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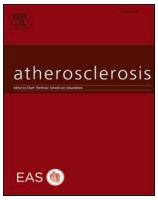

Transportation noise and the cardiometabolic risk

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ABSTRACT

Transportation noise is a widespread and often underestimated environmental pollutant, posing a substantial health risk particularly in urban areas. In contrast to air pollution, the health effects of noise pollution are less extensively documented. Defined as an unwanted and/or harmful sound, noise pollution affects over 20 % of the European Union (EU) population, contributing to an estimated 12,000 premature deaths and 48,000 new cases of ischemic heart disease annually.

Recent epidemiological evidence strengthens the link between transportation noise and cardiovascular disease (CVD). A 2024 Umbrella + review with subsequent meta-analyses found that road traffic noise was associated with risk of CVD, more specifically a 4.1 % higher risk for ischemic heart disease, 4.6 % for stroke, and 4.4 % for heart failure per 10 dB(A). Translational and experimental studies have investigated the biological mechanisms behind noise-induced cardiovascular damage, showing that noise impacts stress and sleep pathways. Human studies reveal that nighttime noise impairs vascular function, elevates stress hormone levels, and triggers inflammation and oxidative stress, particularly in individuals with pre-existing CVD. Animal research corroborates these findings, demonstrating that noise exposure leads to endothelial dysfunction, elevated blood pressure, and oxidative stress through mechanisms shared with traditional cardiovascular risk factors. Mitigation strategies are crucial to reducing the health impacts of environmental noise. For road traffic, transitioning to electric vehicles offers minimal noise reduction, necessitating measures such as noise-reducing asphalt, low-noise tyres, and changes in urban infrastructure, whereas for aircraft noise nighttime flight bans and optimized flight paths are important tools for reducing noise exposure. Addressing co-exposure to noise and air pollution is essential for a comprehensive approach to mitigating the environmental burden on cardiovascular health.

1. Introduction

Over recent decades, the global burden of disease has transitioned from predominantly communicable diseases to chronic non-communicable conditions, such as cardiovascular disease (CVD). While classical risk factors—like diabetes, smoking, and arterial hypertension—have attracted much attention, environmental stressors, including noise and air pollution, are increasingly recognized as significant contributors to CVD development [1,2]. Among these, transportation noise from road traffic, railways, and aircraft poses a pervasive and underestimated health risk.

Noise affects health through complex and multifaceted mechanisms. The "noise reaction model" proposed by Babisch describes an indirect pathway where noise exposure disrupts sleep, communication, and daily activities, triggering annoyance and chronic stress responses via activation of the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system [3]. These stress responses involve the release of cortisol and catecholamines, which promote inflammation, oxidative stress, and endothelial dysfunction [4]. Over time, these effects manifest in increased blood pressure, hyperlipidemia, and hyperglycemia, leading to higher risk of coronary artery disease, heart failure, and stroke [5–7] (Fig. 1).

Epidemiological data reinforce the severity of noise-induced health outcomes. The European Environment Agency (EEA) estimates that high levels of road traffic noise affect at least 20 % of the European Union's urban population, with 113 million individuals exposed to day-evening-night traffic noise levels (L_{den}) of ≥55 dB(A) and 6.5 million experiencing chronic sleep disturbances annually [8]. Nighttime noise (L_{night})

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above 50 dB(A) is particularly harmful, as it disrupts sleep—a critical regulator of cardiovascular health—and has been associated with an increased risk of ischemic heart disease (IHD), stroke, and Takotsubo syndrome, a stress-induced cardiomyopathy [9,10]. However, it is important to keep in mind that recent national studies from Denmark and Switzerland have found no lower threshold for the adverse health effects of transportation noise, indicating that also chronic noise exposure below 50 dB(A) will increase the risk of non-communicable diseases [11–13].

The mechanisms of noise-induced vascular damage are still under investigation, but studies suggest that chronic noise exposure triggers oxidative stress, endothelial dysfunction, and inflammation. Noise reduces nitric oxide bioavailability, essential for vascular health, and heightens sensitivity to stress-induced vasoconstriction, impairing blood flow [14,15]. Furthermore, noise-induced inflammatory responses involve elevated interleukins (e.g., IL-6, IL-1β) and pro-inflammatory monocytes, exacerbating cardiovascular and metabolic dysfunction [16]. The synergistic interaction between noise and traditional risk factors like hypertension and diabetes suggests shared pathogenic pathways that will amplify their combined impact [4].

Despite the significant health burden noise imposes, it remains strongly underrepresented in prevention guidelines from major cardiovascular organizations, including the American Heart Association and the European Society of Cardiology [17]. This is concerning, given projections of increasing urban noise exposure due to population growth and heightened mobility, estimating a 7.8 % rise in road noise and an 11.8 % increase in railway noise exposure by 2030 [8].

The indirect pathways through which noise contributes to cardiovascular health risks—spanning stress responses, and disturbance of sleep—underscore the urgent need for targeted public health interventions. Addressing these challenges requires a multidisciplinary approach, integrating policymakers, researchers, and healthcare professionals to safeguard cardiovascular health in an increasingly noisy world. Effective mitigation strategies are critical for reducing the health burden of noise. These include integration of noise mitigation in urban planning such as optimized land use, improved building insulation, and quieter transportation technologies. However, substantial knowledge gaps remain, particularly regarding the long-term cardiovascular effects of noise in populations outside Europe and the United States, particularly its interaction with other environmental stressors.

With this review, we will summarize the epidemiological evidence on chronic transportation noise exposure and risk of cardiovascular disease as well as provide insight concerning the pathophysiological mechanisms. To this end we will address the most appropriate mitigation therapies, the gaps of knowledge, the need for further studies and the political and societal implications.

2. Historical perspective on noise and adverse health effects

In 1910, Robert Koch, a visionary scientist, presciently stated, “One day mankind will have to fight the burden of noise as relentless as the pest and cholera”. Early recognition of the broader health implications from noise exposure came from Karl D. Kryter’s *Effects of Noise in Man* [18]. Kryter described non-auditory effects, such as impacts on sleep, pain perception, circulation, and work performance, attributing these to activations of the autonomic nervous system, reticular nervous system, and brain centers regulating intellectual performance [18].

Empirical studies supported these concepts. Jansen et al. [19] showed that noise exposure during exercise caused vasoconstriction and variable cardiovascular responses, regardless of whether the stimulus was noise or music [20]. Levi et al. established increased catecholamine excretion in industrial workers, indicating heightened stress [21]. Jansen et al. further reported cardiovascular effects, including peripheral circulation and heart problems, in German industrial workers exposed to

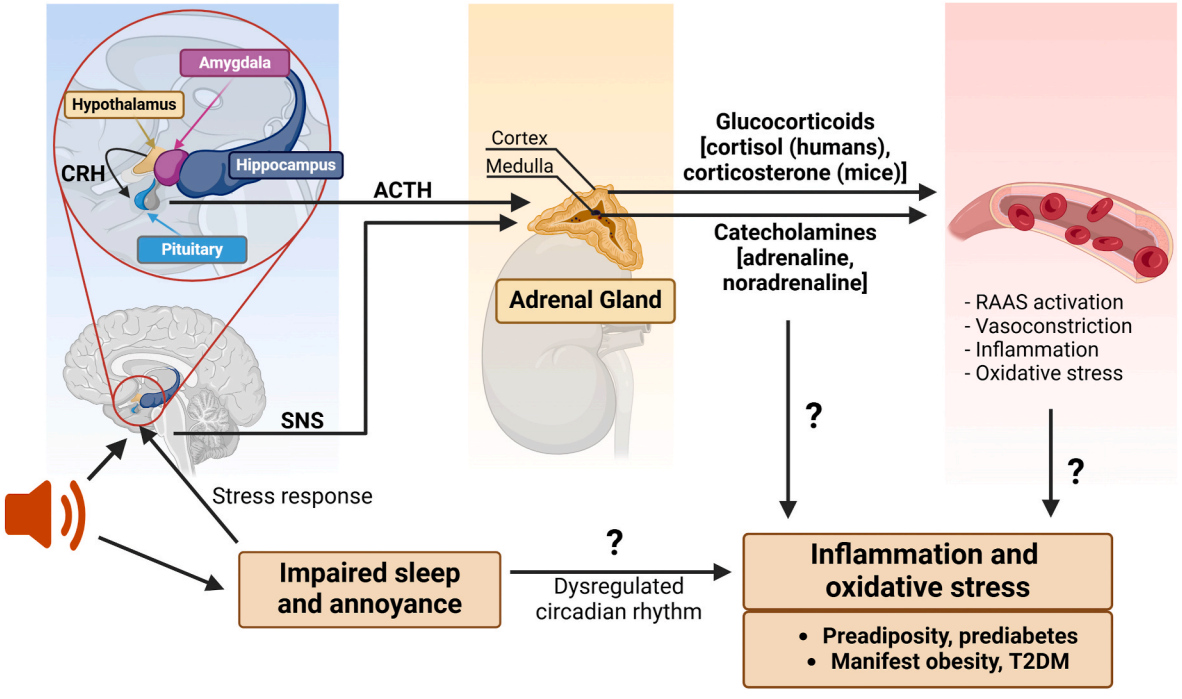

Fig. 1. Pathophysiology of noise-induced cardiovascular, neuropsychiatric and metabolic disease. Neuronal activation (arousal) induced by noise exposure triggers signalling via the hypothalamic–pituitary–adrenal (HPA) axis and sympathetic nervous system (SNS) [4,96]. The release of glucocorticoids and catecholamines, in turn, leads to the activation of other neurohormonal pathways (such as the renin-angiotensin–aldosterone (RAAS) system) as well as to dysregulated circadian rhythm (altered expression of central clock genes such as period 1, cryptochrome 1 and Bmal1/Arntl) and increased inflammation and oxidative stress, which can ultimately have adverse effects on cardiometabolic function and molecular targets [97,98]. Alternatively, noise-induced sleep disorders may have a direct impact on inflammation and oxidative stress. ACTH, adrenocorticotropic hormone; CRH, corticotropin-releasing-hormone; RAAS, renin-angiotensin-aldosterone system; SNS, sympathetic nervous system; T2DM, type 2 diabetes mellitus. The image was created using Biorender.com and modified from Ref. [99] with permission.

high noise levels [22].

Experimental research in the 1990s demonstrated noise-induced stress hormone release [3], notably in response to aircraft [23,24] and road traffic noise [25,26]. Intermittent and low-frequency noise elicited more robust neuroendocrine responses than steady noise [27,28]. Animal studies, though limited, confirmed similar effects, with increased blood pressure observed in white noise-exposed monkeys and rats [29,30]. While early research focused on high-level occupational and military noise, recent studies on the effects of chronic low-level environmental noise on CVD highlight circadian rhythm dysregulation, inflammation and oxidative stress as a critical mechanisms, paving the way for new therapeutic strategies [4].

3. Epidemiological evidence

3.1. Transportation noise and cardiovascular disease and death

Growing evidence highlights the impact of environmental noise on cardiovascular health. Meta-analyses from the WHO's Environmental Noise Guidelines for the European Region (WHO ENG) from 2018 included epidemiological studies up to 2015 [31]. A 2023 Umbrella + review updated these findings by integrating high-quality systematic reviews and original studies published between 2015 and mid-2023 [32]. Only studies meeting stringent criteria, such as reliable exposure assessment methods and robust confounding adjustment, were included. For mortality and incident CVD, cohort studies were prioritised, while case-control and cross-sectional studies were considered for hypertension if population-based and methodologically sound [32]. Meta-analyses based on the Umbrella + review provided updated exposure-response functions for CVD and mortality. Below is a summary of the key findings.

3.2. Cardiovascular mortality

The Umbrella + review identified 61 potentially eligible studies, of which 12 prospective cohort studies on road, railway, and aircraft noise qualified for meta-analysis. Road traffic noise was associated with cardiovascular mortality with a pooled relative risk (RR) of 1.05 (95 % CI: 1.02–1.07) per 10 dB(A) [32]. Railway and aircraft noise showed minimal or no effect on cardiovascular mortality, but this was based on very limited data. Short-term noise exposure may acutely trigger cardiovascular death. A Swiss case-crossover study reported odds ratios (ORs) of 1.33 (95 % CI: 1.05–1.67) and 1.44 (95 % CI: 1.03–2.04) for nighttime aircraft noise levels of 40–50 dB and >50 dB, respectively, within 2 h before CVD death [33]. This suggests both chronic and acute effects of noise on CVD mortality.

3.3. Ischemic heart disease (IHD)

The WHO ENG review identified a significant association between road traffic noise and IHD incidence, with an RR of 1.08 (95 % CI: 1.01–1.15) per 10 dB(A) [34]. Subsequent studies have strengthened this evidence. A pooled analysis of Danish and Swedish cohorts and a Danish nationwide study involving over 2.5 million participants reported hazard ratios (HRs) of 1.03 (95 % CI: 1.00–1.05) and 1.05 (95 % CI: 1.04–1.06), respectively, for road traffic noise [12,35]. Results for railway noise show less consistent results. A meta-analysis combining the WHO ENG review with new data estimated an RR of 1.04 (95 % CI: 1.02–1.06) per 10 dB(A) for road traffic noise. Aircraft and railway noise had weaker associations, with RRs of 1.01 (95 % CI: 0.99–1.03) and 1.00 (95 % CI: 0.93–1.06), respectively [32].

3.4. Stroke

The WHO ENG review identified only one cohort study linking road traffic noise to stroke, reporting an HR of 1.14 (95 % CI: 1.03–1.25) [31]. Subsequent research, including a pooled analysis of Danish and Swedish cohorts, reported an HR of 1.06 (95 % CI: 1.03–1.08) per 10 dB (A) [36]. Based on six cohort studies, the Umbrella + review confirmed this association, finding an RR of 1.05 (95 % CI: 1.01–1.08) for road traffic noise. No significant associations were observed for aircraft or railway noise [32].

3.5. Heart failure

The WHO ENG did not assess heart failure risk from noise. However, recent studies have found road traffic noise to be a risk factor for heart failure [37] and the updated meta-analysis from the Umbrella + review calculated an RR of 1.04 (95 % CI: 1.02–1.07) for road traffic noise. Evidence for railway and aircraft noise remains limited and inconsistent [12,32].

3.6. Arrhythmia

Few studies have explored the link between noise and arrhythmias. A Danish cohort study reported modest associations with road, railway, and aircraft noise, with 1–2% risk increases per 10 dB(A) [38]. The Umbrella + meta-analysis found an RR of 1.01 (95 % CI: 1.00–1.01) for road traffic noise and 1.21 (95 % CI: 0.70–2.08) for aircraft noise [32]. Evidence for railway noise remains sparse.

3.7. Conclusions on cardiovascular risk

The Umbrella + review showed that road traffic noise is associated with higher risk of IHD, stroke, and heart failure, with a joint RR for all CVDs of 1.032 per 10 dB(A) [32]. Evidence for railway and aircraft noise is weaker, potentially due to masking by road traffic noise and lack of studies. Intervention studies are needed to confirm causal relationships and evaluate noise mitigation strategies.

3.8. Lower effect threshold of noise

It remains uncertain what the threshold below which noise has no health effects is. The EU Noise Directive uses 55 dB(A) L_{den} as a threshold for all transportation sources, while WHO recommends 53 dB (A) for road traffic noise and 45 dB(A) for aircraft noise (L_{den}) [31]. Recent large cohort studies suggest that health effects may occur at levels as low as 40–45 dB(A), including stroke, heart failure, cardiovascular mortality and diabetes (Fig. 2) [11,36,39,40]. Determination of this threshold is critical for health impact assessments and policy-making. Health impact assessments in Denmark and Switzerland reveal that lowering the effect threshold from 55 dB(A) to 45 dB(A) triples the estimated number of noise-related IHD and CVD deaths, underscoring the importance of precise threshold identification [41,42].

3.9. Arterial hypertension

A 2021 review evaluated transportation noise in relation to hypertension, deriving pooled estimates based on noise sources and study types [43]. While road traffic noise showed no association in cohort and case-control studies, cross-sectional studies reported a 9 % increased odds per 10 dB(A). Aircraft and railway noise showed no associations. Subsequent studies have provided mixed findings. Two U.S.-based studies found no significant risk for individuals exposed to over 45 dB (A) versus under 45 dB(A) [44,45]. In contrast, a French study reported a HR of 1.36 (95 % CI: 1.02–1.82) per 10 dB(A) L_{den} [46]. Meta-analyses pooling data from various studies suggested that transportation noise marginally increases hypertension risk, with an RR of 1.04 for road noise and 1.03 for aircraft noise per 10 dB(A) [32,43]. Additional longitudinal research is needed.

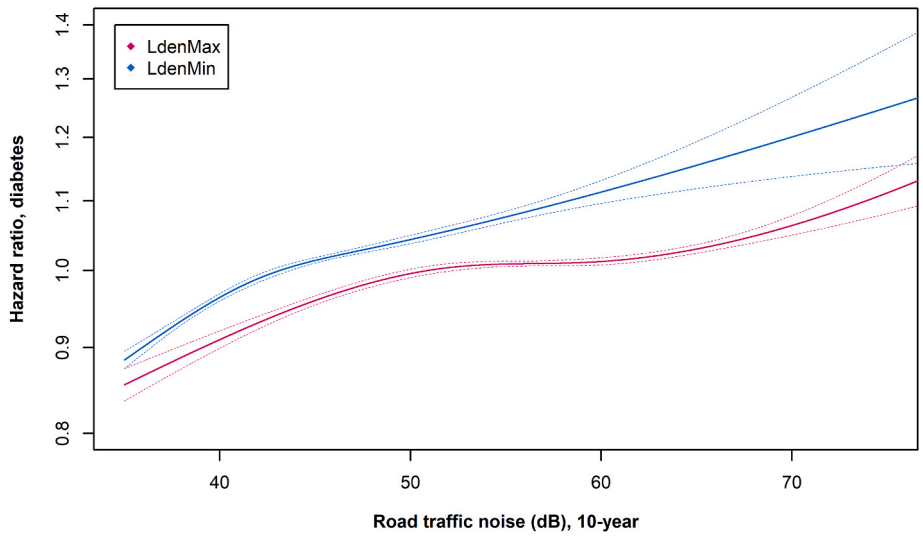

Fig. 2. Association between 10-year mean exposure to road traffic noise at the most (pink line) and at the least (blue line) exposed façade and risk of type 2 diabetes in a cohort covering all of Denmark (3.56 million persons ≥35 years old). Graphs created *de novo* based on the population described in Ref. [47] and reused from Ref. [99] with permission. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

3.10. Diabetes and obesity

Type 2 diabetes and obesity, common CVD comorbidities, have been linked to transportation noise. Recent cohort studies consistently associate road traffic noise with higher diabetes risk, with a meta-analysis reporting an RR of 1.06 per 10 dB(A) [47] (Fig. 2). Studies examining noise exposure at the least-exposed façade—a proxy for bedroom exposure—found more robust associations with diabetes, implicating sleep disruption as a key mechanism [40,48]. Noise-induced endothelial dysfunction further contributes to adverse metabolic effects [49]. Evidence of an association between road traffic noise and adiposity is also emerging, observed in diverse populations, including children and pregnant women [50,51]. These findings suggest that adiposity may mediate noise-related cardiometabolic risks.

3.11. Mental health

Transportation noise also impacts mental health, which may mediate its relationship with CVD risk. A 2020 meta-analysis linked road traffic and aircraft noise to higher depression risks, with RRs of 1.03 and 1.12 per 10 dB(A), respectively [52]. Subsequent studies supported these findings, identifying links to depression, poorer mental well-being, and even suicide [53,54]. Noise annoyance emerged as a partial mediator of these effects [53,55]. Further high-quality prospective studies are essential.

3.12. Sleep disturbance

Sleep disruption, a well-established risk factor for CVD, is exacerbated by noise through arousal and reduced sleep continuity [56,57]. Nocturnal noise exposure impairs vascular function and prevents average nighttime blood pressure dipping, increasing long-term CVD risks [58,59]. Experimental studies reveal that intermittent noise during sleep exacerbates these effects [60]. Research suggests that nocturnal noise may elevate CVD risks through physiological arousal, warranting further investigation [33].

3.13. Noise annoyance

Noise annoyance, an early indicator of potential health risks, is influenced by acoustic and individual factors [61]. WHO guidelines highlight noise annoyance as a key factor in shaping noise policies [62]. Meta-analyses rank aircraft noise as the most annoying, with recent trends indicating rising annoyance levels [63,64]. Addressing annoyance may prevent subsequent health complications, though further research on annoyance as a mediator on the pathway between noise exposure and CVD are highly important to elucidate this.

3.14. Conclusion

In summary, transportation noise is associated with higher risk of diabetes and sleep disturbance, and potentially higher risk of hypertension, obesity, and mental disorders. Further longitudinal and mechanistic studies are needed to strengthen causal inferences and inform mitigation strategies.

4. Translational noise studies in humans

4.1. Noise-induced endothelial dysfunction and oxidative stress markers

Field investigations have demonstrated the adverse effects of nighttime aircraft and railway noise on vascular (endothelial) function, sleep quality, stress hormone release, and inflammatory markers, both in healthy individuals and those with CVD [14,58]. In one study, noise recorded near Düsseldorf Airport was replayed at varying frequencies (30 or 60 events per night) in participants' bedrooms. Exposure to an equivalent sound level (Leq) of 46.3 dB(A) with peaks at 60 dB(A) reduced sleep quality, increased adrenaline levels, and caused endothelial dysfunction, as indicated by impaired flow-mediated dilation (FMD) [14]. These findings were exacerbated by prior noise exposure, suggesting a priming effect rather than habituation.

Vitamin C administration significantly improved endothelial function, implicating reactive oxygen species (ROS) in noise-induced vascular damage. Elevated oxidative stress markers, such as 3-nitrotyrosine (3-NT) and 8-isoprostane, further supported the oxidative stress hypothesis [60]. The effects were particularly pronounced in CVD patients, who exhibited greater susceptibility to endothelial deterioration [58]. Comparable results were observed in studies on nocturnal railway noise, which impaired FMD and influenced plasma proteins associated with oxidative stress, inflammation, and fibrosis [65].

Further exploration of noise patterns showed that both infrequent loud and frequent less loud nighttime aircraft noise resulted in endothelial dysfunction, diastolic heart dysfunction, and altered biomarkers linked to oxidative stress and fibrosis [66]. These findings underscore

the pivotal role of ROS in vascular damage caused by transportation noise.

4.2. Noise-induced epigenetic and immune changes

Transportation noise has been linked to immune system alterations, with studies showing increased levels of interleukin-12 (IL-12) and high-sensitivity C-reactive protein (hsCRP), alongside reduced natural killer cell activity [67,68]. Also, long-term noise exposure in the Swiss SAPALDIA cohort has been associated with DNA methylation changes affecting inflammation pathways [69]. Chronic exposure to nocturnal train or road traffic noise increased arterial stiffness and was associated with subclinical atherosclerosis in participants with early arterial calcification [70,71]. These findings provide molecular and pathophysiological evidence linking noise to CVD.

5. Mechanistic noise studies in animals

5.1. Vascular dysfunction, inflammation and oxidative stress

Animal models have elucidated the mechanisms of noise-induced endothelial dysfunction. If not stated differentially, all noise-exposed mice were on a standard diet. Healthy mice (C57BL/6j) exposed to continuous aircraft noise (Leq 72 dB(A)) had elevated stress hormone levels, increased blood pressure, and vascular oxidative stress driven by NADPH oxidase (NOX-2), the phagocytic isoform mainly expressed in granulocytes and macrophages [15]. Noise exposure also uncoupled endothelial nitric oxide synthase (eNOS) in these mice through S-glutathionylation, thus impairing vascular nitric oxide bioavailability. These effects were absent in similar mice exposed to white noise under comparable conditions, suggesting that noise characteristics—beyond intensity—are critical [15]. Further studies in healthy mice revealed that noise induced microvascular constriction and inflammation, with leukocyte adhesion and oxidative stress normalized in NOX-2 (gp91phox) knockout mice [60,72]. This was also accompanied by elevated prominent inflammatory markers such as interleukins and immune cell markers of LysM-positive inflammatory myelomonocytic cells as confirmed by noise exposure of mice overexpressing a diphtheria toxin receptor in all LysM-positive immune cells (LysMCre^{iDTR}), a genetic tool used for ablation of myelomonocytic cells [73]. Similar mechanisms underlie vascular damage caused by traditional risk factors like diabetes and hypertension, suggesting a shared molecular pathomechanism between noise and other CVD risk factors [74,75]. Inflammation and oxidative stress also promote the progression of diabetes by impaired islet function, insulin activity and glucose homeostasis, increased advanced glycation end product (AGE) and associated receptor RAGE signalling, finally resulting in manifest diabetes and obesity (Fig. 3).

5.2. Gene dysregulation

Noise exposure of healthy mice (C57BL/6j) dysregulated gene networks associated with vascular integrity, including genes involved in TGF-β signalling, autophagy, and inflammation. RNA sequencing identified significant alterations in pathways such as NF-κB, circadian rhythm, and oxidative stress regulation in noise-exposed healthy mice [15,60]. Nighttime noise had a particularly detrimental effect on cardiovascular health, impairing Foxo3 signalling and exacerbating neuroinflammation [60].

5.3. Impact on circadian rhythms

Noise exposure of healthy mice (C57BL/6j) during sleep caused pronounced cardiovascular damage compared to exposure during

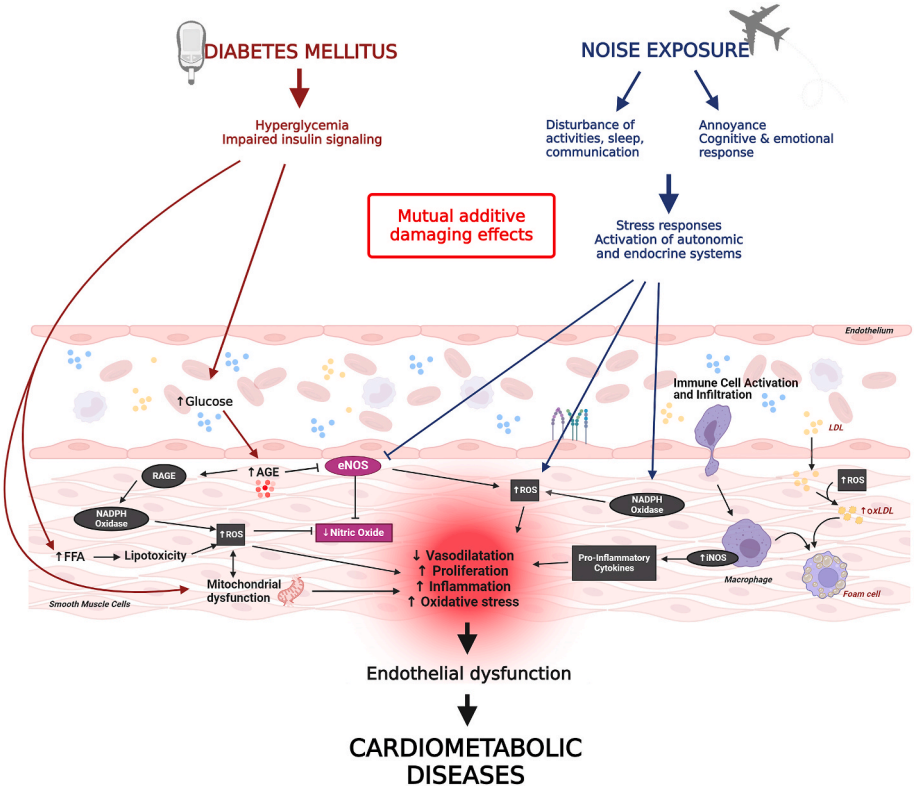

Fig. 3. Postulated central pathomechanisms and additive damage pathways by diabetes and noise exposure. Summarized by using pathways from previous reports and data of the present study. Abbreviations: AGE, advanced glycation end products; RAGE, receptor for AGE; FFA, free fatty acids; ROS, reactive oxygen species; eNOS, endothelial nitric oxide synthase; iNOS, inducible nitric oxide synthase; LDL, low density lipoprotein; oxLDL, oxidized LDL. Generated using biorender .com and reused from Ref. [75] with permission.

waking hours, highlighting the importance of circadian rhythm integrity [60]. Noise increased neurohormonal activity, oxidative stress, and inflammatory responses in both vascular and cerebral systems of these mice [60]. These findings emphasise the need for noise mitigation during sleep.

5.4. Prolonged noise exposure and cardiovascular recovery after noise stress

Chronic noise exposure of healthy mice (C57BL/6j) caused persistent endothelial dysfunction, elevated blood pressure, and oxidative stress, with no evidence of habituation over 28 days [76]. However, a cessation of noise for four days normalized endothelial dysfunction in large vessels of healthy mice (pre-exposed to noise for four days), although microvascular recovery was incomplete [77]. These results suggest that extended periods of quiet may be necessary to fully restore vascular health.

5.5. Noise worsens the cardiovascular side effects of diabetes mellitus

In a recent study, the cardiovascular effects of aircraft noise across three mouse models of diabetes mellitus were investigated, uncovering synergistic adverse effects among the three models (C57BL/6j mice with induction of T1DM by streptozotocin, T2DM by insulin receptor antagonist S961, and T2DM/metabolic syndrome by 20 weeks of high fat diet) [75]. Aircraft noise exacerbated hyperglycaemia in the model simulating metabolic syndrome through a high-fat diet and further impaired both macro- and microvascular endothelial function, evidenced by altered blood pressure and diminished isometric tension in arteries, in all three diabetes models (Fig. 4). This vascular dysfunction correlated with elevated oxidative stress, particularly superoxide production in the aorta, cerebral arterioles, and heart tissue in all diabetic mice, which was increased in an additive manner by aircraft noise exposure. Mitochondrial assessments revealed that diabetic conditions predominantly impaired respiratory chain function, with noise exposure amplifying the reduction in respiratory control ratio across all models. The demonstration that aircraft noise significantly worsens cardiometabolic outcomes in C57BL/6j mice with different forms of diabetes underscores the need for targeted mitigation strategies with special focus on vulnerable people, such as diabetics. These include stricter noise regulations, urban planning to reduce exposure, and medical interventions such as AMP-kinase activators and lifestyle modifications like physical activity and intermittent fasting [78].

5.6. Noise and the neuroendocrine axis

Noise-induced stress pathways involve the renin-angiotensin-aldosterone system (RAAS) and sympathetic nervous system (SNS),

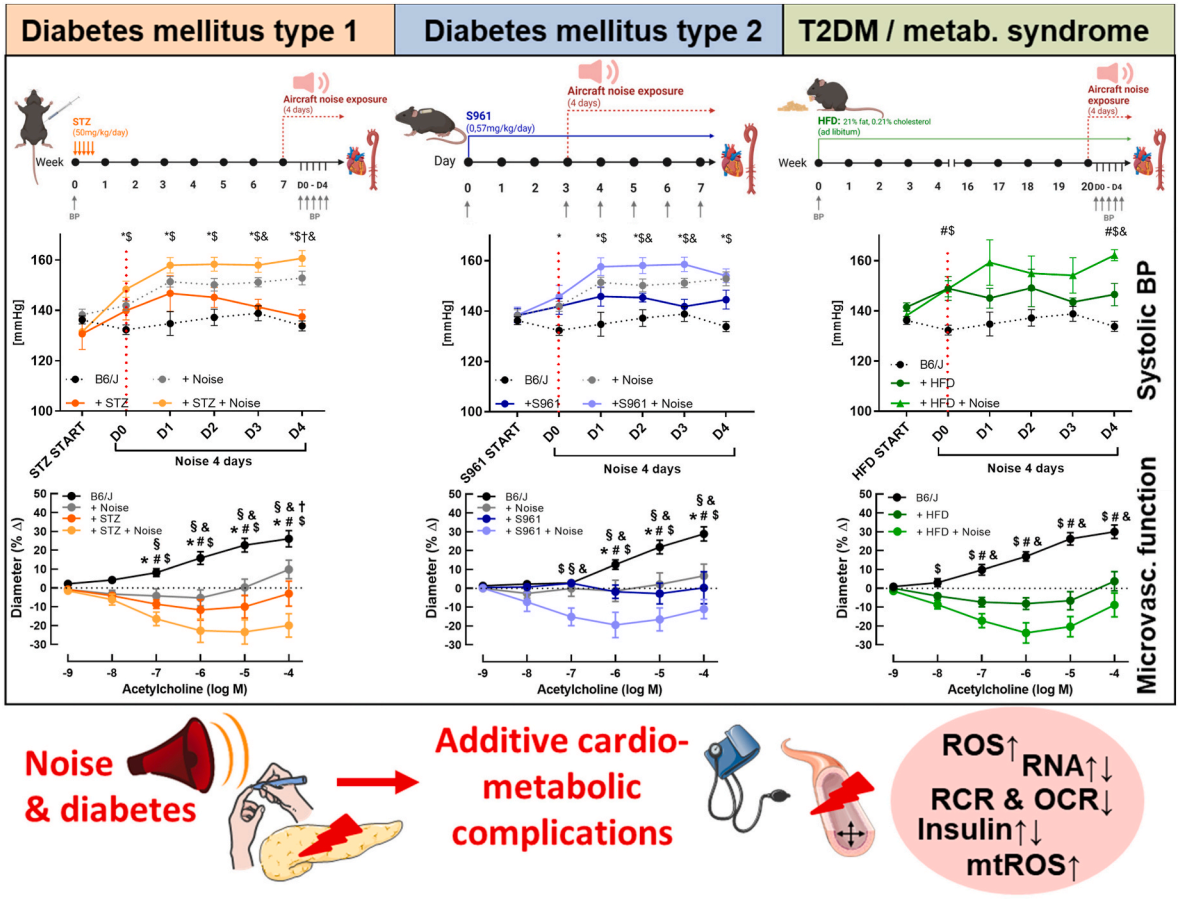

Fig. 4. Key findings in mouse models of diabetes with additional aircraft noise exposure. Noise effects in three models of diabetes: T1DM induced by the islet cell toxin streptozotocin (STZ), T2DM induced by insulin receptor blockade (S961) and metabolic syndrome/T2DM induced by high fat diet (HFD). *(upper panels)* Systolic blood pressure (BP) was measured using non-invasive tail-cuff plethysmography at the start of the treatment and D0-D4 of noise exposure. Noise elevated blood pressure and this increase was further exacerbated in mice with established diabetes. The control curves were merged from all three diabetes models and used in panels *A-C*; the noise only curves were merged from the STZ and S961 models and used in panels *A* and *B* (grey color). The control curves were merged over all models (black color, dotted lines). (*lower panels*) Endothelium-dependent dilation of cerebral arterioles was measured by video microscopy. Noise caused endothelial dysfunction and this increase was further exacerbated in mice with established diabetes. Adapted from Ref. [75] with permission. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

mediated by oxidative stress and NOX-2 activation as shown in healthy mice [15,79]. Noise exposure increased circulating levels of angiotensin-II, endothelin-1, and catecholamines, exacerbating vascular inflammation and oxidative stress [15], also typical features of classical arterial hypertension in rats [80]. Experimental human data highlight the pivotal role of the amygdala in linking noise exposure to stress-induced vascular inflammation and adverse cardiovascular events [81].

5.7. Noise and myocardial infraction

Noise preconditioning of mice, corresponding to a prior noise exposure, exacerbates cardiovascular responses to acute stressors like myocardial infarction (MI). Healthy mice C57BL/6j mice exposed to noise prior to induction of MI exhibited increased inflammatory cell infiltration, oxidative stress, infarct size and cardiac dysfunction [82]. In humans, individuals with high residential aircraft noise exposure had worse prognosis following MI, as evidenced by elevated inflammatory markers and more severely reduced left ventricular ejection fraction [82]. This was also mirrored in a field study by a higher risk by aircraft noise for recurrent cardiovascular events in patients with acute coronary syndrome than in healthy individuals [83].

5.8. Prevention of cardiovascular effects of noise via activation of the endothelial AMP-kinase

Non-pharmacological interventions, such as physical activity and intermittent fasting, and pharmacological activation of α1AMPK, have shown promise in reducing noise-induced vascular damage in healthy mice. Exercise, intermittent fasting and pharmacological AMPK activation restored endothelial function and reduced oxidative stress in noise-exposed healthy mice, supporting these strategies as effective countermeasures [78]. Notably, these mitigation measures failed in endothelial-specific αAMPK knockout mice highlighting the central role of AMPK in the beneficial effects of exercise and intermittent fasting. Endothelial-specific αAMPK knockout mice were obtained from crossing B6.Cg-Tg(Cdh5-cre)7Mlia/J with $\alpha1AMPK^{fl/fl}$ mice.

5.9. Conclusion

Transportation noise poses significant risks to vascular health through mechanisms involving oxidative stress, inflammation, and neuroendocrine dysregulation. Findings from both human and animal studies underscore the critical need for targeted mitigation strategies and further investigation into the long-term effects of noise on risk for cardiometabolic diseases and other major non-communicable diseases such as dementia or cancer.

6. Co-exposure to noise and air pollution

Air pollution and traffic noise are considered the two leading environmental causes of cardiovascular morbidity and mortality [84]. They usually co-exist in urban environments, as road traffic is an essential source of both. Lack of green surroundings and artificial light at night are two other potentially significant co-exposures in urban environments which may affect risk of CVD [85] - green space acting to improve cardiovascular health through higher physical activity and lower stress [86] whereas light at night may cause CVD by disrupting the circadian rhythm [84].

Although these exposures are correlated in urban settings, most studies have focused on one environmental exposure at a time. However, a more realistic, multi-exposure approach is needed to disentangle the effects of the exposures on the cardiovascular system to identify the extent of mutual confounding and potential interactions [87].

In terms of pathophysiology, exposure to noise, and to a lesser extent also air pollution both stimulates the hypothalamic-pituitary-adrenal (HPA) axis, as well as the sympathetic nervous system and subsequent release of the stress hormones cortisol from the adrenal cortex and catecholamines from the adrenal medulla [4,84]. These stress response pathways are directly connected to oxidative stress and inflammation as well as direct cardiovascular effects via glucocorticoid-, α- and β-receptor signalling, and activation of the RAAS, causing direct vasoconstriction by angiotensin-II (Fig. 1).

The combination of exposure to noise and air pollution has been demonstrated to have additive adverse effects on the cardiovascular system in experimental animal models. More specifically, systemic inflammation and oxidative damage in the aorta and heart were additively exacerbated by inhalation of particulate matter in healthy mice (C57BL/6j) and noise-triggered stress hormone signaling resulting from the noise effects on the brain and particulate matter effects on the lung [88]. The additive damage in the aorta was also envisaged by functional impairment of endothelial function and elevated blood pressure.

Furthermore, noise and potentially also air pollution may, like artificial light pollution, disrupt the circadian rhythm, contributing to oxidative stress and vascular inflammation, culminating in endothelial dysfunction [84]. As an example, PM2.5 exposure and shift of light/dark cycle caused additive but also differential circadian rhythm disruption and metabolic dysfunction through epigenetic regulation of circadian targets in C57BL/6j mice [89]. For noise and light at night, circadian rhythm disruption is a direct consequence of impaired sleep [56,60], whereas for air pollution recent studies have indicated an association with dysregulated circadian rhythm, likely as a consequence of oxidative damage of clock core components [90,91]. The absence of green spaces exacerbates these harmful effects by promoting physical inactivity, reducing opportunities for environmental restoration, and intensifying urban heat island effects, thereby amplifying the adverse health impacts of noise, air, and light pollution leading ultimately to cardiometabolic diseases such as hypertension, ischemic heart disease, stroke, heart failure and diabetes [4,87].

While most studies on road traffic noise and CVD have adjusted for air pollution, only a few studies on air pollution have adjusted for road traffic noise. A 2023 systematic review identified 52 publications on transportation noise and CVD that also considered air pollution [92]. The authors concluded that air pollution did not confound the association between noise and CVD, while more studies on potential interactions were needed. Nationwide Danish studies, including residential exposure to various air pollutants, transportation noise and lack of green space, found all exposures independently associated with CVD [93] and type 2 diabetes (Fig. 5). However, for all exposures, the risk estimates in multi-pollutant analyses were lower than in single-pollutant analyses, stressing the importance of a multi-exposure approach to achieve reliable risk estimates. Also important to mention that high quality studies on air pollution and traffic noise adjust for confounding socioeconomic parameters that were reported to significantly affect environmental exposure-health associations of population-based studies [94].

7. Noise mitigation strategies

Effective noise mitigation requires a combination of approaches. For road traffic, noise barriers, noise-reducing asphalt, speed limit adjustments, and low-noise tyres can achieve significant reductions. Electric vehicle transition offers only minor decreases (approximately 1 dB(A)). For aircraft noise, optimized flight paths, night flight bans, and steeper descent approaches can minimize exposure. Railway noise can be mitigated through rail grinding, brake upgrades, and nighttime operational bans near residential zones.

8. Conclusions

Transportation noise is a significant contributor to cardiovascular and cerebrovascular diseases, including myocardial infarction, stroke,

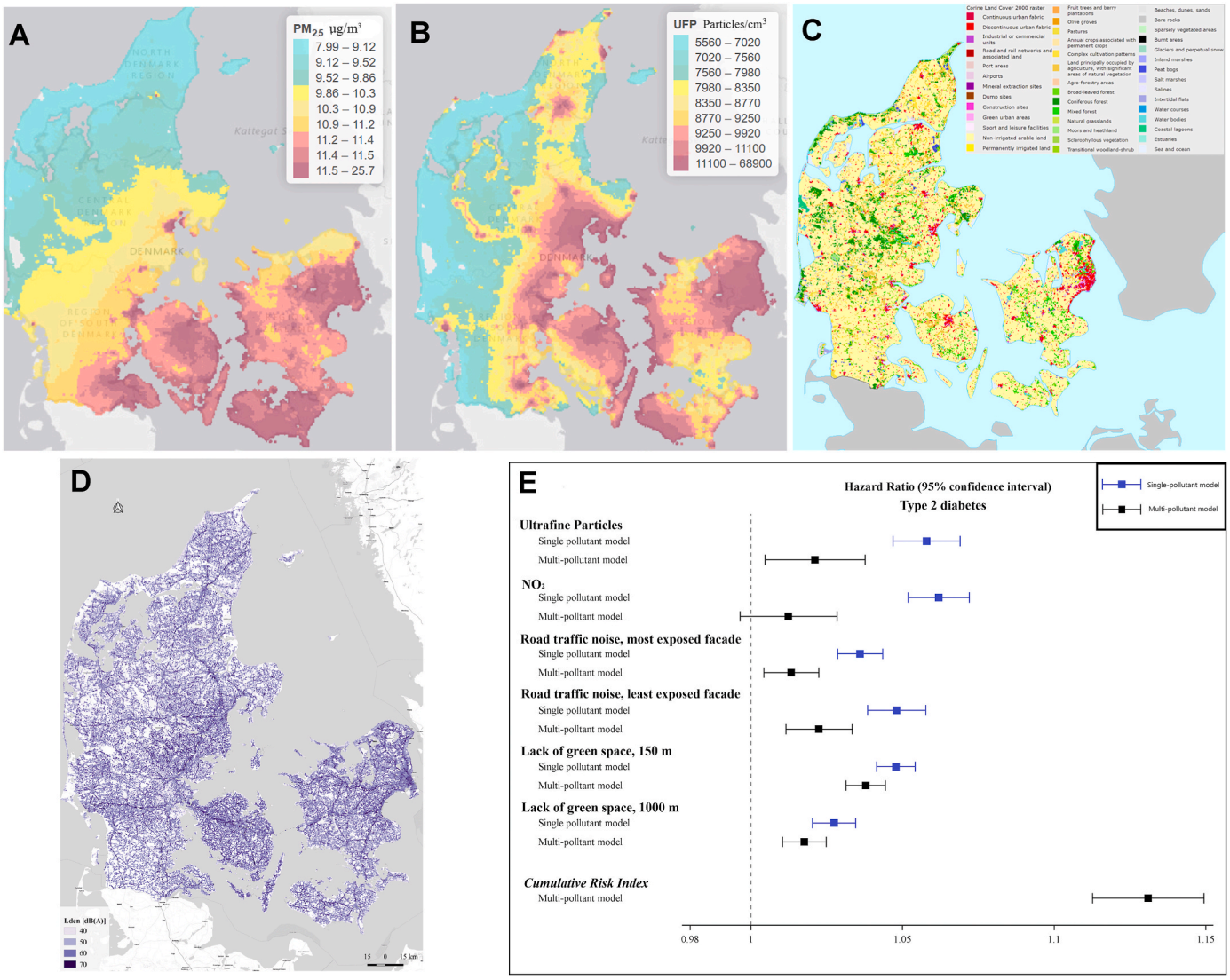

Fig. 5. Co-localization of environmental exposures in Denmark. The maps show the annual mean levels of particulate matter with diameter ≤2.5 μm ($PM_{2.5}$) (part **a**) and ultrafine particles (UFP) (part **b**) in the air in Denmark in 2000, modelled by Aarhus University using the Danish Eulerian Hemispheric Model and the Urban Background Model at 1 × 1 km spatial resolution [100,101]. Corine Land Cover map for Denmark in 2000, providing information for 44 classes of land use such as forest and arable land (part **c**). The European Environment Agency coordinates European Union Corine Land Cover maps. Map of road traffic noise at the most exposed facade at all residential addresses in Denmark in 2015, shown as the day–evening–night noise level (L_{den}), an indicator based on 24-h average sound levels (part **d**). Risk estimates for type 2 diabetes per interquartile range increase in exposure to air pollution, noise pollution and lack of green space in single-exposure and multi-exposure analyses based on a prospective study covering all of Denmark [102] (part **e**). Parts **a** and **b** courtesy of Matthias Ketzel (unpublished data). Part **c** reprinted from Ref. [103], CC BY 2.5. Part **d** courtesy of M.S. (unpublished data). Part **e** reprinted with permission from Ref. [102], Entire figure adapted from Ref. [87] with permission. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

and heart failure. Mechanistic studies indicate that noise exacerbates traditional cardiovascular risk factors by inducing oxidative stress, inflammation, and autonomic disturbances, which are triggered by neuronal activation in the amygdala with subsequent stress responses via the HPA axis and the sympathetic nervous system and down-stream activation of the RAAS (see Graphical Abstract for summary). The correlation between noise and air pollution underscores the need for holistic strategies addressing both exposures.

Political and societal action is imperative. The cardiovascular community must advocate for integrating environmental factors like noise into health risk assessments. Current guidelines often overlook noise pollution despite its significant impact on health [17], although at least impaired sleep quality (as a direct consequence of night-time noise exposure) is mentioned in position papers of some medical societies, e.g. in Ref. [95]. Adopting an exposome approach, which considers all exposures throughout an individual's life, could enhance the precision of CVD risk predictions and improve prevention strategies [87].

Author contributions

All authors were involved in writing the original manuscript and also critically revised it before submission.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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