JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. ■, NO. ■, 2024

Higher Aircraft Noise Exposure Is Linked to Worse Heart Structure and Function by Cardiovascular MRI

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ABSTRACT

BACKGROUND Aircraft noise is a growing concern for communities living near airports.

OBJECTIVES This study aimed to explore the impact of aircraft noise on heart structure and function.

METHODS Nighttime aircraft noise levels (L_{night}) and weighted 24-hour day-evening-night aircraft noise levels (L_{den}) were provided by the UK Civil Aviation Authority for 2011. Health data came from UK Biobank (UKB) participants living near 4 UK major airports (London Heathrow, London Gatwick, Manchester, and Birmingham) who had cardiovascular magnetic resonance (CMR) imaging starting from 2014 and self-reported no hearing difficulties. Generalized linear models investigated the associations between aircraft noise exposure and CMR metrics (derived using a validated convolutional neural network to ensure consistent image segmentations), after adjustment for demographic, socioeconomic, lifestyle, and environmental confounders. Mediation by cardiovascular risk factors was also explored. Downstream associations between CMR metrics and major adverse cardiac events (MACE) were tested in a separate prospective UKB subcohort (n = 21,360), to understand the potential clinical impact of any noise-associated heart remodeling.

RESULTS Of the 3,635 UKB participants included, 3% experienced higher L_{night} (≥45 dB) and 8% higher L_{den} (≥50 dB). Participants exposed to higher L_{night} had 7% (95% CI: 4%-10%) greater left ventricular (LV) mass and 4% (95% CI: 2%-5%) thicker LV walls with a normal septal-to-lateral wall thickness ratio. This concentric LV remodeling is relevant because a 7% greater LV mass associates with a 32% greater risk of MACE. They also had worse LV myocardial dynamics (eg, an 8% [95% CI: 4%-12%] lower global circumferential strain which associates with a 27% higher risk of MACE). Overall, a hypothetical individual experiencing the typical CMR abnormalities associated with a higher L_{night} exposure may have a 4 times higher risk of MACE. Findings were clearest for L_{night} but were broadly similar in analyses using L_{den}. Body mass index and hypertension appeared to mediate 10% to 50% of the observed associations. Participants who did not move home during follow-up and were continuously exposed to higher aircraft noise levels had the worst CMR phenotype.

CONCLUSIONS Higher aircraft noise exposure associates with adverse LV remodeling, potentially due to noise increasing the risk of obesity and hypertension. Findings are consistent with the existing literature on aircraft noise and cardiovascular disease, and need to be considered by policymakers and the aviation industry. (JACC. 2024;■:■–■)

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ISSN 0735-1097 https://doi.org/10.1016/j.jacc.2024.09.1217

ABBREVIATIONS AND ACRONYMS

AHA = American Heart Association

BMI = body mass index

CAD = coronary artery disease

CMR = cardiovascular magnetic resonance

CNN = convolutional neural network

CV = cardiovascular

CVD = cardiovascular disease

ICD-10 = International Classification of Disease–10th Revision

L_{den} = 24-hour day-evening-night aircraft noise levels

L_{night} = nighttime aircraft noise levels

LV = left ventricle/ventricular

$LVEDV_i$ = left ventricular end-diastolic volume indexed to height$^{1.7}$

LVEF = left ventricular ejection fraction

$LVESV_i$ = left ventricular end-systolic volume indexed to height$^{1.7}$

$LVmass_i$ = left ventricular mass indexed to height$^{1.7}$

MACE = major adverse cardiac events

MCF = myocardial contraction fraction

MV = myocardial volume

NO_2 = nitrogen dioxide

$PM_{2.5}$ = particulate matter that is 2.5 μm or less in diameter

SLWR = septal-to-lateral wall thickness ratio

SV = stroke volume

UKB = UK Biobank

WHO = World Health Organization

WT = wall thickness

$\overline{WT}$ = mean wall thickness

The World Health Organization (WHO) estimated in 2011 that >1 million disability-adjusted life-years were lost due to environmental noise in Western Europe.[1] At the same equivalent noise level, human annoyance is greater in response to aircraft noise compared to road or rail traffic noise.[2] This is because aircraft noise has: higher sound pressure levels, leading to auditory discomfort; a rapid rise time compared to the gradual onset of road/rail noise; greater low-frequency content causing stronger vibrations; and unpredictable patterns that hinder habituation. As the aviation industry has expanded, there has been a growing concern in communities living near airports or under flight paths regarding potential impacts on quality of life and sleep. The European Environment Agency noted that >4 million Europeans were exposed to day-evening-night aircraft noise levels (L_{den}) >55 dB in 2017.[3] The 2018 WHO Environmental Noise Guidelines for Europe advocate for the reduction of L_{den} to values below 45 dB and nighttime aircraft noise levels (L_{night}) to values below 40 dB.[4]

Epidemiological studies have consistently shown that environmental noise, especially aircraft noise, is associated with worse cardiovascular (CV) health. For example, those exposed to high levels of aircraft noise by living near Heathrow Airport in London were more likely to experience hospitalizations secondary to stroke or coronary artery disease (CAD).[5] Moreover, the systematic review conducted by van Kempen et al[6] to support the 2018 WHO Environmental Noise Guidelines reported a relative risk of 1.10 for incident CAD per 10-dB increment in L_{den}. Aircraft noise has also been linked to cardiometabolic risk factors such as obesity,[7] diabetes,[8] and hypertension.[9] Although the exact mechanism through which aircraft noise leads to cardiovascular disease (CVD) is yet to be fully established, human experimental and field studies to date have provided valuable insights into the potential pathophysiological pathways. These have indicated that aircraft noise exposure, especially during nighttime, can lead to diastolic dysfunction (increased early mitral inflow velocity to early diastolic mitral annular velocity ratio by echocardiography),[10] higher systolic blood pressure and endothelial dysfunction (lower flow-mediated dilatation of the brachial artery) in patients with or at risk of CAD,[11] increased vascular stiffness,[12,13] more pronounced stress hormone release,[14,15] and greater oxidative stress and inflammation in the vasculature.[14,16]

However, it remains unclear whether aircraft noise independently associates with an adverse cardiac phenotype in terms of heart structure and function, and whether cardiometabolic risk factors at least partly mediate this association. Using cardiovascular magnetic resonance (CMR) imaging outcomes and aircraft noise exposure data from the UK Biobank (UKB), we sought to answer these questions.

METHODS

STUDY POPULATION. A subset of 26,658 participants from the UK Biobank had CMR imaging data. Of these, 3,635 participants lived in 1 of the 44 Local Authority Districts, wholly or partially encompassing the UK Civil Aviation Authority 100 m gridded surface of modeled L_{den} around 4 major international airports (London Heathrow, London Gatwick, Birmingham, and Manchester) in England, after excluding individuals who self-reported hearing difficulties. Aircraft noise exposure data in participants living outside 1 of these 44 Local Authority Districts were not available. For transparency, the data fields used in this study are shown in Supplemental Table 1.

ETHICAL APPROVAL. The Northwest Multi-Centre Research Ethics Committee approved the UKB study initially in 2011 (reference number: 06/MRE08/65), and this approval was renewed in 2016 and 2021.

EXPOSURE: AIRCRAFT NOISE. The UK Civil Aviation Authority provided estimates of ground-level aircraft

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received June 21, 2024; revised manuscript received September 20, 2024, accepted September 26, 2024.

noise derived from version 2 of the Aircraft Noise CONtour (ANCON) model. ANCON considers the average flight path heights and speed profiles, aircraft performance characteristics (as provided by the manufacturers), and takeoff/landing weights.[17] This model was validated against and shown to have a similar performance as the U.S. Federal Aviation Administration's Integrated Noise Model.[18] ANCON estimates were provided for point locations separated by 100 m, running along transects parallel to the airport runways. These were resampled to a regular 100 × 100 m gridded surface by inverse distance-based weighted interpolation of the 4 nearest antilog noise values.

The 100 m aircraft noise raster surfaces were then intersected by the postcode centroids, typically comprising 43 ± 39 residents and 18 ± 15 occupied households. Population-weighted average exposures of the antilog noise values were then calculated for 2011 small-area-level census output areas (COAs) using the postcode-level data. In 2011, the average population of the 181,408 COAs in England and Wales was 309 residents (95% CI: 171-486). COA residents were assumed to have had the same level of noise exposure. We used both the L_{night} and L_{den} indicators, where L_{night} is the A-weighted equivalent noise level over the 8-hour night period between 23:00 and 07:00. In contrast, L_{den} is the A-weighted equivalent noise level over a whole day, but with a penalty of +10 dB (A) for nighttime noise (23:00-07:00) and +5 dB (A) for evening noise (19:00-23:00). The penalties are automatic adjustments applied to measured noise during these specific time periods (Supplemental Equation 1). The UK Civil Aviation Authority provided continuous data to 1 decimal place truncated to a lower level of 45 dB for L_{night} and 50 dB for L_{den} (ie, below these specific noise exposure levels, data are not provided). Thus, we divided participants into either lower or higher noise exposure groups. Higher noise exposure at night was defined as L_{night} ≥45 dB and throughout a 24-hour day as L_{den} ≥50 dB.

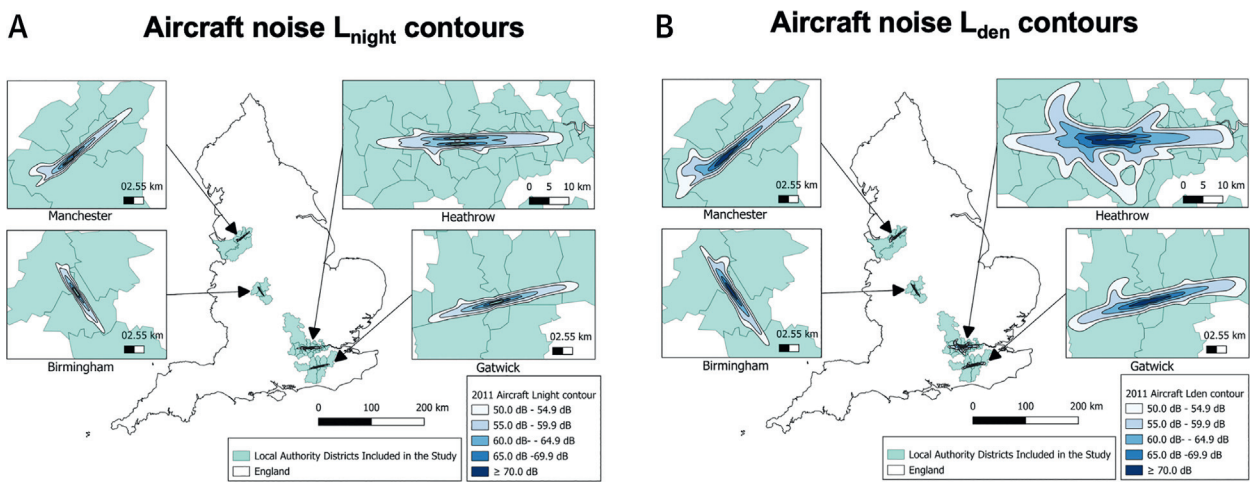
Aircraft noise contours were created from the gridded model outputs to simplify the visual interpretation of exposures around the 4 UK major airports in 2011 (London Heathrow, London Gatwick, Manchester, and Birmingham) (**Figure 1**).

OUTCOMES: CMR DATA. Starting from 2014, CMR images were acquired over 20 minutes using a Siemens 1.5-T scanner. Three long-axis (horizontal, vertical, and left ventricular [LV] outflow tract) and a short-axis cine stack were acquired using balanced steady-state free precession sequences. To ensure consistent and precise cardiac contours, cines were automatically segmented using a deep learning convolutional neural network (CNN).[19] The full details have been described elsewhere.[19] Briefly, the CNN was trained and validated based on 4,875 subjects from the UK Biobank, amounting to 93,500 pixelwise manually annotated images by clinical experts. The subjects were split into training (n = 3,975), validation for model hyperparameter tuning (n = 300), and testing (n = 600) datasets. In the testing dataset, the CNN showed an excellent performance in conducting segmentations for both the LV myocardium and cavity (both mean dice metrics = 0.94; mean contour distances = 1.14 and 1.04, respectively; and mean Hausdorff distances = 3.92 and 3.16, respectively). The contours were postprocessed to calculate the LV end-diastolic and end-systolic volumes, LV stroke volume (SV), LV ejection fraction (LVEF), and LV myocardial mass. The LV relative wall mass was derived as the ratio of LV mass to LV end-diastolic volume. The LV myocardial volume (MV) was calculated from LV mass assuming a myocardial density of 1.05 g/mL.[20] The LV myocardial contraction fraction (MCF) was then derived as the ratio of the LV SV to LV MV. Although indexation to body surface area is common in clinical practice, body surface area is biased in overweight individuals.[21] As around 30% of the UKB population has a body mass index (BMI) >30 kg/m^2, we indexed LV end-diastolic volume, LV end-systolic volume, and LV mass to the standing height raised to the power 1.7 (ie, height$^{1.7}$) to yield the LV end-diastolic volume index ($LVEDV_i$), LV end-systolic volume index ($LVESV_i$), and LV mass index ($LVmass_i$).[21]

The wall thickness (WT) for each of the 16 American Heart Association (AHA) segments was derived using the same CNN[19] as the average perpendicular distance between the endocardial and epicardial surfaces at end-diastole. The LV mean wall thickness ($\overline{WT}$) was calculated as the average WT across the 16 AHA segments, while the LV maximal wall thickness was calculated as the maximum LV WT value. The interventricular septal thickness was calculated as the mean WT of AHA segments 2, 3, 8, 9, and 14, while the lateral WT was calculated as the mean WT of AHA segments 5, 6, 11, 12, and 16. The septal and lateral WT were divided to obtain the septal-to-lateral wall thickness ratio (SLWR). An SLWR >1.3 (or <0.7) was considered abnormal.[22]

Starting from epicardium to endocardium, the myocardium has oblique, circular, and longitudinal muscle fibers, meaning that it undergoes

FIGURE 1 **Aircraft Noise Contours Around the 4 UK Major International Airports**



Local authority districts surrounding the 4 UK major airports (London Heathrow, London Gatwick, Manchester, and Birmingham), along with the noise contours provided by the UK Civil Aviation Authority, are presented for (A) nighttime aircraft noise levels (L_{night}) and (B) 24-hour day-evening-night aircraft noise levels (L_{den}) in 2011.

circumferential, radial, and longitudinal shortening during systole.[23] Changes in LV mass or WT may imply alterations in cardiomyocytes, and their relationships with each other and the extracellular matrix.[24] To explore the mechanical impact of such changes, we also analyzed the global and regional LV circumferential, radial, and longitudinal strain values indexed to $LVmass_i$, as previously described.[25] The unindexed strain values were calculated using a 3-dimensional deformable model of the myocardium.[26] The basal region was defined as AHA segments 1 to 6, mid as AHA segments 7 to 12, and apical as AHA segments 13 to 16. At the time of this study, longitudinal mid and apical strain values were not released by the UKB. Less negative LV circumferential and longitudinal strain values, as well as less positive radial strain values, suggest worse myocardial dynamics.[27] Thus, we used absolute strain values, so lower absolute values can be interpreted as worse myocardial dynamics for all strain metrics.

COVARIATES. Sex was recorded as male or female, while race/ethnicity was recorded as White, Asian or Asian British, Black or Black British, Chinese, mixed, or other. BMI and age at baseline were used. Information regarding the assessment center attended, time spent residing at the current address, and any change in the place of residence were also available from the UKB. Area-level socioeconomic status of participants was captured using the 2011 Townsend deprivation index score. This index is an unweighted composite of 4 UK Census variables (rates of unemployment, overcrowding, private vehicle ownership, and home ownership) measured in each COA community and compared with national averages per COA in England and Wales using z scores.[28] Individual-level socioeconomic status was assessed through the average annual household income before tax in pounds sterling as a categorical variable (<£18,000; £18,000-£30,999; £31,000-£51,999; £52,000-£100,000; and >£100,000). Self-reported lifestyle factors included smoking status (current, never, and former), alcohol consumption (daily or almost daily, 3-4 times/week, 1-2 times/ week, 1-3 times/month, special occasions, or never), and physical activity (the total number of days per week the participant engaged in at least moderately vigorous physical activities).

Details on comorbidities were obtained through self-reported diagnoses, International Classification of Disease-10th Revision (ICD-10) codes from linked medical records, and data from clinic visits. Primary care records were not used to avoid bias, as these data were available in only ~50% of the cohort at the time of this study. The presence of hearing difficulties or deafness, hypertension, diabetes, and CVD were recorded as 1 = present or 0 = absent. Hearing difficulties were self-reported at baseline. Hypertension was based on self-reported doctor-diagnosed cases, high blood pressure (BP) readings during the baseline visit (ie, systolic ≥140 mm Hg or diastolic ≥90 mm Hg), or the use of antihypertensives. Diabetes was defined based on self-reported doctor

diagnosis at baseline. High cholesterol was defined as a baseline total serum cholesterol level ≥6.2 mmol/L. Lipid-lowering drugs were not included in the definition of high cholesterol because they are commonly prescribed to high-risk individuals for primary prevention of CVD and routinely used for secondary prevention (eg, following a percutaneous coronary intervention), even when cholesterol levels are within the normal range. There were no additional cases pertinent to hypertension, diabetes, or high cholesterol derived from hospital records up to 2014. The presence of CVD was based on self-report of angina, myocardial infarction, or stroke, as well as inpatient admissions for ischemic heart diseases (ICD-10 codes I20-I25) or cerebrovascular diseases (ICD-10 codes I60-I69) up to 2014.

Abdominal magnetic resonance imaging was also postprocessed to calculate total trunk fat volume, subcutaneous adipose tissue volume, and visceral adipose tissue volume, as previously described.[29,30]

The environmental covariates included both noise from road and railway sources (L_{den} and L_{night}) as well as ambient air pollution (concentrations of nitrogen dioxide [NO_2] and particulate matter that is 2.5 μm or less in diameter [$PM_{2.5}$]). Road transport noise levels in 2013 from major and minor roads were modeled in accordance to the European Commission's Common Noise Assessment Methods in Europe framework for the loudest façade of the building assigned to each postcode centroid: Annual Average Daily Traffic counts and speed limits across the UK road network enter the model, along with information relating to the surface roughness of land cover, building heights, wind profiles, and average temperatures.[31] The 2011 strategic mapping surfaces of noise from major rail activity in England were provided by the UK Department for Environment, Food and Rural Affairs.[32] The 10 × 10 m noise surfaces extend down to 0 dB and are compliant with the European Union Environmental Noise Directive (Round 3). Of note, this dataset only included the contributions from major corridors, defined as railway lines running 30,000 or more passenger vehicle trips per year. Despite this limitation, the dataset can differentiate between locations that are substantially burdened by railway noise. Population-weighted average exposures for rail transport were calculated for COA communities with postcode centroids containing population counts. In line with our approach for categorizing aircraft noise, we divided samples into higher road traffic noise (L_{night} ≥45 dB or L_{den} ≥50 dB) and lower road traffic noise groups, as well as into higher railway traffic noise (L_{night} ≥45 dB or L_{den} ≥50 dB) and lower railway traffic noise groups. NO_2 (μg/m^3) air concentrations were derived for 2009 using a land use regression model developed by Gulliver et al,[33] which takes into account land cover classifications and road network data. The model was validated against the measured values reported by the Automatic Urban and Rural Network and was able to explain >60% of the variability in measurements (ie, R^2 >0.6). $PM_{2.5}$ air concentrations used were those modeled using the land use regression model developed by the European Study of Cohorts for Air Pollution Effects.[34]

STATISTICAL ANALYSES. All analyses were performed in STATA version 18 (StataCorp). For all estimates, 95% CIs are provided.

Because hearing impairment potentially modifies the biological response to noise, we excluded participants who self-reported either having hearing difficulties or deafness.[35] Then, we compared participants with higher and lower aircraft noise exposure, conducting separate analyses for L_{night} and L_{den}. Given the positively skewed distributions of CMR metrics, generalized linear models with a gamma distribution and log link were used to investigate the associations between higher aircraft noise exposure as the independent variable and the cardiac phenotype by CMR as the dependent variable. All models were adjusted for demographic (age, sex, and race/ethnicity), cohort-related (assessment center, nonmover status, and length at the current address), socioeconomic (Townsend deprivation index and household income before tax), lifestyle (smoking status, alcohol consumption, and physical activity), and environmental (road noise, rail noise, and concentrations of NO_2 and $PM_{2.5}$ in the air) confounders. Because strain is sensitive to changes in BP, strain analyses were additionally adjusted for antihypertensive drug use. Data missingness was <1% for all covariates, except for household income, for which 9% of participants preferred not to answer. This potentially implies data missingness not at random, which could bias multiple imputation approaches, so we had to exclude participants with missing data.

We explored to what extent the relationship between higher aircraft noise exposure and the worse cardiac CMR phenotype observed was explained by CV risk factors and CVD. Separate mediation analyses were conducted for BMI, the presence of hypertension, and the presence of high cholesterol using the Imai, Tingley, and Yamamoto framework of causal inference.[36] We could not conduct formal mediation analyses for the presence of diabetes or the presence of CVD due to the small number of recorded events. For these, we present separate regression results, in which we further adjusted for either diabetes or CVD

TABLE 1 Characteristics of Participants Who Lived Near 1 of the 4 UK Airports, Had CMR, and Reported No Hearing Difficulties

	Aircraft Noise Exposure in 2011					
	L_{den} ≥50 dB	L_{den} <50 dB	*P* Value	L_{night} ≥45 dB	L_{night} <45 dB	*P* Value
Participants	304 (8.4)	3,331 (91.6)		107 (2.9)	3,528 (97.1)	
Demographics						
Age at baseline, y	52 (44-58)	53 (46-59)	0.020[a]	51 (43-58)	53 (46-59)	0.072
Male	134 (44.1)	1,511 (45.4)	0.667	51 (47.7)	1,594 (45.2)	0.611
Race/ethnicity						
White	291 (96.7)	3,157 (95.0)	0.057	101 (95.3)	3,347 (95.2)	0.856
Mixed	5 (1.7)	20 (0.6)		<5	24 (0.7)	
Asian or Asian British	<5	61 (1.8)		<5	62 (1.8)	
Black or Black British	<5	50 (1.5)		<5	50 (1.4)	
Chinese	<5	15 (0.5)		<5	15 (0.4)	
Other	<5	19 (0.6)		<5	19 (0.5)	
Townsend deprivation index in 2011 (lower values indicate less deprivation)	−2.01 (−3.8 to 0.4)	−2.57 (−4.0 to −0.4)	0.015[a]	−1.56 (−3.1 to 1.7)	−2.57 (−4.0 to −0.4)	<0.001[a]
Household income						
<£18,000	32 (11.6)	319 (10.5)	0.873	12 (12.6)	339 (10.6)	0.562
£18,000-30,999	61 (22.2)	628 (20.7)		24 (25.3)	665 (20.7)	
£31,000-£51,999	77 (28.0)	892 (29.4)		29 (30.5)	940 (29.3)	
£52,000-£100,000	78 (28.4)	919 (30.4)		22 (23.2)	975 (30.4)	
>£100,000	27 (9.8)	273 (9.0)		8 (8.4)	292 (9.0)	
Lifestyle						
Smoking status						
Current	21 (6.9)	249 (7.5)	0.219	10 (9.3)	260 (7.4)	0.030[a]
Former	107 (35.2)	1,010 (30.4)		44 (41.2)	1,073 (30.5)	
Never	176 (57.9)	2,066 (62.1)		53 (49.5)	2,189 (62.1)	
Alcohol consumption						
Daily	75 (24.8)	768 (23.1)	0.540	27 (25.2)	816 (23.1)	0.119
3-4 times/wk	79 (26.0)	911 (27.3)		18 (16.8)	972 (27.6)	
1-2 times/wk	72 (23.8)	801 (24.0)		32 (29.9)	841 (23.8)	
1-3 times/mo	33 (10.9)	385 (11.6)		11 (10.3)	407 (11.6)	
Occasional	33 (10.9)	285 (8.6)		14 (13.1)	304 (8.6)	
Never	11 (3.6)	181 (5.4)		5 (4.7)	187 (5.3)	
Physical activity, d/wk	3 (2-5)	3 (2-5)	0.682	4 (2-5)	3 (2-5)	0.603
Other environmental exposures						
Road noise in 2013						
L_{den} ≥50 dB	221 (72.7)	2,396 (71.9)	0.776	N/A	N/A	
L_{den} <50 dB	83 (27.3)	935 (28.1)		N/A	N/A	
L_{night} ≥45 dB	N/A	N/A		62 (57.9)	1,858 (52.7)	0.281
L_{night} <45 dB	N/A	N/A		45 (42.1)	1,670 (47.3)	
Rail noise in 2011						
L_{den} ≥50 dB	24 (7.9)	95 (2.9)	<0.001[a]	N/A	N/A	
L_{den} <50 dB	280 (92.1)	3,236 (97.1)		N/A	N/A	
L_{night} ≥45 dB	N/A	N/A		6 (5.6)	87 (2.5)	0.043[a]
L_{night} <45 dB	N/A	N/A		101 (94.4)	3,441 (97.5)	
NO_2 air concentrations in 2009, μg/m^3	33.8 (29.8-40.3)	32.2 (27.6-36.2)	<0.001[a]	33.4 (30.1-46.4)	32.3 (27.6-36.3)	<0.001[a]
$PM_{2.5}$ air concentrations in 2010, μg/m^3	9.9 (9.3-10.4)	9.9 (9.3-10.5)	0.640	10.2 (9.6-10.7)	9.9 (9.3-10.5)	0.054

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beyond demographic, cohort-related, socioeconomic, lifestyle, and environmental variables, and comment on coefficient attenuation. As a higher BMI appeared to explain most associations between a higher aircraft noise exposure and worse CMR metrics, we further examined any potential mediating effects of total trunk fat volume, subcutaneous adipose tissue volume, and visceral adipose tissue volume to better understand the influence of adiposity itself on these associations. To calculate the total effects, we

TABLE 1 Continued

	Aircraft Noise Exposure in 2011					
	L_{den} ≥50 dB	L_{den} <50 dB	*P* Value	L_{night} ≥45 dB	L_{night} <45 dB	*P* Value
Cardiometabolic risk factors						
BMI, kg/m^2	26.1 (23.5-29.4)	25.9 (23.4-28.7)	0.100	26.2 (23.5-30.1)	25.9 (23.5-28.7)	0.200
Hypertension	146 (48.0)	1,431 (43.0)	0.088	45 (42.1)	1,532 (43.4)	0.778
Diabetes	8 (2.6)	98 (2.9)	0.758	<5	104 (2.9)	0.514
High cholesterol	101 (33.2)	1,134 (34.0)	0.773	46 (43.0)	1,189 (33.7)	0.046[a]
CVD	11 (3.6)	143 (4.3)	0.576	<5	152 (4.3)	0.217
CMR heart structure and function metrics						
$LVEDV_i$, mL/m$^{1.7}$	59.9 (52.9-67.6)	59.1 (52.6-67)	0.833	60.2 (53.1-69.0)	59.2 (52.5-66.9)	0.128
$LVESV_i$, mL/m$^{1.7}$	23.8 (19.9-28.3)	23.7 (20.1-28)	0.764	24.1 (20.4-28.9)	23.8 (20.1-28.0)	0.116
$LVmass_i$, g/m$^{1.7}$	33.6 (29.3-39.0)	33.5 (29.2-38.9)	0.647	34.4 (30.5-40.5)	33.5 (29.1-38.9)	0.062
LV MV, mL	78.5 (65.1-95.6)	77.4 (64.5-95.9)	0.621	79.9 (69.4-95.8)	77.4 (64.5-95.9)	0.094
LV $\overline{WT}$, mm	5.5 (5.1-6.1)	5.5 (5.0-6.1)	0.515	5.6 (5.1-6.2)	5.5 (5.0-6.1)	0.118
LV MWT, mm	6.9 (6.2-7.69)	6.9 (6.2-7.6)	0.698	7.0 (6.3-7.9)	6.9 (6.2-7.6)	0.215
IVST, mm	5.6 (5.0-6.1)	5.5 (4.9-6.1)	0.528	5.5 (5.1-6.1)	5.5 (4.9-6.1)	0.187
LV lateral WT, mm	5.6 (5.2-6.2)	5.6 (5.1-6.2)	0.588	5.7 (5.2-6.3)	5.6 (5.1-6.2)	0.059
SLWR	1.0 (0.9-1.0)	1.0 (0.9-1.0)	0.834	1.0 (0.9-1.0)	1.0 (0.9-1.0)	0.418
LV RWM, g/mL	0.6 (0.5-0.6)	0.6 (0.5-0.6)	0.592	0.6 (0.5-0.6)	0.6 (0.5-0.6)	0.368
LV MCF	1.1 (1.0-1.2)	1.1 (1.0-1.2)	0.884	1.1 (1.0-1.2)	1.1 (1.0-1.2)	0.420
LVEF, %	60.1 (56.3-63.9)	59.6 (55.9-63.5)	0.878	59.7 (57.0-63.4)	59.6 (55.9-63.6)	0.637
Absolute LV circumferential strain index, m$^{1.7}$/g						
Global	0.7 (0.5-0.8)	0.7 (0.5-0.8)	0.571	0.6 (0.5-0.8)	0.7 (0.5-0.8)	0.040[a]
Basal	0.7 (0.6-0.8)	0.7 (0.6-0.8)	0.552	0.7 (0.5-0.8)	0.7 (0.6-0.8)	0.022[a]
Mid	0.6 (0.5-0.8)	0.7 (0.5-0.8)	0.407	0.6 (0.5-0.8)	0.7 (0.5-0.8)	0.038[a]
Apical	0.8 (0.6-1.0)	0.8 (0.6-1.0)	0.823	0.8 (0.6-0.9)	0.8 (0.6-1.0)	0.092
Absolute LV radial strain index, m$^{1.7}$/g						
Global	1.3 (1.1-1.6)	1.3 (1.1-1.6)	0.321	1.3 (1.0-1.5)	1.3 (1.1-1.6)	0.088
Basal	1.4 (1.0-1.7)	1.4 (1.1-1.7)	0.414	1.4 (1.0-1.6)	1.4 (1.1-1.7)	0.109
Mid	1.4 (1.1-1.7)	1.4 (1.1-1.8)	0.341	1.4 (1.1-1.6)	1.4 (1.1-1.8)	0.074
Apical	1.5 (1.2-1.8)	1.5 (1.2-1.8)	0.529	1.5 (1.2-1.8)	1.5 (1.2-1.8)	0.252
Absolute LV longitudinal strain index, m$^{1.7}$/g						
Global	0.5 (0.5-0.7)	0.6 (0.5-0.7)	0.945	0.5 (0.4-0.6)	0.6 (0.5-0.7)	0.066
Basal	0.6 (0.5-0.7)	0.6 (0.5-0.7)	0.953	0.6 (0.5-0.7)	0.6 (0.5-0.7)	0.097
Mid	N/A	N/A	N/A	N/A	N/A	N/A
Apical	N/A	N/A	N/A	N/A	N/A	N/A
Major adverse cardiac events						
MACE, events/1,000 person-years	3.9	1.6	N/A	3.8	2.1	N/A

Values are n (%), median (Q1-Q3), or n. Comparisons were made using the chi-square test with Yates continuity correction for categorical variables and Mann-Whitney *U* test for continuous variables. LV end-diastolic volume, LV end-systolic volume, and LV mass were indexed to height$^{1.7}$. Strain metrics were indexed to $LVmass_i$. [a]Significant *P* value.

BMI = body mass index; CMR = cardiovascular magnetic resonance; IVST = interventricular septal wall thickness; L_{den} = 24-hour day-evening-night aircraft noise levels; L_{night} = nighttime aircraft noise levels; LV = left ventricular; $LVEDV_i$ = left ventricular end-diastolic volume indexed to height$^{1.7}$; LVEF = left ventricular ejection fraction; $LVESV_i$ = left ventricular end-systolic volume indexed to height$^{1.7}$; $LVmass_i$ = left ventricular mass indexed to height$^{1.7}$; MACE = major adverse cardiac events; MCF = myocardial contraction fraction; MV= myocardial volume; MWT = maximal wall thickness; N/A = not available; NO_2 =nitrogen dioxide; $PM_{2.5}$ = particulate matter that is ≤2.5 μm in diameter; RWM = relative wall mass; SLWR = septal-to-lateral wall thickness ratio; WT = wall thickness; $\overline{WT}$ = mean wall thickness.

regressed the aircraft noise exposure on the CMR outcomes. To calculate the effect of the independent variable on the mediator (the mediator model), we regressed the aircraft noise exposure on the CV risk factors. To calculate the effect of the mediator on the dependent variable (the outcome model), we regressed the CV risk factors on the CMR outcomes. All models were adjusted for demographic, cohort-related, socioeconomic, lifestyle, and environmental confounders. This allowed us to derive the total effects, average causal mediation effects, and average direct effects. The proportion of mediation was calculated as the ratio of average causal mediation effects to total effects expressed as a percentage. CV

TABLE 2 Percentage Differences in CMR Metrics Between Those Exposed and Unexposed to Higher Aircraft Noise Levels

CMR Structure and Function Metrics	LV Volumes			LV Structure							LV Systolic Function	
	$LVEDV_i$	$LVESV_i$	LV MV	$LVmass_i$	LV $\overline{WT}$	LV MWT	IVST	LV lateral WT	SLWR	LV RWM	LVEF	LV MCF
Aircraft noise L_{night} ≥45 dB												
% difference (95% CI)	4.47 (3.52-5.43)	6.99 (1.97-12.25)	7.14 (3.98-10.39)	6.84 (3.84-9.92)	3.49 (1.86-5.15)	3.13 (1.83-4.45)	3.28 (1.65-4.93)	4.20 (2.07-6.38)	−0.73 (−1.27 to −0.18)	1.83 (0.31-3.37)	−1.25 (−4.15 to 1.74)	−2.57 (−6.33 to 1.34)
P value	<0.001[a]	0.006[a]	<0.001[a]	<0.001[a]	<0.001[a]	<0.001[a]	<0.001[a]	<0.001[a]	0.009[a]	0.018[a]	0.407	0.194
n	3,149	3,149	3,153	3,149	3,151	3,151	3,151	3,151	3,151	3,153	3,153	3,153
Aircraft noise L_{den} ≥50 dB												
% difference (95% CI)	1.57 (1.25-1.89)	2.24 (0.24-4.28)	3.33 (1.21-5.48)	3.49 (1.17-5.87)	2.13 (0.42-3.86)	2.03 (−0.42 to 4.54)	2.31 (0.79-3.85)	2.05 (0.04-4.11)	0.30 (−0.34 to 0.95)	1.69 (−0.61 to 4.04)	−0.48 (−1.89 to 0.96)	−1.93 (−2.70 to −1.15)
P value	<0.001[a]	0.028[a]	0.002[a]	0.003[a]	0.014[a]	0.104	0.003[a]	0.046[a]	0.354	0.150	0.512	<0.001[a]
n	3,149	3,149	3,153	3,149	3,151	3,151	3,151	3,151	3,151	3,153	3,153	3,153

CMR Absolute Strain Index Metrics	LV Circumferential				LV Radial				LV Longitudinal	
	Global	Basal	Mid	Apical	Global	Basal	Mid	Apical	Global	Basal
Aircraft noise L_{night} ≥45 dB										
% difference (95% CI)	−7.76 (−11.75 to −3.58)	−8.04 (−12.40 to −3.47)	−7.71 (−11.39 to −3.88)	−7.17 (−11.13 to −3.03)	−6.96 (−10.21 to −3.59)	−7.31 (−9.84 to −4.71)	−6.87 (−10.91 to −2.64)	−5.35 (−9.77 to −0.71)	−6.29 (−8.74 to −3.78)	−5.85 (−8.75 to −2.86)
P value	<0.001[a]	0.001[a]	<0.001[a]	0.001[a]	<0.001[a]	<0.001[a]	0.002[a]	0.024[a]	<0.001[a]	<0.001[a]
n	3,145	3,145	3,145	3,145	3,145	3,145	3,145	3,145	3,029	3,029
Aircraft noise L_{den} ≥50 dB										
% difference (95% CI)	−4.03 (−5.10 to −2.95)	−3.71 (−5.17 to −2.23)	−4.04 (−4.77 to −3.30)	−3.89 (−6.25 to −1.48)	−4.93 (−6.10 to −3.74)	−4.68 (−5.70 to −3.65)	−4.70 (−5.69 to −3.69)	−4.21 (−5.53 to −2.87)	−2.71 (−5.40 to 0.07)	−2.84 (−5.10 to −0.53)
P value	<0.001[a]	<0.001[a]	<0.001[a]	0.002[a]	<0.001[a]	<0.001[a]	<0.001[a]	<0.001[a]	0.056	0.016[a]
n	3,145	3,145	3,145	3,145	3,145	3,145	3,145	3,145	3,029	3,029

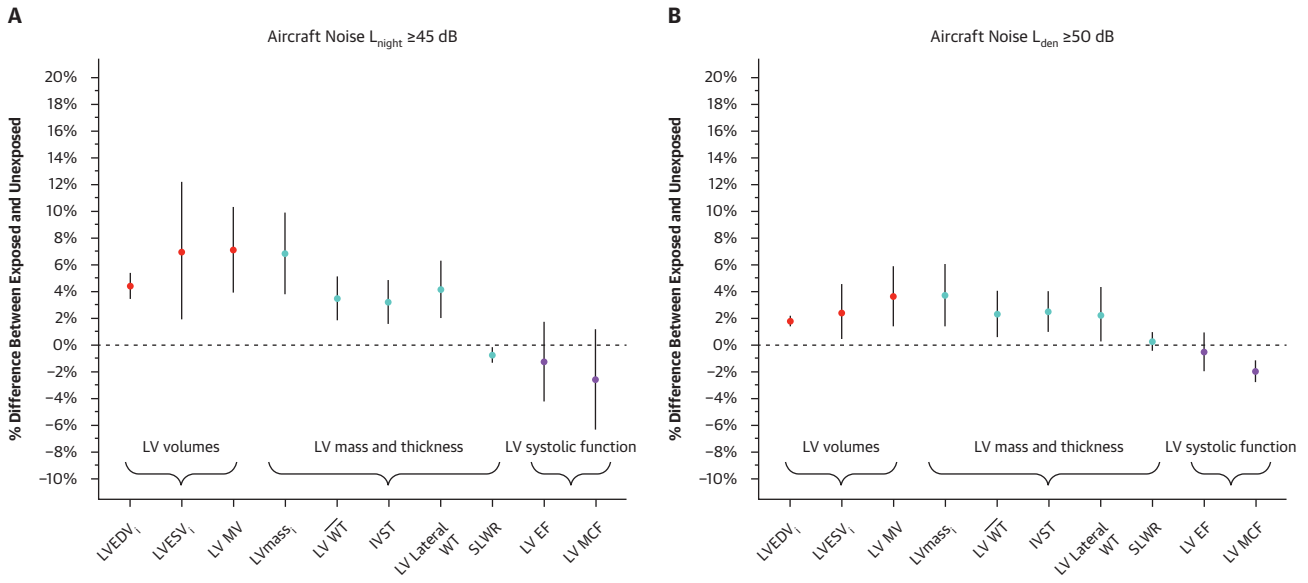
LV end-diastolic volume, LV end-systolic volume, and LV mass were indexed to height$^{1.7}$. All strain metrics were indexed to $LVmass_i$. All reported analyses consisted of generalized linear models with a gamma distribution and log link. The % difference between those exposed and unexposed to higher aircraft noise levels was calculated as 100*(*exp β-1)*. Each model was adjusted for demographic (age, sex, and race/ethnicity), cohort-related (assessment center, nonmover status, and length at the current address), socioeconomic (Townsend deprivation index and household income before tax), lifestyle (smoking status, alcohol consumption, and physical activity), and environmental (road and rail noise, and concentrations of NO_2 and $PM_{2.5}$ in the air) confounders. Strain models were also adjusted for the use of antihypertensives. [a]Significant *P* value.

Abbreviations as in Table 1.

risk factors with significant proportions of mediation were considered significant mediators. A graphical representation of the Imai, Tingley, and Yamamoto mediation framework is provided in Supplemental Figure 1.

To understand the potential clinical impact of the detected magnitude of noise-related LV remodeling, we explored the associations between CMR metrics and a prospectively collected major adverse cardiac events (MACE) outcome. The MACE data were sourced from the recorded ICD-10 codes based on linked medical records. This analysis was conducted in the UKB subcohort in which both CMR and MACE data were available. To ensure this subcohort's independence, individuals included in the aircraft noise substudy were excluded. UKB participants with known cardiomyopathies were also excluded. Any individual experiencing CV death or a hospitalization for ischemic heart diseases (ICD-10 codes I20-I25, which include acute coronary syndromes and stable angina), cerebrovascular diseases (ICD-10 codes I60-I69, which include ischemic stroke and intracranial hemorrhages), arrhythmias (ICD-10 codes I47-I49, which include supraventricular tachycardias, atrial fibrillation, atrial flutter, ventricular tachycardias, and ventricular fibrillation), or heart failure (ICD-10 code I50) was considered to have reached our MACE endpoint. We used Cox regression models using the CMR metrics as the independent variables and the MACE outcome as the dependent variable. The follow-up period was calculated as the difference between the time of MACE or the time of the last encounter and the time of CMR. The CMR metrics were minimum-maximum rescaled to be distributed between 0 and 100, so the HR for MACE per 1% adverse change in each CMR metric can be calculated. Because the differences in CMR metrics between those exposed and unexposed to higher aircraft noise levels are expressed as percentage differences, the clinical impact of observed differences can be estimated. For example, if the HR per 1% adverse change is x, a y% difference between the exposed and

FIGURE 2 **Associations Between Higher Aircraft Noise Exposure (L_{night} ≥45 dB and L_{den} ≥50 dB) and CMR Heart Structure and Function Metrics**



Plots are presented for 3,635 UK Biobank participants living near 1 of the 4 UK major airports showing the percentage differences (central dots), along with their 95% CIs (whiskers), in cardiovascular magnetic resonance (CMR) metrics between those exposed and unexposed to higher (A) L_{night} ≥45 dB and (B) L_{den} ≥50 dB, after adjusting for demographic, cohort-related, socioeconomic, lifestyle, and environmental confounders. IVST = interventricular septal wall thickness; LV = left ventricular; $LVEDV_i$ = left ventricular end-diastolic volume indexed to height$^{1.7}$; LVEF = left ventricular ejection fraction; $LVESV_i$ = left ventricular end-systolic volume indexed to height$^{1.7}$; $LVmass_i$ = left ventricular mass indexed to height$^{1.7}$; MCF = myocardial contraction fraction; MV = myocardial volume; SLWR = septal-to-lateral wall thickness ratio; WT = wall thickness; $\overline{WT}$ = mean wall thickness; other abbreviations as in Figure 1.

unexposed translates into a x^y higher risk. Model 1 was adjusted for demographic, cohort-related, socioeconomic, and lifestyle confounders. Model 2 was additionally adjusted for BMI as well as the presence of high cholesterol, hypertension, diabetes, and CVD at the time of the CMR.

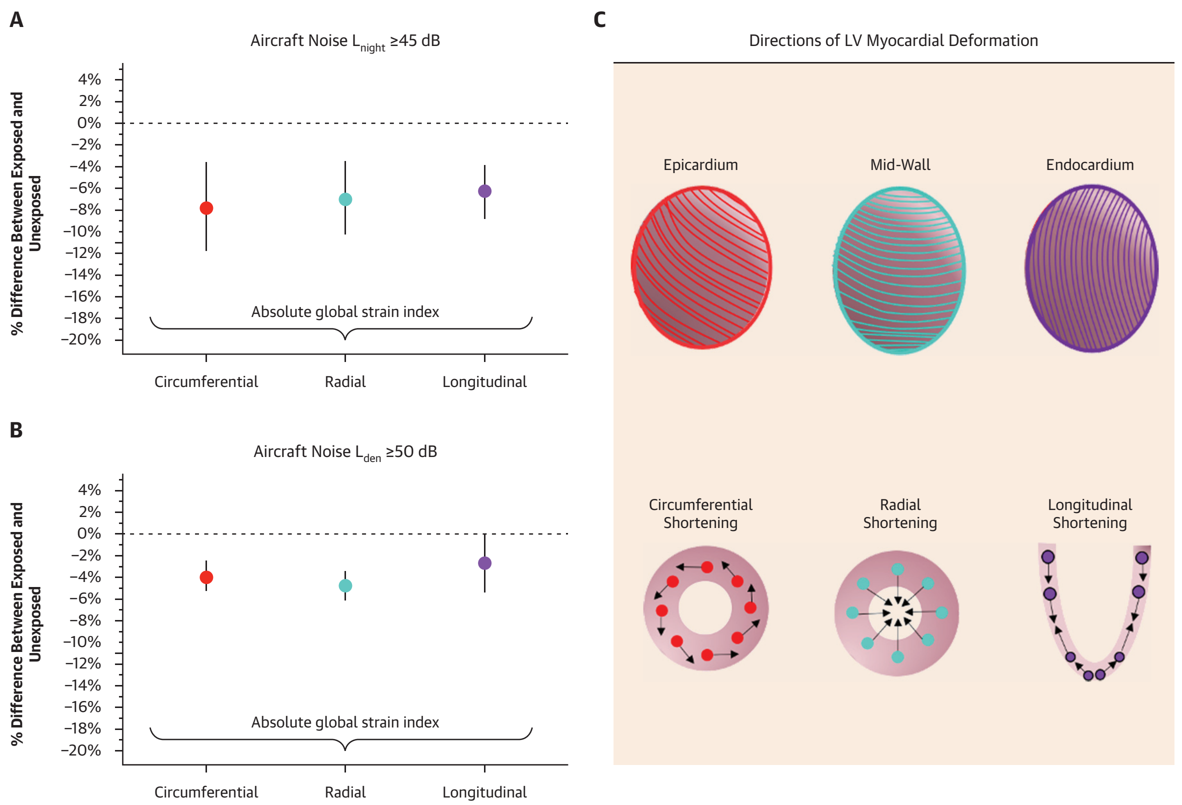
As most individuals were in the unexposed group (97% for L_{night} and 92% for L_{den}), differences in covariate distributions between the unexposed and exposed groups could bias the results, despite standard regression model adjustments. To verify the reliability of our results, we therefore repeated the analyses using generalized linear models weighted with propensity-matched scores. The propensity scores were calculated using the psmatch2 STATA package.[37]

To verify the robustness of our results, we repeated all the analyses in UKB participants who did not move home since recruitment and were potentially continuously exposed to higher aircraft noise levels. Models were adjusted as before for demographic, cohort-related, socioeconomic, lifestyle, and environmental confounders, with strain models being additionally adjusted for the use of antihypertensives. Separate analyses were conducted for L_{night} and L_{den}.

RESULTS

PARTICIPANT CHARACTERISTICS. A total of 3,635 UKB participants who lived near 1 of the 4 major UK airports, had CMR imaging data, and self-reported no hearing difficulties or deafness were included. Higher L_{night} (≥45 dB) or higher L_{den} (≥50 dB) were experienced by 2.9% and 8.4% of participants, respectively. Participant characteristics stratified by noise exposure status are presented in Table 1. Both aircraft noise L_{night} and L_{den} were very weakly correlated with $PM_{2.5}$ air concentrations (correlation coefficients <0.15), but not correlated with road noise, rail noise, or NO_2 air concentrations (Supplemental Table 2). The characteristics of the

FIGURE 3 **Associations Between Higher Aircraft Noise Exposure (L_{night} ≥45 dB and L_{den} ≥50 dB) and CMR Strain Metrics**



Plots are presented for 3,635 UK Biobank participants living near 1 of the 4 UK major airports showing the percentage differences (central dots), along with their 95% CIs (whiskers), in CMR absolute strain metrics between those exposed and unexposed to higher (A) L_{night} ≥45 dB and (B) L_{den} ≥50 dB, after adjusting for demographic, cohort-related, socioeconomic, lifestyle, and environmental confounders, as well as the use of antihypertensives. All strain metrics were indexed to $LVmass_i$. (C) The directions of myocardial deformation corresponding to these strain metrics are visually displayed. Abbreviations as in Figures 1 and 2.

21,360 individuals who had both CMR and MACE outcome data, but were not included in the aircraft noise substudy are presented in Supplemental Table 3. Of these, 1,272 (6%) experienced MACE.

ASSOCIATIONS BETWEEN AIRCRAFT NOISE EXPOSURE AND THE CMR PHENOTYPE. Among those who did not self-report any hearing difficulties, participants exposed to higher aircraft L_{night} had larger LV volumes (all $P \leq 0.006$), including 5% (95% CI: 4%-6%) greater $LVEDV_i$, 7% (95% CI: 2%-12%) greater $LVESV_i$, and 7% (95% CI: 4%-10%) greater MV, after adjusting for demographic, socioeconomic, cohort-related, lifestyle, and environmental confounders (including road and rail noise, and concentrations of NO_2 and $PM_{2.5}$ in the air). The absolute value differences corresponding to these percentage differences are presented in Supplemental Table 4. In addition, they also had concentrically thicker hearts, as suggested by the 7% (95% CI: 4%-10%) greater $LVmass_i$ and 4% (95% CI: 2%-5%) greater LV $\overline{WT}$ with a SLWR of ~1 (Table 2, Figure 2A). They also had worse LV dynamics, as suggested by the lower absolute LV global strain indices. These were 8% (95% CI: 4%-12%) lower for circumferential, 7% (95% CI: 4%-10%) lower for radial, and 6% (95% CI: 4%-9%) lower for longitudinal strain in the exposed group, after adjusting for confounders as before (Table 2, Figure 3A). In general, the differences between the exposed and unexposed groups were greater at the base/mid segments compared to the apex. Although those exposed also had 1% smaller LVEF and 3% smaller LV MCF, these associations were not significant (both $P > 0.194$). The results were similar when the generalized linear models were weighted using propensity-matched scores (Supplemental Table 5).

TABLE 3 Associations Between CMR Metrics and MACE in Those With No Aircraft Noise Exposure

CMR Metrics	Model 1			Model 2		
	HR (95% CI)	*P* Value	n	HR (95% CI)	*P* Value	n
$LVEDV_i$	1.02 (1.00-1.04)	0.012[a]	18,380	1.02 (1.00-1.03)	0.052	18,368
$LVESV_i$	1.03 (1.01-1.05)	0.014[a]	18,380	1.02 (1.00-1.04)	0.034[a]	18,368
LV MV	1.04 (1.03-1.05)	<0.001[a]	18,391	1.04 (1.02-1.05)	<0.001[a]	18,368
$LVmass_i$	1.04 (1.03-1.06)	<0.001[a]	18,380	1.04 (1.03-1.06)	<0.001[a]	18,368
LV $\overline{WT}$	1.04 (1.03-1.05)	<0.001[a]	18,388	1.04 (1.03-1.05)	<0.001[a]	18,365
LV MWT	1.04 (1.03-1.06)	<0.001[a]	18,388	1.04 (1.02-1.05)	<0.001[a]	18,365
IVST	1.04 (1.02-1.05)	<0.001[a]	18,388	1.03 (1.02-1.04)	<0.001[a]	18,365
LV lateral WT	1.04 (1.03-1.05)	<0.001[a]	18,388	1.04 (1.02-1.05)	<0.001[a]	18,365
LVEF	0.99 (0.98-1.01)	0.291	18,391	0.99 (0.98-1.01)	0.234	18,368
LV MCF	0.97 (0.96-0.98)	<0.001[a]	18,391	0.97 (0.96-0.99)	<0.001[a]	18,368
Global absolute LV circumferential strain index	0.96 (0.95-0.98)	<0.001[a]	18,368	0.97 (0.95-0.98)	<0.001[a]	18,356
Global absolute LV radial strain index	0.97 (0.95-0.98)	<0.001[a]	18,368	0.97 (0.96-0.98)	<0.001[a]	18,356
Global absolute LV longitudinal strain index	0.97 (0.95-0.98)	<0.001[a]	17,719	0.97 (0.96-0.98)	<0.001[a]	17,707

Our MACE outcome consisted of cardiovascular deaths or inpatient hospitalizations for acute coronary syndromes, stable angina, stroke, intracranial hemorrhage, atrial fibrillation or flutter, supraventricular tachycardias, life-threatening ventricular arrythmias, or heart failure. All reported analyses consisted of Cox regression models. The CMR metrics were minimum-maximum rescaled to be distributed between 0 and 100, so the HR for MACE per 1% increase in each CMR metric could be reported. Please note that a 1% increase in the LVEF, LV MCF, and LV strain metrics reflects a change to a more desirable phenotype. Model 1 was adjusted for demographic (age, sex, and race/ethnicity), cohort-related (assessment center, nonmover status, and length at the current address), socioeconomic (Townsend deprivation index and household income before tax), and lifestyle (smoking status, alcohol consumption, and physical activity) confounders. Model 2 was additionally adjusted for BMI and the presence of hypertension, diabetes, high cholesterol, and cardiovascular disease. [a]Significant *P* value.

Abbreviations as in Table 1.

In mediation analyses, BMI appeared to mediate 25% to 46% of the relationships between higher L_{night} and the observed CMR phenotype, especially for LV volumes, $LVmass_i$, and LV strain values (**Table 4**). Interestingly, total trunk fat volume (Supplemental Table 6), abdominal subcutaneous adipose tissue volume (Supplemental Table 7), and visceral adipose tissue volume (Supplemental Table 8) (all reflecting adiposity) also appeared to be significant mediators, with similar proportions of mediation as BMI. However, no mediating effects through hypertension (Supplemental Table 9) or high cholesterol (Supplemental Table 10) were seen when using L_{night}. Further adjusting for diabetes or CVD beyond demographic, socioeconomic, cohort-related, lifestyle, and environmental covariates did not attenuate the regression coefficients (Supplemental Table 11).

Observed changes are potentially clinically relevant, as each 1% adverse change in any single one of these CMR metrics (except for LVEF) was associated with a higher risk of MACE. The HR was 1.02 for each 1% adverse change in $LVEDV_i$ ($P = 0.052$) and $LVESV_i$ ($P = 0.034$); 1.03 for interventricular septal thickness, LV MCF, and all global LV strain metrics (all $P < 0.001$); and 1.04 for LV MV, $LVmass_i$, LV $\overline{WT}$, LV maximal wall thickness, and LV lateral WT (all $P < 0.001$), after adjusting for demographic, cohort-related, socioeconomic, and lifestyle confounders, as well as BMI and the presence of high cholesterol, hypertension, diabetes, and CVD (**Table 3**). For example, a 7% greater $LVmass_i$ independently associated with a 32% higher risk of MACE, while a 4% greater LV $\overline{WT}$ associated with a 17% higher risk of MACE. Moreover, an 8% lower circumferential strain independently associated with a 27% higher risk and a 7% lower radial strain with a 23% higher risk, while a 6% lower longitudinal strain associated with a 19% higher risk of MACE. Overall, a hypothetical individual experiencing the typical CMR abnormalities associated with higher L_{night} in $LVEDV_i$, $LVESV_i$, $LVmass_i$, LV $\overline{WT}$, and LV strain may have a 4 times higher risk of MACE.

In general, findings were mostly replicated in those exposed to higher aircraft L_{den}, but the effect sizes were smaller (**Table 2**, **Figures 2B and 3B**). Importantly, those exposed to higher aircraft L_{den} also had a 2% (95% CI: 1%-3%) lower LV MCF. In mediation analyses, BMI appeared to mediate 29% to 54% (**Table 4**), while hypertension appeared to mediate 9% to 36% (Supplemental Table 9), of the relationships between higher L_{den} and the CMR metrics. The abdominal magnetic resonance imaging-based adiposity metrics had mediating effects comparable to BMI (Supplemental Tables 6 to 8). High cholesterol was not a significant mediator (Supplemental Table 10). Further adjusting for diabetes or CVD beyond demographic, socioeconomic, cohort-related, lifestyle, and environmental covariates did not attenuate the regression coefficients (Supplemental Table 11). A hypothetical individual experiencing the typical CMR

TABLE 4 Mediation Analyses for BMI

	L_{night} ≥45 dB					
	ACME		Total Effects		PoM	
CMR Metrics	β (95% CI)	*P* Value	β (95% CI)	*P* Value	Proportion (95% CI) (%)	*P* Value
$LVEDV_i$	0.96 (0.77-1.15)	<0.001[a]	2.66 (2.17-3.16)	<0.001[a]	36 (23-49)	<0.001[a]
$LVESV_i$	0.61 (0.48-0.75)	<0.001[a]	1.72 (0.63-2.8)	0.002	36 (7-65)	0.017[a]
LV MV	2.20 (0.89-3.52)	0.001[a]	5.37 (3.22-7.52)	<0.001[a]	41 (2-80)	0.040[a]
$LVmass_i$	0.89 (0.33-1.45)	0.002[a]	2.19 (1.32-3.06)	<0.001[a]	41 (−1 to 82)	0.054
LV $\overline{WT}$	0.07 (0.01-0.13)	0.029[a]	0.18 (0.11-0.26)	<0.001[a]	37 (−10 to 83)	0.121
LV MWT	0.09 (0.01-0.17)	0.029[a]	0.20 (0.12-0.28)	<0.001[a]	46 (−13 to 104)	0.130
IVST	0.06 (0.01-0.12)	0.030[a]	0.17 (0.09-0.24)	<0.001[a]	38 (−11 to 87)	0.127
LV lateral WT	0.07 (0.01-0.14)	0.035[a]	0.23 (0.13-0.33)	<0.001[a]	32 (−10 to 74)	0.133
LVEF	−0.26 (−0.40 to −0.12)	<0.001[a]	−0.75 (−2.27 to 0.76)	0.328	35 (−31 to 101)	0.302
LV MCF	−0.01 (−0.03 to 0)	0.087	−0.03 (−0.07 to 0.01)	0.110	41 (−42 to 124)	0.335
Global absolute LV circumferential strain index	−0.02 (−0.02 to −0.01)	<0.001[a]	−0.06 (−0.08 to −0.03)	<0.001[a]	30 (8-52)	0.009[a]
Global absolute LV radial strain index	−0.03 (−0.05 to −0.02)	<0.001[a]	−0.1 (−0.14 to −0.06)	<0.001[a]	35 (11-58)	0.004[a]
Global absolute LV longitudinal strain index	−0.01 (−0.02 to 0)	0.020[a]	−0.04 (−0.05 to −0.03)	<0.001[a]	25 (4-54)	0.009[a]

We aimed to explore to what extent BMI explains the relationships between higher aircraft noise exposure and worse heart structure and function CMR metrics using the Imai, Tingley, and Yamamoto framework of causal inference. We calculated the ACME of BMI and total effects, and then determined the PoM via BMI as their ratio, expressed as a percentage. Models were adjusted for demographic (age, sex, and race/ethnicity), cohort-related (assessment center, local authority district, nonmover status, and length at the current address), socioeconomic (Townsend deprivation index and household income before tax), lifestyle (smoking status, alcohol consumption, and physical activity), and environmental (road and rail noise, and concentrations of NO_2 and $PM_{2.5}$ in the air) confounders. [a]Significant *P* value.

ACME = average causal mediation effect; PoM = proportion of mediation; other abbreviations as in Table 1.

Continued on the next page

abnormalities associated with higher L_{den} in $LVEDV_i$, $LVESV_i$, $LVmass_i$, LV $\overline{WT}$, and LV strain may have a doubled risk of MACE.

ASSOCIATIONS BETWEEN AIRCRAFT NOISE EXPOSURE AND THE CMR PHENOTYPE IN NONMOVERS. Out of the 3,635 study participants included, 2,532 (70%) did not move home from recruitment up until 2022, and were continuously exposed to higher aircraft noise levels. These nonmovers were slightly older (53 vs 51 years of age) and lived in less deprived neighborhoods compared to those who moved home (Supplemental Table 12). However, the prevalence of comorbidities was similar at baseline. In general, the study findings were replicated in this subgroup of nonmovers, with similar or even larger effect sizes for all CMR heart structure and function metrics (Supplemental Table 13). However, the 95% CIs were generally wider due to the smaller sample size.

DISCUSSION

In this study in which cardiac imaging was acquired at least 3 years after noise data was collected, we found that higher aircraft noise exposure was associated with adverse cardiac remodeling in the form of concentric hypertrophy, worse myocardial dynamics, and impaired systolic performance, potentially due to noise increasing the risk of obesity and hypertension. This noise-related LV remodeling is clinically relevant, as it is associated with a higher risk of MACE.

CARDIAC REMODELING PATTERNS ASSOCIATED WITH HIGHER AIRCRAFT NOISE EXPOSURE. Using CMR, the gold standard imaging modality to assess heart structure and function, we found that higher aircraft noise levels at residential addresses were associated with a higher LV mass and $\overline{WT}$ but with a SLWR of ∼1, suggesting a pattern of concentric LV remodeling. Hypertension and BMI/adiposity appeared to mediate 10% to 50% of the observed associations between higher aircraft noise exposure and this concentric remodeling phenotype, suggesting their potential role in the mechanistic pathway. Noise can lead to the overactivation of the sympathetic nervous system, increasing the BP,[38] and induce a stress response characterized by higher cortisol levels,[14,15,39] which can promote weight gain.[40] By increasing LV afterload, hypertension can cause concentric remodeling. In addition, concentric hypertrophy is the most common pattern of LV hypertrophy in overweight individuals.[41] LV hypertrophy can lead to diastolic dysfunction, and this has been

TABLE 4 Continued

L_{den} ≥50 dB					
ACME		Total effects		PoM	
β (95% CI)	*P* Value	β (95% CI)	*P* Value	Proportion (95% CI) (%)	*P* Value
0.53 (0.26-0.8)	<0.001[a]	0.97 (0.86-1.09)	<0.001[a]	54 (24-85)	0.001[a]
0.30 (0.14-0.46)	<0.001[a]	0.67 (0.24-1.10)	0.002[a]	45 (4-86)	0.031[a]
1.35 (0.20-2.50)	0.022[a]	2.62 (1.07-4.16)	0.001[a]	51 (0-100)	0.049[a]
0.59 (0.08-1.10)	0.023[a]	1.15 (0.41-1.90)	0.003[a]	51 (−8 to 111)	0.090
0.05 (0-0.11)	0.054	0.11 (0.03-0.20)	0.008[a]	47 (−15 to 108)	0.135
0.07 (0-0.15)	0.058	0.13 (−0.02 to 0.29)	0.090	54 (−5 to 112)	0.073
0.05 (−0.01 to 0.11)	0.079	0.12 (0.05-0.20)	0.001[a]	41 (−10 to 92)	0.114
0.05 (0-0.10)	0.039[a]	0.11 (0.01-0.21)	0.034[a]	48 (−24 to 120)	0.189
−0.12 (−0.22 to −0.02)	0.017[a]	−0.29 (−1.01 to 0.43)	0.430	41 (−48 to 130)	0.369
−0.01 (−0.02 to 0)	0.104	−0.02 (−0.03 to −0.01)	<0.001[a]	45 (−15 to 106)	0.141
−0.01 (−0.02 to 0)	0.012[a]	−0.03 (−0.03 to −0.02)	<0.001[a]	40 (2-78)	0.041[a]
−0.02 (−0.03 to −0.01)	0.005[a]	−0.07 (−0.08 to −0.05)	<0.001[a]	29 (9-49)	0.005[a]
−0.01 (−0.01 to 0)	0.034[a]	−0.02 (−0.03 to 0)	0.008	48 (37-59)	<0.001[a]

observed in those exposed to higher aircraft noise levels.[10] Moreover, there is already good epidemiological data linking noise with obesity[7,42] and hypertension.[9] Considering the growing body of evidence suggesting a relationship between noise exposure and CVD, as well as highlighting plausible biological mechanisms, it is possible that a causal relationship may exist. Hypertension and obesity can adversely affect the heart by increasing LV mass and worsening systolic function, as suggested by the existing CMR literature.[43,44] Given the established link between aircraft noise and both hypertension and obesity, it should not be surprising that these CV risk factors could mediate the relationship between a higher aircraft noise exposure and worse heart structure and function, as observed in this study.

CLINICAL IMPACT OF AIRCRAFT NOISE-RELATED CARDIAC REMODELING. The observed aircraft noise-associated LV remodeling may be pathological. LV MCF is an index of LV myocardial shortening that captures maladaptive LV hypertrophy, with low values previously linked to negative outcomes even in the presence of a normal LVEF,[20] indicating its utility as a subclinical disease biomarker. In those exposed to higher aircraft noise L_{den}, MCF was lower, suggesting a measurable decline in LV systolic function. Similarly, a higher aircraft noise exposure could be linked to worse myocardial dynamics, as highlighted by the 6% to 8% worse circumferential, radial, and longitudinal global strain indices. All of these changes are potentially clinically relevant because they are associated with a higher risk of a MACE composite of CV deaths or hospitalizations (for coronary syndromes, stroke, supraventricular or ventricular arrhythmias, or heart failure). For example, an 8% isolated decrease in global circumferential strain increases the risk of MACE by 27%. However, when considering compounding, the risk of MACE increases exponentially. For example, a hypothetical individual in whom all CMR volume, mass, and strain metrics exhibit the average worsening associated with a higher L_{night} aircraft noise exposure may see their risk of MACE increase 4 times.

IMPLICATIONS FOR TRANSPORT POLICY. The European Environment Agency predicts an almost 50% increase in passenger numbers in the aviation industry by 2040 in Europe,[45] and many airports have made plans to build new runways or terminals, or to expand their current ones, to accommodate this predicted increased demand. For example, the UK government approved the expansion of Heathrow's third runway through the Airports National Policy Statement,[46] and further expansion of London City Airport is also planned. In Europe, the United States, and many countries worldwide, there are no regulatory limits for noise exposure, although there are policies in place to reduce aircraft noise. Our results suggest that higher aircraft noise associates with adverse cardiac remodeling, with the worst phenotype seen with nighttime exposure. This is consistent with the growing body of evidence linking aircraft noise with worse cardiovascular health.[47,48] Moving forward, the

impacts of aircraft noise on health need to be carefully considered as part of transport planning to protect communities living near airports or under flight paths.

STUDY STRENGTHS AND LIMITATIONS. This is the first CMR-based study to examine the associations between a higher aircraft noise exposure and heart structure and function. While our regression models were extensively adjusted for confounders, including the sensitivity analyses using propensity scores, and our results are compatible with the body of evidence linking transport noise with cardiovascular disease, we cannot fully exclude residual confounding as a partial explanation for the observed associations. Further, while our noise exposure estimates precede imaging, we were unable to investigate incidence, as this would require results from repeated imaging. An important limitation is that we were unable to explore the dose-response effects of aircraft noise exposure, which would provide increased plausibility for a causal association. We compared higher vs lower noise exposures because of the relatively small numbers exposed to high aircraft noise, and given that CAA does not supply noise estimates <50 dB for L_{den} and <45 dB for L_{night}. This data truncation prevented us from using the cutoffs recommended by the WHO in their health-based guidelines for noise exposure. As these are 5 dB lower (ie, 45 dB for L_{den} and 40 dB for L_{night}), we may underestimate the number of individuals who are exposed to higher aircraft noise levels and its impact on heart structure and function. Given the previous limitations, it is difficult to directly quantify potential clinical implications if associations are causal. However, we provide an investigation of the clinical impact of noise-related LV remodeling in terms of MACE risk. In this study, we could only include UKB participants who had both aircraft noise and CMR data meaning that selection and collider bias can exist. Misclassification of noise levels remains possible as noise exposure was evaluated at the group level based on postcodes and census units. In addition, we could not estimate the noise levels in the bedroom or living room, where participants potentially spend most of their time. Moreover, we were also unable to consider house soundproofing or earplug use. This misclassification is likely to lead to a bias toward the null in associations. Because imaging occurred a few years after the aircraft noise collection, those who were exposed to the highest noise levels may have moved residence and been lost to follow-up. Similarly, they could have had the most adverse cardiac phenotype and passed away, missing the chance to attend the imaging clinic. While our results are consistent with the existing evidence on physical effects of noise, causality regarding impacts on the heart cannot be inferred from this first study examining associations between aircraft noise exposure and LV structure and function.

CONCLUSIONS

Our study suggests that a higher aircraft noise exposure, especially at night, is associated with adverse cardiac remodeling in the form of concentric LV hypertrophy and reduced LV systolic function, independent of clinical and environmental confounders. This phenotype was associated with MACE, and both obesity and hypertension may be contributing to it. In the context of a growing body of evidence linking transport noise with CVD, our findings also support the negative impacts of aircraft noise on the human heart, with important implications for noise reduction policies.

ACKNOWLEDGMENTS The authors thank and acknowledge the UK Civil Aviation Authority, who provided aircraft noise data, calculated using the Aircraft Noise CONtour (ANCON) model. The authors gratefully acknowledge the Noise and Statutory Nuisance Team at the Department for Environment, Food and Rural Affairs for the creation and provision of the Environmental Noise Regulations Round 2 exposure surfaces of rail transport in England. The authors thank the members of the advisory board for the Medical Research Council ANCO (Aircraft Noise and Cardiovascular Outcomes) study for their input on the methodological aspects. The advisory board includes representation from relevant government departments and agencies, community groups, nongovernmental organizations, and industry. The views expressed in this paper are those of the authors and may not reflect those of the advisory board members or their respective organizations. This research has been conducted using the UK Biobank Resource under Application Number 59129. The UK Biobank data are available from https://www.ukbiobank.ac.uk/. Upon publication, the final STATA script will be made publicly available on GitHub.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

This project was funded by the Medical Research Council (MRC) ANCO (Aircraft Noise and Cardiovascular Outcomes) study grant (principal investigator: Dr Hansell). Dr Topriceanu was supported by a British Cardiovascular Society Heart Research UK Fellowship and by a University College London (UCL) Charlotte and Yule Bogue Research Fellowship. Dr Captur was supported by the British Heart Foundation (MyoFit46 Special Programme Grant SP/20/2/34841), a National

Institute for Health and Care Research (NIHR) iFAST grant (187075), and by the NIHR UCL Hospitals Biomedical Research Centre. Drs Hansell, Gulliver, and Gong were funded by the NIHR Health Protection Research Unit in Environmental Exposures and Health at the University of Leicester development award, a partnership between the UK Health Security Agency, the Health and Safety Executive, and the University of Leicester. Dr Hansell was funded by the NIHR Leicester Biomedical Research Centre. Dr Blangiardo was partially supported by the MRC Centre for Environment and Health funded by the UK Medical Research Council (grant no. MR/L01341X/1). Dr Hughes was supported by the British Heart Foundation, the Horizon 2020 and Horizon Europe Programmes of the European Union, the NIHR UCL Hospitals Biomedical Research Centre, the UK Medical Research Council, the NIHR, and the Wellcome Trust, and works in a unit that receives support from the UK Medical Research Council. None of the funders were involved in the study design, collection, analysis, interpretation of the data, or decision to submit the article for publication. The views expressed in this publication are those of the authors and not necessarily those of the funders. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS aircraft noise, cardiac hypertrophy, cardiac remodeling, worse systolic function

APPENDIX For a supplemental equation, supplemental tables and a figure, please see the online version of this paper.