SUPPLEMENTAL MATERIAL

Individual Day-Time Noise Exposure During Routine Activities and Heart Rate Variability in Adults: A Repeated Measures Study

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**Detailed description of the diary and physical activity**

During the measurement period between 7:30 a.m. and 3 p.m. participants were free to go wherever they liked and to pursue their daily routines. All their activities and whereabouts were recorded in a diary. In doing so, participants always made a diary entry when they changed their whereabouts or activity. Times were recorded precisely to the minute. A diary entry included a free text description of the activity. Furthermore, participants had to tick whether they were indoors, outside and not in traffic (e.g. in a park), or in traffic. Additionally, persons were asked to note when they felt annoyed by noise and to rate this annoyance on a scale with five levels ranging from “minor” to “extreme”. After returning to the study center the nurses checked the diary for readability, completeness and conclusiveness. Every ambiguity was directly solved in discussion together with the participant. Dichotomous variables for the whereabouts where built.

To ensure that diary data can be aligned on the same timescale with exposure and outcome data, each participant got a wrist watch that was regularly synchronized with a radio controlled clock. The clocks of the exposure devices were likewise synchronized before starting the measurement. Furthermore, the study nurses recorded start and end times of the measurement periods in a protocol. Before combining the data times were compared with the times that were recorded by the study nurses.
### TABLE S1. Final confounder models for each ECG parameter.

| ECG parameter | Confounder model                                                                 |
|---------------|-----------------------------------------------------------------------------------|
| HR            | lagged HR, long-term time trend (linear), daily time trend based on every five minutes (smooth), physical activity (categorical) |
| SDNN          | lagged SDNN, long-term time trend (polynomial, 2nd order), daily time trend based on every 30 minutes (polynomial, 4th order), physical activity (categorical), HR |
| LF power      | lagged LF power, long-term time trend (linear), daily time trend based on every 15 minutes (polynomial, 4th order), physical activity (categorical), HR |
| HF power      | lagged HF power, long-term time trend (linear), daily time trend based on every 15 minutes (polynomial, 4th order), physical activity (categorical), HR |
| LF/HF ratio   | lagged LF/HF ratio, long-term time trend (polynomial 3rd order), daily time trend based on every 5 minutes (smooth), physical activity (categorical), HR |

Abbreviations: HF, high frequency; HR, heart rate; LF, low frequency; SDNN, standard deviation of normal-to-normal intervals
| Characteristic                                      | Men |           | Women |           | P     |
|---------------------------------------------------|-----|-----------|-------|-----------|-------|
|                                                  | N   | (% or    | N     | (% or    |       |
|                                                  |     | mean ± SD|       | mean ± SD|       |
| Age [yrs]                                         | 69  | (63.7 ± 11.1) | 41    | (58.1 ± 11.9) | 0.016e |
| Body mass index [kg/m²]                           | 69  | (28.8 ± 4.7) | 41    | (28.2 ± 6.4) | 0.59e  |
| Smoking history                                   |     |           |       |           |       |
| Never smoker                                      | 45  | (65.2)    | 14    | (34.1)    |       |
| Ex smoker                                         | 24  | (34.8)    | 27    | (65.9)    | 0.0016f |
| Metabolic disorder (T2D⁷ or IGT⁸)                 | 42  | (60.9)    | 22    | (53.7)    | 0.46f  |
| Self-reported history                             |     |           |       |           |       |
| Myocardial infarction                             | 6   | (8.7)     | 0     | (0.0)     | 0.08g  |
| Angina pectoris                                   | 2   | (2.9)     | 4     | (9.8)     | 0.19g  |
| Coronary heart disease                            | 6   | (8.7)     | 1     | (2.4)     | 0.25g  |
| Hypertension                                      | 42  | (60.9)    | 19    | (46.3)    | 0.14f  |
| Use of medication                                 |     |           |       |           |       |
| Agents acting on renin-angiotensin-system         | 27  | (39.1)    | 13    | (31.7)    | 0.43f  |
| Beta blocker                                      | 21  | (30.4)    | 7     | (17.1)    | 0.12f  |
| Calcium channel blockers                          | 8   | (11.6)    | 3     | (7.32)    | 0.53g  |
| Antidiabetics                                     | 14  | (20.3)    | 4     | (9.8)     | 0.15f  |
| Diuretics                                         | 24  | (34.8)    | 12    | (29.3)    | 0.55f  |
| Nitrites                                          | 1   | (1.5)     | 0     | (0.0)     | 1.00g  |
| Statins                                           | 16  | (23.2)    | 3     | (7.3)     | 0.033f |
| Antihypertensive drugs                            | 38  | (55.1)    | 16    | (39.0)    | 0.10f  |
| Hearing impairment ‡ (%)                          | 12  | (17.4)    | 3     | (7.3)     | 0.14f  |
| If yes: Physician diagnosed                       | 9   | (13.0)    | 3     | (7.3)     | 1.00g  |
| Wearing hearing aid                               | 2   | (2.9)     | 0     | (7.3)     | 1.00g  |
| Employed (%)                                      | 24  | (34.8)    | 17    | (41.5)    | 0.48f  |

⁷Participants with T2D were classified based on self-report of a diagnosis by a physician, self-reported medication use, or a fasting glucose level >125mg/dl or 2h glucose level ≥200mg/dl in an oral glucose tolerance test (OGTT). IGT was specified as having 2h OGTT glucose levels ≥140mg/dl but <200mg/dl.

⁸Ever physician diagnosed.

‡At least once during the study period (Mar 17th 2007 to Dec 17th 2008).

P-values determined with eStudent’s t-test, fchi-square test or gFisher’s exact test.

Abbreviations: T2D, type 2 diabetes; IGT, impaired glucose tolerance; SD, standard deviation.
TABLE S3. Baseline characteristics of the study population by age-group.

| Characteristic                                      | < 65 years             | ≥ 65 years             | P    |
|-----------------------------------------------------|------------------------|------------------------|------|
|                                                     | N (% or mean ± SD)     | N (% or mean ± SD)     |      |
| Age [yrs]                                           | 55 (52.1 ± 8.6)        | 55 (58.1 ± 11.9)       | <.0001<sup>d</sup> |
| Body mass index [kg/m<sup>2</sup>]                  | 55 (28.3 ± 6.3)        | 55 (28.9 ± 4.3)        | 0.55<sup>d</sup>  |
| Men                                                 | 29 (52.7)              | 40 (72.7)              | 0.030<sup>e</sup> |
| Smoking history                                     |                        |                        |      |
| Never smoker                                        | 28 (50.9)              | 23 (41.8)              |      |
| Ex smoker                                           | 27 (49.1)              | 32 (58.2)              | 0.34<sup>e</sup>  |
| Metabolic disorder (T2D<sup>a</sup> or IGT<sup>a</sup>) | 23 (41.8)              | 41 (74.6)              | 0.0005<sup>f</sup> |
| Self-reported history<sup>b</sup>                   |                        |                        |      |
| Myocardial infarction                               | 1 (1.8)                | 5 (9.1)                | 0.21<sup>f</sup>  |
| Angina pectoris                                     | 4 (7.3)                | 2 (3.6)                | 0.68<sup>f</sup>  |
| Coronary heart disease                              | 4 (7.3)                | 3 (5.5)                | 1.00<sup>f</sup>  |
| Hypertension                                        | 23 (41.8)              | 38 (69.1)              | 0.0040<sup>e</sup>|
| Use of medication<sup>c</sup>                       |                        |                        |      |
| Agents acting on renin-angiotensin-system           | 14 (25.5)              | 26 (47.3)              | 0.017<sup>e</sup> |
| Beta blocker                                        | 7 (12.7)               | 21 (38.2)              | 0.0022<sup>e</sup>|
| Calcium channel blockers                            | 3 (5.5)                | 8 (15.6)               | 0.11<sup>e</sup>  |
| Antidiabetics                                       | 7 (12.7)               | 11 (20.0)              | 0.30<sup>e</sup>  |
| Diuretics                                           | 12 (21.8)              | 24 (43.6)              | 0.015<sup>e</sup> |
| Nitrates                                            | 0 (0.0)                | 1 (1.8)                | 1.00<sup>f</sup>  |
| Statins                                             | 4 (7.3)                | 15 (27.3)              | 0.0055<sup>e</sup>|
| Antihypertensive drugs                              | 18 (32.7)              | 36 (65.5)              | 0.0006<sup>e</sup>|
| Hearing impairment%<sup>d</sup>                     | 1 (1.8)                | 14 (25.5)              | 0.0003<sup>e</sup>|
| If yes: Physician diagnosed                         | 1 (100.0)              | 11 (78.6)              | 1.00<sup>f</sup>  |
| Wearing hearing aid                                 | 0 (0.0)                | 2 (14.3)               | 1.00<sup>f</sup>  |
| Employed%                                           | 38 (69.09)             | 3 (5.5)                | <.0001<sup>e</sup>|

<sup>a</sup>Participants with T2D were classified based on self-report of a diagnosis by a physician, self-reported medication use, or a fasting glucose level >125mg/dl or 2h glucose level ≥200mg/dl in an oral glucose tolerance test (OGTT). IGT was specified as having 2h OGTT glucose levels ≥140mg/dl but <200mg/dl.

<sup>b</sup>Ever physician diagnosed.

<sup>c</sup>At least once during the study period (Mar 17<sup>th</sup> 2007 to Dec 17<sup>th</sup> 2008).

<sup>d</sup>Not validated.

P-values determined with <sup>e</sup>Student's t-test, or <sup>f</sup>chi-square test.

Abbreviations: T2D, type 2 diabetes; IGT, impaired glucose tolerance; SD, standard deviation.
### TABLE S4. Description of diary entries (N=4,148).

| Diary based information         | Diary entries N (%) | 5-minute segments N (%) |
|----------------------------------|---------------------|-------------------------|
| Whereabouts                      |                     |                         |
| Indoors                          | 2,268 (54.78)       | 14,020 (65.5)           |
| Outside, not in traffic          | 159 (3.8)           | 917 (4.3)               |
| In traffic                       | 1,687 (40.7)        | 4,904 (22.9)            |
| Unclear                          | 34 (0.8)            | 1,578 (7.4)             |
| Physical activity                |                     |                         |
| Sleeping/Reclining               | 110 (2.7)           | 329 (1.5)               |
| Very light/light exertion        | 3,766 (90.8)        | 20,032 (93.5)           |
| Moderate/vigorous/heavy exertion| 272 (6.6)           | 1,058 (4.9)             |

### TABLE S5. Spearman correlation coefficients for ECG parameters.

| ECG measures   | HR  | SDNN | LF   | HF   | LF/HF Ratio |
|----------------|-----|------|------|------|-------------|
| HR             | 1   |      | -0.22| -0.18|             |
| SDNN           |     | 1    |      | -0.21| -0.16       |
| LF             |     | 1    | 0.41 |      | 0.40        |
| HF             |     |      | 1    |      | -0.59       |
| LF/HF Ratio    |     |      |      | 1    |             |

Abbreviations: HF, high frequency; HR, heart rate; LF, low frequency; SDNN, standard deviation of normal-to-normal intervals.
TABLE S6. Adjusted immediate and delayed associations between five-minute averages of $L_{eq}$ and ECG measures.

| ECG measures | % change (95%CI) | % change (95%CI) |
|--------------|-----------------|-----------------|
|              | $< 65$ dB(A)    | $\geq 65$ dB(A) |
| **HR**       |                 |                 |
| concurrent   | 1.48 (1.37, 1.60)* | 0.18 (0.05, 0.31)* |
| 0-5min       | 0.29 (0.17, 0.41)* | 0.09 (-0.04, 0.22) |
| 5-10min      | 0.12 (0.01, 0.24)* | 0.08 (-0.04, 0.21) |
| 10-15min     | 0.09 (-0.02, 0.21) | 0.15 (0.02, 0.28)* |
| **SDNN**     |                 |                 |
| concurrent   | 5.74 (5.13, 6.36)* | -0.67 (-1.30, -0.04)* |
| 0-5min       | -0.53 (-1.12, 0.05) | -0.08 (-0.71, 0.56) |
| 5-10min      | -0.69 (-1.26, -0.12)* | -0.09 (-0.73, 0.54) |
| 10-15min     | -0.67 (-1.26, -0.13)* | -0.21 (-0.84, 0.43) |
| **LF power** |                 |                 |
| concurrent   | -3.77 (-5.49, -2.02)* | 4.42 (2.59, 6.32)* |
| 0-5min       | 0.26 (-1.53, 2.09) | 3.69 (1.86, 5.56)* |
| 5-10min      | 2.14 (0.37, 3.95) | 1.50 (-0.30, 3.33) |
| 10-15min     | 2.24 (0.49, 4.02)* | 1.74 (-0.07, 3.57) |
| **HF power** |                 |                 |
| concurrent   | -8.56 (-10.31, -6.78)* | 2.89 (0.95, 4.87)* |
| 0-5min       | -1.31 (-3.21, 0.62) | 3.45 (1.50, 5.44)* |
| 5-10min      | 0.87 (-1.01, 2.79) | 1.58 (-0.34, 3.55) |
| 10-15min     | 1.90 (-0.04, 3.80) | 1.67 (-0.26, 3.63) |
| **LF/HF ratio** |               |                 |
| concurrent   | 4.89 (3.48, 6.32)* | 1.38 (0.03, 2.75)* |
| 0-5min       | 0.98 (-0.38, 2.36) | -0.09 (-1.43, 1.26) |
| 5-10min      | 0.96 (-0.36, 2.31) | -0.18 (-1.52, 1.17) |
| 10-15min     | 0.12 (-1.17, 1.43) | 0.05 (-1.29, 1.40) |

*P-value of fixed effect for $L_{eq}$ as piecewise linear term in additive mixed model < 0.05

Abbreviations: dB(A), A-weighted decibels; change, change of outcome mean per 5 dB(A) increase in noise exposure; CI, confidence interval; HR, heart rate; SDNN, standard deviation of normal-to-normal intervals; HF, high frequency; LF, low frequency; min, minute
Table S7. Associations of physical activity on HR as well as physical activity and HR on HRV parameters.

| outcome | exposure   | % change$^a$ | (95% CI)       |
|---------|------------|--------------|----------------|
| HR      | moderate PA| 1.67*        | (0.67, 2.67)   |
|         | high PA    | 6.49*        | (5.38, 7.59)   |
| SDNN    | HR         | -0.35*       | (-2.03, -1.42) |
|         | moderate PA| -10.50*      | (-54.22, -27.93) |
|         | high PA    | -15.85*      | (-67.56, -45.09) |
| LF power| HR         | -3.92*       | (-18.83, -17.39) |
|         | moderate PA| 12.31        | (-13.54, 269.41) |
|         | high PA    | 28.36*       | (55.03, 682.96) |
| HF power| HR         | -4.22*       | (-20.13, -18.62) |
|         | moderate PA| -1.48        | (-57.25, 101.58) |
|         | high PA    | 8.36         | (-37.08, 254.73) |
| LF/HF ratio | HR         | 0.34*        | (1.02, 2.35)   |
|         | moderate PA| 11.24        | (-1.33, 194.06) |
|         | high PA    | 15.43*       | (11.43, 276.75) |

$^a$-% change in outcome mean per increase in physical activity category compared to the lowest activity level and per increase of 1 beat/min in HR, respectively.

*p-value<0.05

Abbreviations: CI, confidence interval; HR, heart rate; SDNN, standard deviation of normal-to-normal intervals; HF, high frequency; LF, low frequency; PA, physical activity
FIGURE S1. Number of observations (upper left panel) and estimated exposure-response functions of immediate associations between five-minute averages of $L_{eq}$ and ECG measures. Abbreviations: CI, confidence interval; dB(A), A-weighted decibels; HF, high frequency; HR, heart rate; $L_{eq}$, equivalent continuous sound pressure levels; LF, low frequency; nu, normalized units; SDNN, standard deviation of normal-to-normal intervals.