Exhibit B — Medscape (2024). Noise Pollution and Chronic Disease Slideshow. https://reference.medscape.com/slideshow/Noise-Pollution-Chronic-Disease-6019132

Pollution and Cardiovascular Disease

Increasing evidence shows that various forms of pollution, including noise, air, water, soil, and light, are linked to an increased risk of cardiovascular morbidity and mortality.[1,2] In 2022, the *Lancet* Commission progress report on pollution and health found that pollution continued to account for 9 million deaths per year — or 1 in 6 deaths worldwide — stating that "the impact of pollution on health remains much greater than that of war, terrorism, malaria, HIV, tuberculosis, drugs, and alcohol, and the number of deaths caused by pollution are on par with those caused by smoking."[3]

Given that cardiovascular disease (CVD) is the single largest contributor to the burden of noncommunicable disease, the cardiovascular consequences of pollution in all its forms have a significant unfavorable impact on global health.[4]

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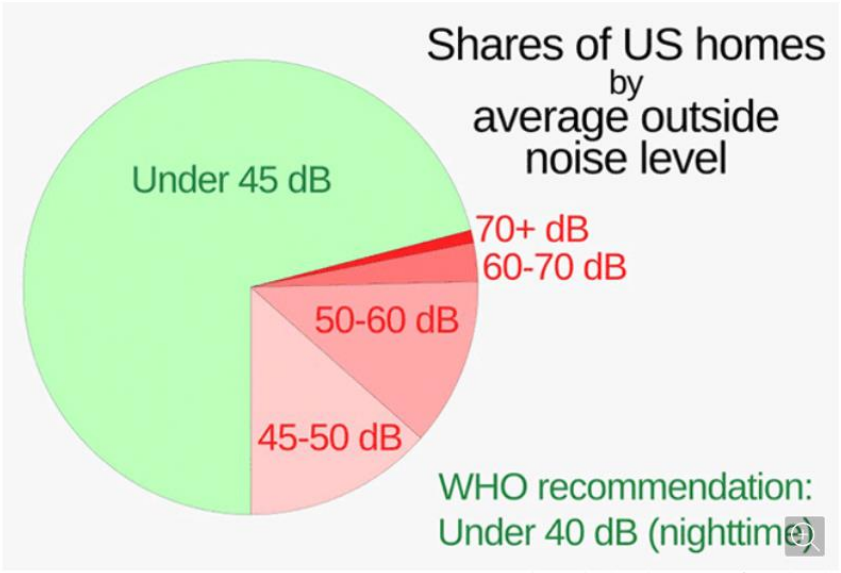

Average outside noise levels, US homes. Image from Wikimedia

The Burden of Noise Pollution

Noise Pollution and Chronic Disease

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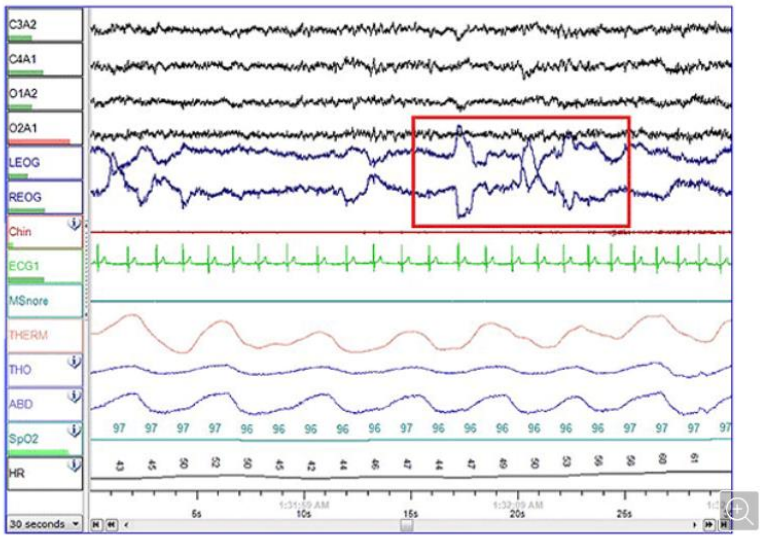
The Burden of Noise Pollution

Noise pollution has only recently been recognized as a form of pollution that contributes to the risk of chronic diseases, such as CVD. A substantial number of people worldwide are now exposed to high noise levels; for instance, in 2020, the European Environment Agency (EEA) reported that at least 20% of the population in the European Union lives in settings where traffic noise levels are harmful to health.[5] According to the EEA report, an estimated 113 million people are affected by long-term traffic noise levels of at least 55 dB throughout the day and night, and 22 million are exposed to high levels of railway noise, with another 4 million exposed to high levels of aircraft noise and slightly less than 1 million subjected to high levels of industrial noise pollution.[5]



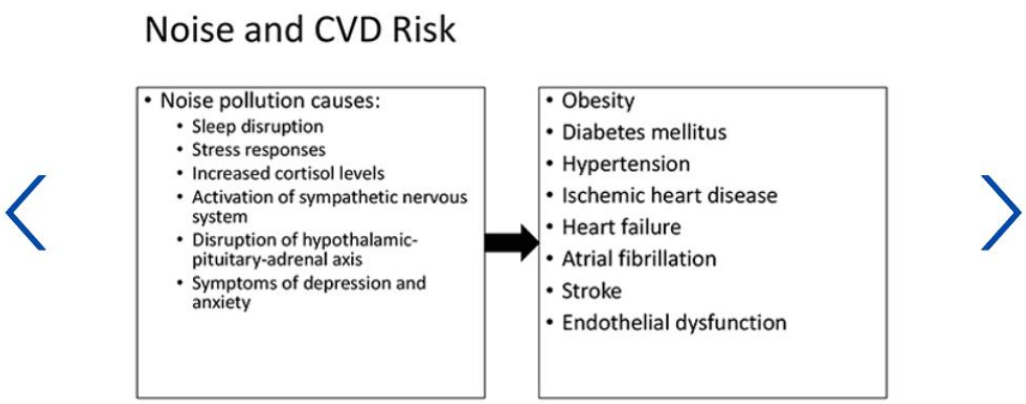
Polysomnograph demonstrating REM sleep (red box). Image from Wikimedia

Noise Pollution and Sleep Disturbance

Polysomnograph demonstrating REM sleep (red box). Image from Wikimedia

Noise Pollution and Sleep Disturbance

Nighttime noise levels at or above 50 dB can cause sleep disturbance, and the link between disturbed sleep and poor CVD outcomes has been extensively studied and demonstrated.[1] The indirect pathway of the noise stress concept introduced by Wolfgang Babisch describes the stress reaction in response to noise levels between 50 and 60 dB.[6] Although direct hearing damage occurs at sound pressure levels above 100 dB, the lower noise levels that activate the indirect pathway can disturb communication and sleep. This, in turn, can lead to emotional stress, which is associated with increased cortisol levels and activation of the sympathetic nervous system, all of which increase CVD risk.[1,6]



Noise pollution causes physiologic responses that increase CVD risk. Image from Dr Yasmine Ali

Noise Pollution and Chronic Disease

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Noise pollution causes physiologic responses that increase CVD risk. Image from Dr Yasmine Ali

Noise and CVD Risk Factors

Noise pollution increases CVD risk through the development of CVD risk factors as well as CVD itself. As previously noted, sleep disruption due to noise pollution is associated with the development of obesity, diabetes, hypertension, and atrial fibrillation.[6] The World Health Organization has also reported that the most significant connection between noise pollution and CVD is the development of ischemic heart disease.[6,7] There is also a moderate association between noise and heart failure as well as stroke.[7] Studies have demonstrated an association between the incidence and mortality of heart failure and transportation noise from road traffic, railway, and aircraft, ranging from a 2% to 8% increased risk per 10 dB.[6]

Noise Pollution and Chronic Disease

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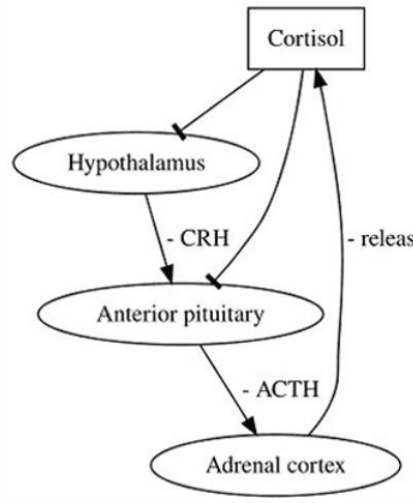

Hypothalamic-pituitary-adrenal axis. Image from Wikimedia

Noise Pollution and Chronic Disease

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Hypothalamic-pituitary-adrenal axis. Image from Wikimedia

Noise and Metabolic Risk Factors

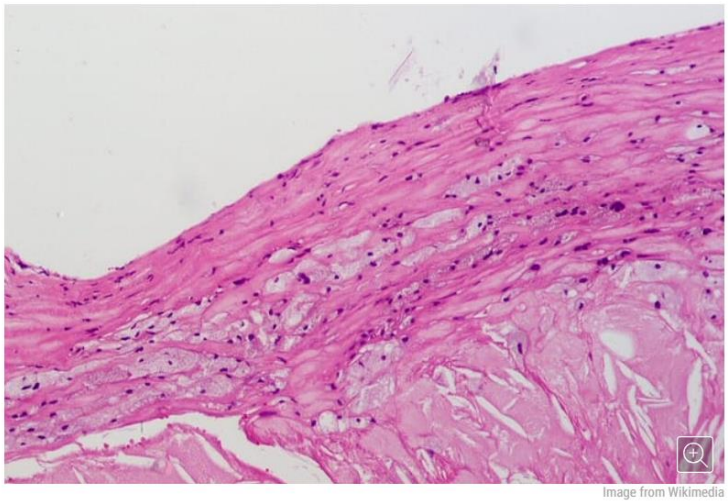
Both psychological stress and sleep disturbance caused by noise pollution can disrupt the hypothalamic-pituitary-adrenal (HPA) axis, leading to increased serum cortisol, which in turn can result in metabolic disease.[1,6] Chronic elevation of cortisol promotes visceral adiposity, insulin resistance, and dyslipidemia through enhanced gluconeogenesis and lipogenesis while simultaneously impairing glucose uptake in peripheral tissues.

Additionally, sustained HPA axis activation contributes to endothelial dysfunction and increased sympathetic nervous system activity, creating a pathophysiologic cascade that elevates cardiovascular risk independent of traditional risk factors.[1,8]

Symptoms of diabetes. Image from Wikimedia

Noise Exposure Increases Risk of Diabetes

Given the disruption of the HPA axis and resulting insulin resistance with impaired glucose uptake in peripheral tissues, it is unsurprising that the risk of type 2 diabetes, a known risk factor for CVD, is also increased by noise exposure.[1] A meta-analysis of observational studies found a 6% increase in diabetes risk per 5 dB increase in noise exposure, with particularly strong associations for aircraft noise (17% increase per 5 dB) and road traffic noise (7% increase per 5 dB).[9]



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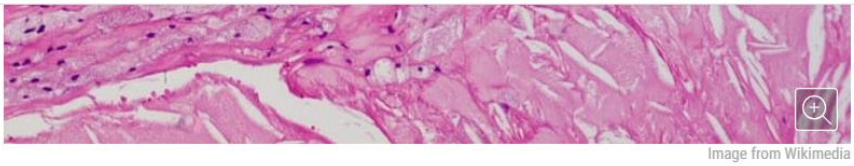

Image from Wikimedia

Noise Causes Endothelial Dysfunction

Noise exposure also causes endothelial dysfunction and resulting atherosclerosis through the mechanisms noted above and the development of arterial stiffness and worsened hypertension.[1] This is compounded by sleep disruption caused by excess noise exposure and by metabolic dysfunction caused by the sleep disruption, as well as by inflammation and oxidative stress resulting from all of the above.[10] Oxidative stress has been implicated as an underlying mechanism of the endothelial dysfunction caused by aircraft and railway noise, and a finding that this dysfunction responds to the antioxidant vitamin C.[1]

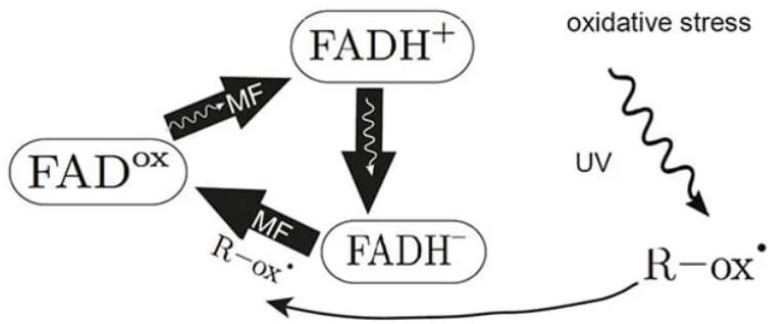

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Image from Wikimedia

Oxidative Stress From Noise Pollution

Prolonged exposure to noise-induced stress causes oxidative stress and chronic inflammation, which are involved in the progression of noise-induced vascular dysfunction, circadian rhythm disruption, mitochondrial dysfunction, cell death, and accelerated aging, all of which contribute to increased CVD risk.[10] Oxidative stress and inflammation have been found to contribute to traffic noise-induced vascular and cerebral dysfunction through uncoupling of nitric oxide synthases.[11]

Noise Pollution and Chronic Disease

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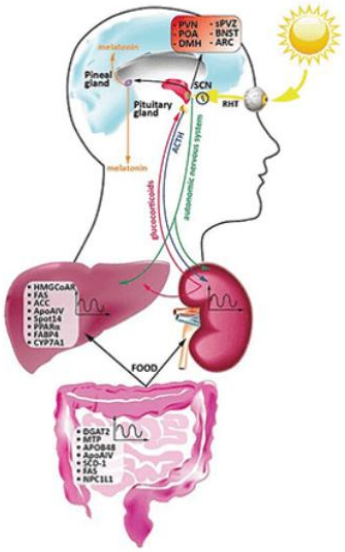

Noise pollution disrupts the interplay between the central and peripheral circadian clocks and the autonomic nervous system. Image from Wikimedia/National Institutes of Health

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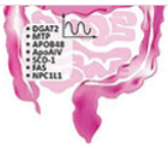

Noise pollution disrupts the interplay between the central and peripheral circadian clocks and the autonomic nervous system. Image from Wikimedia/National Institutes of Health

Noise Pollution Disrupts Circadian Rhythm

Mechanistic studies have found that transportation noise causes disturbances of the cerebral and vascular circadian rhythm. Dysregulation of circadian clock genes in the aorta and kidney after noise exposure has been observed, along with increased DNA-methylation and upregulation of pathways related to inflammation and immune responses.[1,12]

Noise Pollution and Chronic Disease

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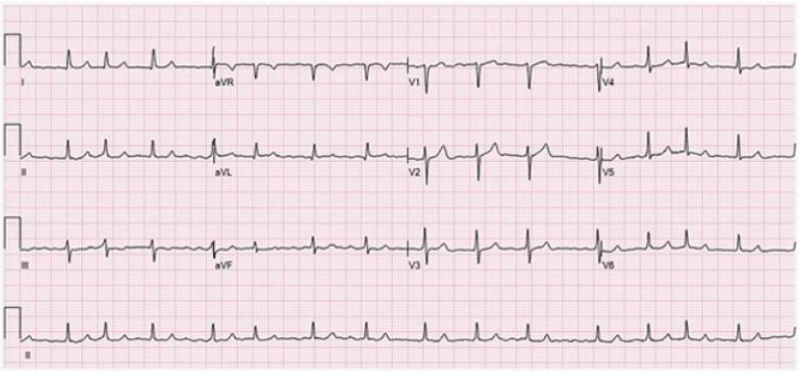

Atrial fibrillation with controlled ventricular response. Image from Wikimedia

Noise Pollution and Chronic Disease

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Atrial fibrillation with controlled ventricular response. Image from Wikimedia

Noise Exposure and Atrial Fibrillation

Sleep disruption, psychological stress, metabolic dysfunction, hypertension, and endothelial and vascular dysfunction all resulting from noise pollution cause an increased risk of atrial fibrillation.[1] A meta-analysis of cohort studies demonstrated that exposure to the highest levels of environmental noise was associated with a significant 5% increased risk of atrial fibrillation, with each 10 dB increment in noise exposure conferring an additional 1%-2% increase in risk.[13]

Noise Pollution and Chronic Disease

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Social determinants of health. Image from CDC

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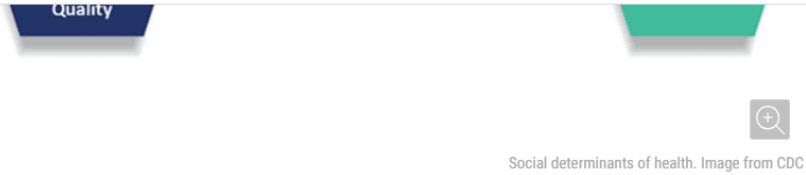

Social determinants of health. Image from CDC

Sociodemographic Disparities in Noise Exposure

Significant sociodemographic disparities exist in noise exposure. Studies show associations between noise levels and neighborhood racial and economic composition, with noise pollution being found at greater levels in historically redlined areas and communities of color,[14] further compounding cardiovascular health disparities created by social determinants of health.[15] Experts suggest these findings "can inform efforts to address these disparities through noise pollution policymaking." [14]

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iv. Image from Dr Yasmine Ali

v. https://commons.wikimedia.org/wiki/File:HPA-axis_-_Hypothalamus,_Pituitary_and_Adrenal_cortex_Axis.svg

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