023 Feb 1;858(Pt 2):159857. doi: 10.1016/j.scitotenv.2022.159857. Epub 2022 Oct 31. PMID: 36328253.

335. Gariazzo C, Renzi M, Marinaccio A, Michelozzi P, Massari S, Silibello C, Carlino G, Rossi PG, Maio S, Viegi G, Stafoggia M; BIGEPI Collaborative Group. Association between short-term exposure to air pollutants and cause-specific daily mortality in Italy. A nationwide analysis. *Environ Res*. 2023 Jan 1;216(Pt 3):114676. doi: 10.1016/j.envres.2022.114676. Epub 2022 Oct 31. PMID: 36328229.

336. Lei X, Zhang Y, Wang Z, Lu Z, Pan C, Zhang S, Chen Q, Yuan T, Zhang J, Gao Y, Tian Y; Shanghai Birth Cohort Study. Effects of prenatal exposure to PM2.5 and its composition on cognitive and motor functions in children at 12 months of age: The Shanghai Birth Cohort Study. *Environ Int*. 2022 Dec;170:107597. doi: 10.1016/j.envint.2022.107597. Epub 2022 Oct 21. PMID: 36327589.

337. Kim H, Samet JM, Bell ML. Association between Short-Term Exposure to Air Pollution and COVID-19 Mortality: A Population-Based Case-Crossover Study Using Individual-Level Mortality Registry Confirmed by Medical Examiners. *Environ Health Perspect*. 2022 Nov;130(11):117006. doi: 10.1289/EHP10836. Epub 2022 Nov 11. PMID: 36367781; PMCID: PMC965118

338. Ran J, Sun S, Han L, Zhao S, Chen D, Guo F, Li J, Qiu H, Lei Y, Tian L. Fine particulate matter and cause-specific mortality in the Hong Kong elder patients with chronic kidney disease. *Chemosphere*. 2020 May;247:125913. doi: 10.1016/j.chemosphere.2020.125913. Epub 2020 Jan 13. PMID: 31962222.

339. Zhao W, Zhao Y, Wang P, Zhou Y, Meng X, Ma W, Li J, Zhang Y. PM2.5 exposure associated with prenatal anxiety and depression in pregnant women. *Ecotoxicol Environ Saf.* 2022 Dec 15;248:114284. doi: 10.1016/j.ecoenv.2022.114284. Epub 2022 Nov 14. PMID: 36395653.
340. Pérez Velasco R, Jarosińska D. Update of the WHO global air quality guidelines: Systematic reviews - An introduction. *Environ Int.* 2022 Dec;170:107556. doi: 10.1016/j.envint.2022.107556. Epub 2022 Oct 1. PMID: 36395555; PMCID: PMC9720155.
341. Kang N, Wu R, Liao W, Zhang C, Liu X, Mao Z, Huo W, Hou J, Zhang K, Tian H, Lin H, Wang C. Association of long-term exposure to PM2.5 constituents with glucose metabolism in Chinese rural population. *Sci Total Environ.* 2023 Feb 10;859(Pt 2):160364. doi: 10.1016/j.scitotenv.2022.160364. Epub 2022 Nov 22. PMID: 36427733.
342. Thompson R, Smith RB, Karim YB, Shen C, Drummond K, Teng C, Toledano MB. Air pollution and human cognition: A systematic review and meta-analysis. *Sci Total Environ.* 2023 Feb 10;859(Pt 2):160234. doi: 10.1016/j.scitotenv.2022.160234. Epub 2022 Nov 23. PMID: 36427724.
343. Cai J, Shen Y, Meng X, Zhao Y, Niu Y, Chen R, Du W, Quan G, Barnett AL, Jones G, Kan H, Hua J. Association of developmental coordination disorder with early-life exposure to fine particulate matter in Chinese preschoolers. *Innovation (Camb).* 2022 Nov 4;4(1):100347. doi: 10.1016/j.xinn.2022.100347. PMID: 36425095; PMCID: PMC9678769.
344. Dora Cserbik, Jiu-Chiuan Chen, Rob McConnell, Kiros Berhane, Elizabeth R. Sowell, Joel Schwartz, Daniel A. Hackman, Eric Kan, Chun C. Fan, Megan M. Herting, Fine particulate matter exposure during childhood relates to hemispheric-specific differences in brain structure, *Environment International*, Volume 143, 2020, 105933,ISSN 0160-4120
345. Hu M, Wei J, Hu Y, Guo X, Li Z, Liu Y, Li S, Xue Y, Li Y, Liu M, Wang L, Liu X. Long-term effect of submicronic particulate matter (PM1) and intermodal particulate matter (PM1-2.5) on incident dyslipidemia in China: A nationwide 5-year cohort study. *Environ Res.* 2023 Jan 15;217:114860. doi: 10.1016/j.envres.2022.114860. Epub 2022 Nov 21. PMID: 36423667.
346. Lowe ME, Akhtari FS, Potter TA, Fargo DC, Schmitt CP, Schurman SH, Eccles KM, Motsinger-Reif A, Hall JE, Messier KP. The skin is no barrier to mixtures: Air pollutant mixtures and reported psoriasis or eczema in the Personalized Environment and Genes Study (PEGS). *J Expo Sci Environ Epidemiol.* 2022 Dec 2. doi: 10.1038/s41370-022-00502-0. Epub ahead of print. PMID: 36460922.
347. Odo DB, Yang IA, Dey S, Hammer MS, van Donkelaar A, Martin RV, Dong GH, Yang BY, Hystad P, Knibbs LD. A cross-sectional analysis of long-term exposure to ambient air pollution and cognitive development in children aged 3-4 years living in 12 low- and middle-income countries. *Environ Pollut.* 2023 Feb 1;318:120916. doi: 10.1016/j.envpol.2022.120916. Epub 2022 Dec 20. PMID: 36563987.

348. Chang YT, Jung CR, Chang YC, Chuang BR, Chen ML, Hwang BF. Prenatal and postnatal exposure to PM_{2.5} and the risk of tic disorders. *Paediatr Perinat Epidemiol*. 2022 Dec 23. doi: 10.1111/ppe.12943. Epub ahead of print. PMID: 36562434.
349. Chen EW, Ahmad K, Erqou S, Wu WC. Particulate matter 2.5, metropolitan status, and heart failure outcomes in US counties: A nationwide ecologic analysis. *PLoS One*. 2022 Dec 30;17(12):e0279777. doi: 10.1371/journal.pone.0279777. PMID: 36584210; PMCID: PMC9803275.
350. Qi, Y.; Wei, S.; Chen, Y.; Pu, Y.; Liu, S.; Liu, Y. Intrusion of inhaled exotic ultrafine particles into the knee joint in humans and animals: a risk to the joint and surrounding tissues. *Nano Today* 2022, 43, 101426, DOI: 10.1016/j.nantod.2022.101426
351. Ma, J.; Liu, X.; Yang, Y.; Qiu, J.; Dong, Z.; Ren, Q.; Zuo, Y. Y.; Xia, T.; Chen, W.; Liu, S. Binding of benzo[a]pyrene alters the bioreactivity of fine biochar particles toward macrophages leading to deregulated macrophagic defense and autophagy. *ACS Nano* 2021, 15, 9717– 9731, DOI: 10.1021/acsnano.1c00324
352. Calderon-Garciduenas, L.; Gonzalez-Maciel, A.; Reynoso-Robles, R.; Hammond, J.; Kulesza, R.; Lachmann, I.; Torres-Jardon, R.; Mukherjee, P. S.; Maher, B. A. Quadruple abnormal protein aggregates in brainstem pathology and exogenous, metal-rich and magnetic nanoparticles (and engineered Ti-rich nanorods). The substantia nigrae is a very early target in young urbanites and the gastrointestinal tract likely a key brainstem portal. *Environ. Res.* 2020, 191, 110139, DOI: 10.1016/j.envres.2020.110139
353. Kulick ER, Kaufman JD, Sack C. Ambient Air Pollution and Stroke: An Updated Review. *Stroke*. 2023 Mar;54(3):882-893. doi: 10.1161/STROKEAHA.122.035498. Epub 2022 Dec 29. PMID: 36579640.
354. Frye, R.E.; Cakir, J.; Rose, S.; Delhey, L.; Bennuri, S.C.; Tippett, M.; Melnyk, S.; James, S.J.; Palmer, R.F.; Austin, C.; et al. Prenatal air pollution influences neurodevelopment and behavior in autism spectrum disorder by modulating mitochondrial physiology. *Mol. Psychiatry* 2021, 26, 1561–1577
355. Frye RE, Cakir J, McCarty PJ, Rose S, Delhey LM, Palmer RF, Austin C, Curtin P, Yitshak-Sade M, Arora M. Air Pollution and Maximum Temperature Are Associated with Neurodevelopmental Regressive Events in Autism Spectrum Disorder. *J Pers Med*. 2022 Nov 1;12(11):1809. doi: 10.3390/jpm12111809. PMID: 36579525; PMCID: PMC9696106.
356. Zhao T, Li X, Qian H, Miao X, Zhu Y, Wang J, Hui J, Zhou L, Ye L. PM_{2.5} induces the abnormal lipid metabolism and leads to atherosclerosis via Notch signaling pathway in rats. *Toxicology*. 2023 Feb;485:153415. doi: 10.1016/j.tox.2022.153415. Epub 2023 Jan 2. PMID: 36603807.

357. Mozafarian N, Hashemipour M, Yazdi M, Hani Tabaei Zavareh M, Hovsepian S, Heidarpour M, Taheri E. The Association between Exposure to Air Pollution and Type 1 Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Adv Biomed Res.* 2022 Nov 28;11:103. doi: 10.4103/abr.abr_80_21. PMID: 36660754; PMCID: PMC9843592.
358. Li J, Liu F, Liang F, Yang Y, Lu X, Gu D. Air pollution exposure and vascular endothelial function: a systematic review and meta-analysis. *Environ Sci Pollut Res Int.* 2023 Mar;30(11):28525-28549. doi: 10.1007/s11356-023-25156-9. Epub 2023 Jan 27. PMID: 36702984.
359. Della Guardia L, Wang L. Fine particulate matter induces adipose tissue expansion and weight gain: Pathophysiology. *Obes Rev.* 2023 Apr;24(4):e13552. doi: 10.1111/obr.13552. Epub 2023 Jan 26. PMID: 36700515.
360. Wang X, Chen L, Cai M, Tian F, Zou H, Qian ZM, Zhang Z, Li H, Wang C, Howard SW, Peng Y, Zhang L, Bingheim E, Lin H, Zou Y. Air pollution associated with incidence and progression trajectory of chronic lung diseases: a population-based cohort study. *Thorax.* 2023 Feb 2;thorax-2022-219489. doi: 10.1136/thorax-2022-219489. Epub ahead of print. PMID: 36732083.
361. Yang M, Wu K, Wu Q, Huang C, Xu Z, Ho HC, Tao J, Zheng H, Hossain MZ, Zhang W, Wang N, Su H, Cheng J. A systematic review and meta-analysis of air pollution and angina pectoris attacks: identification of hazardous pollutant, short-term effect, and vulnerable population. *Environ Sci Pollut Res Int.* 2023 Feb 3. doi: 10.1007/s11356-023-25658-6. Epub ahead of print. PMID: 36735120.
362. Qiu X, Shi L, Kubzansky LD, Wei Y, Castro E, Li H, Weisskopf MG, Schwartz JD. Association of Long-term Exposure to Air Pollution With Late-Life Depression in Older Adults in the US. *JAMA Netw Open.* 2023 Feb 1;6(2):e2253668. doi: 10.1001/jamanetworkopen.2022.53668. PMID: 36763364; PMCID: PMC9918878.
363. Gong Y, Zhang X, Zhao X, Chang H, Zhang J, Gao Z, Mi Y, Chen Y, Zhang H, Huang C, Yu Z. Global ambient particulate matter pollution and neurodegenerative disorders: a systematic review of literature and meta-analysis. *Environ Sci Pollut Res Int.* 2023 Feb 10. doi: 10.1007/s11356-023-25731-0. Epub ahead of print. PMID: 36763275.
364. Alexeeff SE, Deosaransingh K, Van Den Eeden S, Schwartz J, Liao NS, Sidney S. Association of Long-term Exposure to Particulate Air Pollution With Cardiovascular Events in California. *JAMA Netw Open.* 2023 Feb 1;6(2):e230561. doi: 10.1001/jamanetworkopen.2023.0561. PMID: 36826819; PMCID: PMC9958530.
365. Dzekem BS, Aschebrook-Kilfoy B, Olopade CO. Air Pollution and Racial Disparities in Pregnancy Outcomes in the United States: A Systematic Review. *J Racial Ethn Health Disparities.* 2023 Mar 10. doi: 10.1007/s40615-023-01539-z. Epub ahead of print. PMID: 36897527.

366. Ronaldson A, Arias de la Torre J, Ashworth M, Hansell AL, Hotopf M, Mudway I, Stewart R, Dregan A, Bakolis I. Associations between air pollution and multimorbidity in the UK Biobank: A cross-sectional study. *Front Public Health*. 2022 Dec 2;10:1035415. doi: 10.3389/fpubh.2022.1035415. PMID: 36530697; PMCID: PMC9755180.
367. Weichenthal S, Pinault L, Christidis T, Burnett RT, Brook JR, Chu Y, Crouse DL, Erickson AC, Hystad P, Li C, Martin RV, Meng J, Pappin AJ, Tjepkema M, van Donkelaar A, Weagle CL, Brauer M. How low can you go? Air pollution affects mortality at very low levels. *Sci Adv*. 2022 Sep 30;8(39):eabo3381. doi: 10.1126/sciadv.abo3381. Epub 2022 Sep 28. PMID: 36170354; PMCID: PMC9519036.
368. Abolhasani E, Hachinski V, Ghazaleh N, Azarpazhooh MR, Mokhber N, Martin J. Air Pollution and Incidence of Dementia: A Systematic Review and Meta-analysis. *Neurology*. 2023 Jan 10;100(2):e242-e254. doi: 10.1212/WNL.0000000000201419. Epub 2022 Oct 26. PMID: 36288998.
369. Binter AC, Kusters MSW, van den Dries MA, Alonso L, Lubczyńska MJ, Hoek G, White T, Iñiguez C, Tiemeier H, Guxens M. Air pollution, white matter microstructure, and brain volumes: Periods of susceptibility from pregnancy to preadolescence. *Environ Pollut*. 2022 Nov 15;313:120109. doi: 10.1016/j.envpol.2022.120109. Epub 2022 Sep 22. PMID: 36155148.
370. Bailey MJ, Holzhausen EA, Morgan ZEM, Naik N, Shaffer JP, Liang D, Chang HH, Sarnat J, Sun S, Berger PK, Schmidt KA, Lurmann F, Goran MI, Alderete TL. Postnatal exposure to ambient air pollutants is associated with the composition of the infant gut microbiota at 6-months of age. *Gut Microbes*. 2022 Jan-Dec;14(1):2105096. doi: 10.1080/19490976.2022.2105096. PMID: 35968805; PMCID: PMC9466616.
371. Yu Z, et al. Ambient air pollution exposure linked to long COVID among young adults: a nested survey in a population-based cohort in Sweden. *The Lancet Regional Health/Europe*. Published: March 07, 2023 DOI: <https://doi.org/10.1016/j.lanepe.2023.100608>
372. Kim H, Kim WH, Kim YY, Park HY. Air Pollution and Central Nervous System Disease: A Review of the Impact of Fine Particulate Matter on Neurological Disorders. *Front Public Health*. 2020 Dec 16;8:575330. doi: 10.3389/fpubh.2020.575330. PMID: 33392129; PMCID: PMC7772244.
373. Johnson, N.M.; Hoffmann, A.R.; Behlen, J.C.; Lau, C.; Pendleton, D.; Harvey, N.; Shore, R.; Li, Y.; Chen, J.; Tian, Y.; et al. Air pollution and children's health-a review of adverse effects associated with prenatal exposure from fine to ultrafine particulate matter. *Environ. Health Prev. Med*. 2021, 26, 72.
374. Yuan X, et al. Maternal Exposure to PM2.5 and the Risk of Congenital Heart Defects in 1.4 Million Births: A Nationwide Surveillance-Based Study. *Circulation*, Vol. 147, No. 7. Originally

published 13 Feb 2023 <https://doi.org/10.1161/CIRCULATIONAHA.122.061245> Circulation. 2023;147:565–574

375. Kuiper IN, et al. Preconception air pollution exposure and early onset asthma and hay fever in the offspring. *European Respiratory Journal* Sep 2019, 54 (suppl 63) PA4453; DOI: 10.1183/13993003.congress-2019.PA4453

376. Crump C. An overview of adult health outcomes after preterm birth. *Early Hum Dev.* 2020 Nov;150:105187. doi: 10.1016/j.earlhumdev.2020.105187. Epub 2020 Sep 9. PMID: 32948365; PMCID: PMC7480736.

377. Aguilera, R., Corringham, T., Gershunov, A. et al. Wildfire smoke impacts respiratory health more than fine particles from other sources: observational evidence from Southern California. *Nat Commun* 12, 1493 (2021). <https://doi.org/10.1038/s41467-021-21708-0>

378. Schünemann HJ, Dorn J, Grant BJ, Winkelstein W Jr, Trevisan M. Pulmonary function is a long-term predictor of mortality in the general population: 29-year follow-up of the Buffalo Health Study. *Chest.* 2000 Sep;118(3):656–64. doi: 10.1378/chest.118.3.656. PMID: 10988186.

379. Yu Z, et al. Associations of improved air quality with lung function growth from childhood to adulthood: The BAMSE study. *European Respiratory Journal*, 2023; 2201783 DOI: 10.1183/13993003.01783-2022

380. Tibuakuu M, Michos ED, Navas-Acien A, Jones MR. Air Pollution and Cardiovascular Disease: A Focus on Vulnerable Populations Worldwide. *Curr Epidemiol Rep.* 2018 Dec;5(4):370–378. doi: 10.1007/s40471-018-0166-8. Epub 2018 Sep 19. PMID: 30931239; PMCID: PMC6435302.

381. Zhang J, Wang X, Yan M, Shan A, Wang C, Yang X, Tang N. Sex Differences in Cardiovascular Risk Associated With Long-Term PM_{2.5} Exposure: A Systematic Review and Meta-Analysis of Cohort Studies. *Front Public Health.* 2022 Feb 2;10:802167. doi: 10.3389/fpubh.2022.802167. PMID: 35186842; PMCID: PMC8847390.

382. <https://give.brighamandwomens.org/7-differences-between-men-and-women/>

383. <https://www.propublica.org/article/toxic-chemicals-epa-regulation-failures>

384. OECD, *The Economic Consequences of Outdoor Air Pollution* 2016

385. US EPA, “The benefits and costs of the Clean Air Act from 1990 to 2020. Final report – Rev. A,” Technical Report 2011.

386. OECD, *The Economic Consequences of Outdoor Air Pollution* 2016.

387. Graff Zivin, Joshua and Matthew Neidell, "Air pollution's hidden impacts," *Science*, 2018, 359 (6371), 39–40.
388. Graff Zivin, Joshua and Matthew Neidell, "The impact of pollution on worker productivity," *The American Economic Review*, 2012, 102 (7), 3652–3673.
389. Adhvaryu, Achyuta, Namrata Kala, and Anant Nyshadham, "Management and shocks to worker productivity," Technical Report, National Bureau of Economic Research 2019.
390. Chang, Tom, Joshua Graff Zivin, Tal Gross, and Matthew Neidell, "Particulate Pollution and the Productivity of Pear Packers," *American Economic Journal: Economic Policy*, 2016, 8 (3), 141–69.
391. Ebenstein, Avraham, Victor Lavy, and Sefi Roth, "The long-run economic consequences of high-stakes examinations: evidence from transitory variation in pollution," *American Economic Journal: Applied Economics*, 2016, 8 (4), 36–65.
392. Heyes, Anthony, Matthew Neidell, and Soodeh Saberian, "The Effect of Air Pollution on Investor Behavior: Evidence from the S&P 500," Technical Report 22753, National Bureau of Economic Research 2016.
393. Fu, Shihe, V Brian Viard, and Peng Zhang, "Air quality and manufacturing firm productivity: comprehensive evidence from China," 2017.
394. Dechezlepretre, Antoine; Rivers, Nicholas; Stadler, Balazs, The economic cost of air pollution: Evidence from Europe. November 2, 2020.
395. Fu, Shihe, V Brian Viard, and Peng Zhang, "Air quality and manufacturing firm productivity: comprehensive evidence from China," 2017.
396. Borgschulte, Mark, David Molitor, and Eric Zou, "Air pollution and the labor market: Evidence from wildfire smoke," Technical Report, Technical report. Working Paper 2020.
397. Reilly, Sean, "EPA blueprint: Soot proposal would affect Calif. the most," *Greenwire*, republished in the *E&E News*, January 9, 2023, available at <https://www.eenews.net/articles/epa-blueprint-soot-proposal-would-affect-calif-the-most/>.
398. American Lung Association, State of the Air, Reports Cards tab, available at <https://www.lung.org/research/sota/city-rankings/states/utah/salt-lake>

399. IQAir, Air quality index (AQI) and PM2.5 air pollution in Salt Lake City, available at <https://www.lung.org/research/sota/city-rankings/states/utah/salt-lake>.

400. *Id.*

401. Utah Department of Environmental Quality, Metrics, Metrics: Air Quality tab, available at <https://deq.utah.gov/metrics/metrics-air-quality>.

402. IQAir, Air quality index (AQI) and PM2.5 air pollution in Salt Lake City, available at <https://www.lung.org/research/sota/city-rankings/states/utah/salt-lake>.

403. Utah Department of Environmental Quality, Metrics, Metrics: Air Quality tab, available at <https://deq.utah.gov/metrics/metrics-air-quality>.

404. See https://en.wikipedia.org/wiki/Human_Development_Index. and https://en.wikipedia.org/wiki/United_Nations_Development_Programme,

405. United State Census Bureau, Utah: 2020 Census, available at <https://www.census.gov/library/stories/state-by-state/utah-population-change-between-census-decade.html>.

406. FRED, Economic Data, St. Louis Fed, Gross Domestic Product: All Industry Total in Utah, available at <https://fred.stlouisfed.org/series/UTNGSP>.

407. Errigo, Isabella, et al., Human Health and Economic Costs of Air Pollution in Utah: An Expert Assessment, *Atmosphere* 2020, 11(11), 1238; <https://doi.org/10.3390/atmos11111238>.

