# APPENDICES AVAILABLE ON THE HEI WEB SITE

## Research Report 186

## Ambient and Controlled Particle Exposures as Triggers for Acute ECG Changes

**D. Q. Rich, A. Peters, et al.**

## Appendices A–T

Note: Appendices available only on the Web have been reviewed solely for spelling, grammar, and cross-references to the main text. They have not been formatted or fully edited by HEI.

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This document was reviewed by the HEI Health Review Committee.

APPENDICES A–T

## APPENDIX A. Total Antioxidant Capacity

**Methods:** Using the $n = 464$ blood samples from the Augsburg Panel Study and the $n = 657$ blood samples from the Rochester REHAB Study described above, we measured total antioxidant capacity. We used a commercial assay, Cell Biolabs OxiSelect Total Antioxidant Capacity (TAC) Assay Kit (San Diego, CA), to determine TAC within each blood sample. The assay is based on the reduction of copper (II) to copper (I) by antioxidants in the sample, such as uric acid. Upon reduction, the copper (I) ion further reacts with a coupling chromogenic reagent that produces a color with a maximum absorbance at 490 nm. The results for unknown samples were compared to a standard curve prepared from known uric acid concentrations. Results are expressed as mM Uric Acid Equivalents. The copper assay method detects all classes of antioxidants, including thiols, with marginal radical interference. Based on 44 human samples, the reference values of TAC were estimated to be 1.175 ± 0.007 mM (Kampa et al. 2002).

The associations between 24-hour averages of air pollution and TAC, done in the Augsburg Panel and Rochester REHAB studies only, were analyzed using additive mixed models with a random participant effect and a compound symmetry covariance structure in order to account for the dependencies between the repeated measurements. All models in the Augsburg Panel Study were adjusted for long-term time trend, temperature (lag day 1), relative humidity (lag day 1, P-Spline), and barometric pressure (lag day 0). In the Rochester REHAB Study, we included these same variables, as well as indicator variables for visit month, weekday, and hour of the day of the clinic visit. Immediate (lag day 0) and lagged (1 to 4 days) effects of 24-hour averages of $PM_{2.5}$, BC, UFP, and AMP were separately added to the confounder model and the effects were estimated linearly. For the Augsburg Panel Study, we checked whether the association between particulate air pollution and the ECG parameters differed between participants with diabetes or IGT and individuals with a genetic predisposition by conducting a stratified analysis.

**Results:** We hypothesized that increased 24 hour particulate pollutant concentrations in the few days before each blood sample, in which we assayed total antioxidant status, would be associated with decreased total antioxidant capacity (TAC). In both subject groups in the Augsburg Panel Study, we did not observe a consistent pattern of increased TAC or decreased TAC associated with IQR increases in 24 hour UFP, AMP, $PM_{2.5}$, or BC concentration in the previous 120 hours (5 days). In contrast, in the Rochester REHAB Study, we observed more decreases in TAC associated with increased 24 hour average UFP, AMP, and $PM_{2.5}$ concentrations in the previous 120 hours, the largest of which was a -0.80% reduction in TAC (95% CI -1.46%, -0.15%) associated with each IQR increase in UFP concentration lagged 96–119 hours. Therefore, we scored this as “No association or agreement,” and concluded that this hypothesis was not confirmed (Table 9).

**Table A.1.** Percent change in total antioxidant capacity per interquartile range increase in 24-hour average pollution concentrations in participants in the Augsburg panel Study (A: Diabetes/IGT group, B: Genetic Susceptibility group) and C: Rochester REHAB Study.

**A: Augsburg Panel Study: Diabetes/IGT group.**

| | | UFP IQR = 5722 particles/$cm^3$ | | | AMP IQR = 1532 particles/$cm^3$ | | | $PM_{2.5}$ IQR = 11.1 μg/$m^3$ | | | Black Carbon IQR = 1.2 μg/$m^3$ | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Pollutant averaging time** | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** |
| Lag 0–23h | 266 | –0.26 | (–1.38, 0.87) | 266 | 0.37 | (–0.75, 1.49) | 272 | 0.08 | (–1.07, 1.22) | 228 | –0.48 | (–1.83, 0.87) |
| Lag 24–47h | 263 | 0.35 | (–0.71, 1.42) | 263 | 0.42 | (–0.58, 1.41) | 272 | 0.12 | (–1.03, 1.26) | 229 | 0.47 | (–0.66, 1.60) |
| Lag 48–71h | 263 | 0.31 | (–0.95, 1.57) | 263 | 0.72 | (–0.42, 1.85) | 271 | 0.45 | (–0.80, 1.71) | 221 | 0.69 | (–0.74, 2.11) |
| Lag 72–95h | 259 | –0.43 | (–1.66, 0.80) | 259 | 0.54 | (–0.63, 1.71) | 270 | 0.37 | (–0.86, 1.59) | 221 | –0.37 | (–1.70, 0.96) |
| Lag 96–119h | 260 | 0.47 | (–0.78, 1.72) | 260 | 0.53 | (–0.61, 1.67) | 271 | –0.19 | (–1.36, 0.97) | 224 | –0.07 | (–1.35, 1.20) |

**B: Augsburg Panel Study: Genetic Susceptibility group.**

| Pollutant averaging time | UFP IQR = 5722 particles/$cm^3$ | | | AMP IQR = 1532 particles/$cm^3$ | | | $PM_{2.5}$ IQR = 11.1 µg/$m^3$ | | | Black Carbon IQR = 1.2 µg/$m^3$ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** |
| Lag 0–23h | 160 | 0.65 | (–0.87, 2.17) | 160 | 0.01 | (–1.51, 1.53) | 170 | –0.25 | (–1.96, 1.46) | 169 | –0.20 | (–1.60, 1.19) |
| Lag 24–47h | 157 | 1.03 | (–0.52, 2.59) | 157 | 0.68 | (–0.63, 1.98) | 170 | 0.70 | (–0.76, 2.17) | 166 | 0.49 | (–0.83, 1.81) |
| Lag 48–71h | 156 | 0.39 | (–1.04, 1.83) | 156 | 0.64 | (–0.64, 1.91) | 170 | 1.78 | (0.33, 3.22) | 166 | 0.94 | (–0.40, 2.28) |
| Lag 72–95h | 162 | –0.08 | (–1.68, 1.52) | 162 | 0.23 | (–1.14, 1.60) | 170 | 0.90 | (–0.67, 2.47) | 163 | 0.13 | (–1.32, 1.57) |
| Lag 96–119h | 159 | 0.38 | (–1.24, 2.00) | 159 | –0.12 | (–1.59, 1.35) | 169 | –0.65 | (–2.13, 0.84) | 166 | –0.26 | (–1.89, 1.37) |

## C: Rochester REHAB Study.

| Pollutant averaging time | UFP IQR = 2699 particles/cm$^3$ | | | AMP IQR = 836 particles/cm$^3$ | | | $PM_{2.5}$ IQR = 6.3 μg/m$^3$ | | | Black Carbon IQR = 0.47 μg/m$^3$ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** |
| Lag 0–23h | 1354 | –0.72* | (–1.34, –0.10) | 1354 | 0.20 | (–0.37, 0.78) | 1255 | 0.49 | (–0.10, 1.07) | 1219 | 0.05 | (–0.40, 0.51) |
| Lag 24–47h | 1354 | 0.17 | (–0.42, 0.77) | 1354 | 0.31 | (–0.25, 0.86) | 1234 | 0.56# | (–0.03, 1.16) | 1214 | 0.20 | (–0.19, 0.59) |
| Lag 48–71h | 1356 | 0.21 | (–0.38, 0.79) | 1356 | –0.46 | (–1.01, 0.10) | 1234 | –0.22 | (–0.86, 0.42) | 1214 | 0.20 | (–0.18, 0.57) |
| Lag 72–95h | 1356 | –0.17 | (–0.78, 0.44) | 1356 | –0.47# | (–1.00, 0.06) | 1238 | –0.57# | (–1.17, 0.03) | 1213 | 0.15 | (–0.23, 0.53) |
| Lag 96–119h | 1356 | –0.80* | (–1.46, –0.15) | 1356 | 0.13 | (–0.42, 0.68) | 1249 | –0.10 | (–0.62, 0.42) | 1211 | 0.21 | (–0.17, 0.59) |

# $P < 0.10$; * $P < 0.05$; ** $P < 0.01$.

**Discussion:** Reactive oxygen species are produced in metabolic and physiological processes, and harmful oxidative reactions may occur in organisms that remove them via antioxidant mechanisms (Erel 2004). One mechanism by which PM may affect human health is by inducing oxidative stress, shifting the oxidative/antioxidative balance towards the oxidative status. Antioxidant molecules prevent or inhibit these harmful reactions and the measure of total antioxidant capacity is a comprehensive assessment of the antioxidant effects of different separate antioxidant molecules. Low antioxidant capacity could therefore be indicative of oxidative stress or increased susceptibility to oxidative damage (Young and Woodside 2001). Other studies have provided evidence that oxidative stress may be a mechanism underlying any air pollution effects on heart rate, HRV, and repolarization (Brook et al. 2010). These effects may also be different in one or more population subgroups with different host defenses against an oxidative stress challenge. To our knowledge, no study to date has evaluated whether immediate ECG responses are beneficially modified by a subject's antioxidant capacity, a blood marker indicative of oxidative stress or increased susceptibility to oxidative damage. However, in both the Augsburg Panel Study and the Rochester REHAB Study, we did not find that TAC modified any PM/outcome association. Further, in only the Rochester REHAB Study did we find that increased UFP, $PM_{2.5}$, and AMP concentrations were associated with a decrease in TAC. However, further analyses in the Rochester REHAB Study can examine whether TAC levels modified markers (e.g. C-reactive protein, fibrinogen) of other mechanisms (e.g. systemic inflammation) thought to underlie any acute cardiovascular response to short-term increases in PM.

**References**

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## APPENDIX B. Factor Analysis Methods and Results

**Methods:** This project involved the analysis of data from four studies: Augsburg Panel Study, and the Rochester REHAB, UPDIABETES, and UPCON studies. The Augsburg Panel study (*N* = 109) was conducted between March 2007 and December 2008 to determine the effect of fine particle matter (PM) and UFP on cardiac rhythm outcomes. It included three distinct subgroups: Subjects with type 2 diabetes mellitus (*n* = 32); subjects with impaired glucose tolerance (*n* = 32); and subjects with a genetic pre-disposition to oxidative stress (*n* = 45). An ECG Holter recording device was used to continuously monitor each subject every 4–6 weeks. The outcomes measured in this study include: HR, SDNN, RMSSD, T-wave complexity (Tcomp), DC, HF, LF, TP, VLF, QTc, and T-wave amplitude (Tamp). The Rochester REHAB Study was a panel study to assess the effects of ambient pollutants on cardio-respiratory outcomes in 76 subjects with acute coronary artery syndromes experiencing cardiac rehabilitation. There were 20 rehabilitation visits per subject with continuously recorded ECGs. The outcomes measured in the REHAB study were: HF, LF, T-wave complexity (Tcomp), DC, TP, VLF, NN, PNN50, RMSSD, and SDNN. The Rochester UPCON and UPDIABETES Studies were controlled exposure studies in which subjects were examined to determine the effect UFP inhalation on cardiovascular function. The outcome measures used in these studies were HF, LF, DC, TP, VLF, NN, Tcomp, PNN50, QTc, SD QTpeak duration (QTp_sd), RMSSD, SDNN, and Tamp. The UPCON study was a double blind, randomized, 2 by 2 crossover trial with clean air and UFP as the control and exposure, respectively. There were 20 healthy subjects in the study who had never smoked, and had no symptoms of or signs of cardiovascular disease. In the UPCON Study, continuous ECG Holter recordings were made starting two hours before the exposure and continuing for 24 hours through and after exposure. The outcomes used include measurements taken from 24 hour ECG recording at each exposure period. A measurement was taken every 5 minutes during this period. The UPDIABETES study was a double-blind, randomized, 2-by-2 crossover trial consisting of 19 diabetic subjects with clean air and UFP as the control and exposure, respectively. Continuous ECG Holter recordings were made starting 2 hours before the exposure and continuing for 48 hours through and after exposure.

Factor analysis was used to assess the assumptions of biological relationships of outcomes in these studies. We also searched for underlying relationships between the outcomes that might suggest new ways of analyzing or interpreting the results. We used the orthogonal factor model:

$$\boldsymbol{X} = \mu + \boldsymbol{LF} + \boldsymbol{\varepsilon}$$

where $\boldsymbol{X}$ represented a $p$-dimensional observable random vector, $\boldsymbol{F}$ was a $m(\leq p)$ dimensional vector of unobservable random variables called common factors, and $\boldsymbol{\varepsilon}$ was a $p$-dimensional vector of random error variables. $\boldsymbol{L}$ was the matrix of factor loadings or factor regression coefficients. $\boldsymbol{F}$ and $\boldsymbol{\varepsilon}$ were independent, $E(\boldsymbol{F}) = \mathbf{0}$), $cov(\boldsymbol{F}) = \boldsymbol{I}$, $E(\boldsymbol{\varepsilon}) = \mathbf{0}$), $cov(\boldsymbol{\varepsilon}) = \psi$, where $\psi$ was a diagonal matrix and $cov(X, F) = L$. Principal components analysis was used to estimate $L$, and the varimax criterion was used to estimate the factor rotation. We have $cov(X) = LL' + \psi$, and the diagonal elements of $LL'$ are called *communalities*. The communalities represent proportion of the variance that can be explained by the factor loadings.

Each element of the factor loading matrix, L, represents the covariance (in our case correlation) between the outcome/dependent variable, $X_i$, $i = 1, \ldots, p$ and the independent (latent) factor variable $F_j$, $j = 1, \ldots, m$. Therefore variables that have large loading estimates on the same factor are variables that are correlated with the same factor. If these variables also have small estimated loadings on all the other factors then we will say that this factor represents this set of variables.

A 4-factor model was applied to the hourly outcome measurements from the REHAB study and Augsburg panel study. A 5-factor model was applied to the two controlled exposure studies. The number of factors that were used in the model was determined by the number of factors that provided an interpretation which corresponded to biological phenomena.  A factor loading of 0.6 or higher was used to determine whether an outcome was represented by a factor. Once the factor–outcome association was determined, a single outcome was used to represent that factor. This outcome was chosen based on its correlation with the factor and the interpretability of that outcome. This approach allows the discussion of the results of the study to be streamlined by allowing each biologically relevant factor to be represented by a single outcome.

**Results:** The portion of the total variation observed in the data that was explained by the orthogonal factor models estimated for the Rochester UPCON, UPDIABETES, and REHAB Studies, and Augsburg Panel Study, using 1-hour ECG outcome values are shown in Figures B.1–4. The factor loadings are displayed in Tables B.1–4.

In the application of the 5 factor model to UPCON endpoints, the scree plot of Figure B.1 shows the contribution of each factor to the total variability in the sample. The second plot in the figure shows that the 5-factor model explains 86.37% of the total variation. The results showed that for the 5-factor model (Table B.1) the factor loading estimates of HF, LF, PNN50, and RMSSD on factor 1 were large and positive. Therefore factor 1 represented HF, LF, NN, PNN50, and RMSSD. Factor 1 can be interpreted as representing *parasympathetic regulation of the heart* since most of these parameters represent parasympathetic modulation of the heart and LF is also significantly modulated by changes in parasympathetic modulations. We chose RMSSD as the primary marker of this factor. The estimated factor loadings of LF, TP, VLF, and SDNN on factor 2 were large and positive. So similarly, factor 2 represents LF, TP, VLF, and SDNN. The interpretation of factor 2 was *overall heart rate variability*. Again, SDNN, TP, and VLF seem to reflect overall HRV. LF contributes to both Factor 1 and Factor 2 since it reflects baroreflex sensitivity. Since the estimated factor loadings of Tcomp, QTp_sd, and Tamp on factor 3 were high, factor 3 represents these variables. The interpretation of Factor 3 was *T-wave morphology* and *QT variability*. T wave amplitude, T-wave complexity and QTpeak variability represent similar repolarization phenomena dependent on T-wave morphology. The variables NN and DC load high on factor 4 so the interpretation of this factor is *Heart Rate*. Both the NN interval and DC are reflections of heart rate and heart rate behavior. The variable QTc had a large positive estimated loading on the factor 5. Therefore factor 5 represented

QTc. The interpretation of factor 5 was *QTc*. The variables TP, VLF, QTc, and SDNN all had communalities larger than 0.9. This means that this factor model captured over 90% of the variability in these variables.

In the analysis of the UPDIABETES endpoints, we found that the pattern of loadings in the *overall heart rate variability* factor, *T-wave morphology* factor, and the QTc factor were all very similar to the pattern of factor loadings in the UPCON analysis, but the two other factors were not. Instead of having a large loading on the parasympathetic regulation of the heart, the endpoints PNN50 and RMSSD both had a large loading on the *heart rate* factor.

The REHAB analysis contained a subset of the endpoints analyzed in the other studies. As a result a 4 factor model was used to the endpoints in the REHAB analysis. Because there was no QTc in this study, there was no QTc factor. The pattern of factor loadings in the other 4 factors used in the UPCON analysis were similar to that of the REHAB analysis.

In comparison to the UPCON analysis, results of the orthogonal factor model application to the Augsburg panel data showed that the *overall heart rate variability* factor had the same pattern of factor loadings. The pattern of factor loadings for the *T-wave morphology* factor in the Augsburg factor model was similar to the *T-wave morphology* factor and the *QTc* factor merged together from the UPCON factor model. Similarly the *parasympathetic regulation of the heart* factor in the Augsburg model had a high loading for HF and RMSSD but not LF. The Augsburg model did not have the variables PNN50 and QTp_sd. So factors in the UPCON analysis that contained high loadings for these variables naturally did not have the same pattern as Augsburg. The Augsburg factor model introduced a new factor, *baroreflex sensitivity,* which had high loadings for both DC and LF. The LF power is believed to predominantly reflect baroreflex sensitivity, and since LF had the highest loading, this term was used to describe this factor.

**Summary:** Application of this methodology has allowed us to reduce the number of outcomes to be considered in the primary analysis of the three Rochester studies from 13 to 5 (UPCON and UPDIABETES) and 10 to 4 (REHAB), respectively. For Augsburg, the number of outcomes could be reduced to 4. Specifically in the Rochester UPCON and UPDIABETES Studies, the variables chosen to represent the five factors of *parasympathetic regulation of the heart, overall heart rate variability*, *T-wave morphology, heart rate,* and *QTc* were RMSSD, SDNN, T-wave complexity, NN, and QTc, respectively. In the Rochester REHAB Study the variables chosen to represent the *parasympathetic regulation of the heart, overall heart rate variability, T-wave morphology*, and *heart rate* were RMSSD, SDNN, T-wave complexity, and NN, respectively. In the Augsburg Study the variables chosen to represent the 4 factors of *parasympathetic regulation of the heart, overall heart rate variability, T-wave morphology*, and *baroreflex sensitivity*, were RMSSD, SDNN, T-wave complexity, and LF, respectively.

**Table B.1:** Factor loadings for 5 factor orthogonal model in the UPCON 1 hour study

| Variable | Parasympathetic Regulation | Overall HRV | T-wave Morphology | Heart Rate | QTc | Communalities |
|---|---|---|---|---|---|---|
| HF | 0.891** | 0.288 | –0.048 | 0.112 | 0.045 | 0.89384 |
| LF | 0.630** | 0.502 | –0.112 | 0.217 | –0.087 | 0.71679 |
| DC | 0.260 | 0.280 | –0.090 | 0.745** | –0.115 | 0.72194 |
| TP | 0.233 | 0.952** | –0.048 | 0.059 | 0.035 | 0.96816 |
| VLF | 0.302 | 0.894** | –0.109 | 0.220 | 0.005 | 0.95153 |
| NN | 0.317 | 0.093 | –0.072 | 0.815** | 0.222 | 0.82771 |
| Tcomp | 0.014 | 0.021 | 0.879** | –0.107 | –0.039 | 0.78551 |
| PNN50 | 0.842** | 0.252 | –0.125 | 0.306 | 0.048 | 0.88433 |
| QTc | 0.057 | 0.009 | –0.059 | 0.063 | 0.979** | 0.96865 |
| QTp_sd | –0.097 | –0.044 | 0.870** | 0.125 | –0.075 | 0.78873 |
| RMSSD | 0.858** | 0.284 | –0.126 | 0.286 | 0.078 | 0.92016 |
| SDNN | 0.354 | 0.884** | –0.064 | 0.177 | –0.005 | 0.94191 |
| Tamp | 0.228 | 0.237 | –0.816** | 0.283 | –0.058 | 0.85823 |

** = factor loading ≥ 0.60.

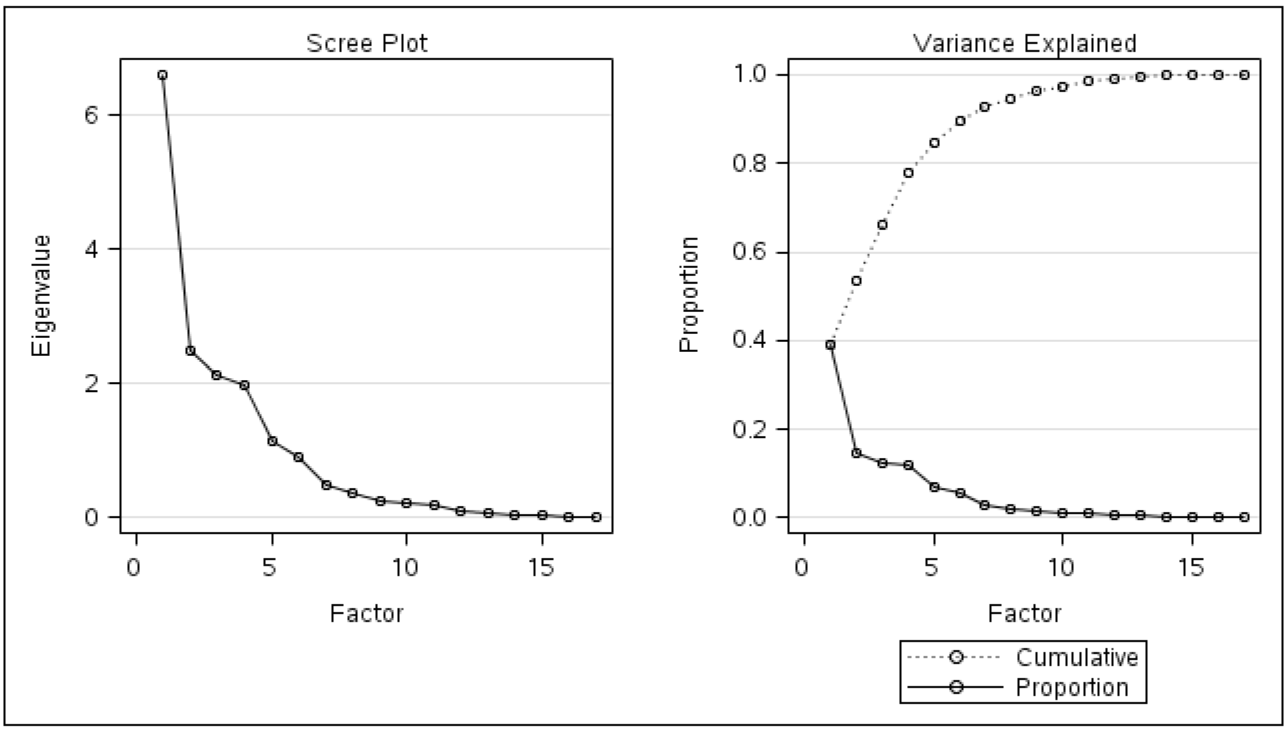



**Figure B.1: Scree plot and a plot of the variance explained by each additional factor in the UPCON 1-hour study.**

**Table B.2:** Factor loadings for 5 factor orthogonal model in the UPDIABETES 1 hour study

| Variable | Overall HRV | Heart Rate | T-wave Morphology | Parasympathetic Regulation | QTc | Communalities |
|---|---|---|---|---|---|---|
| HF | 0.171 | 0.286 | –0.044 | 0.897** | 0.009 | 0.91746 |
| LF | 0.386 | 0.192 | –0.081 | 0.823** | 0.076 | 0.87508 |
| DC | 0.323 | 0.566 | –0.205 | 0.211 | 0.186 | 0.54606 |
| TP | 0.928** | 0.185 | –0.074 | 0.246 | 0.003 | 0.96059 |
| VLF | 0.920** | 0.271 | –0.091 | 0.143 | 0.019 | 0.94878 |
| NN | 0.228 | 0.794** | 0.078 | –0.054 | 0.245 | 0.75236 |
| Tcomp | –0.007 | –0.057 | 0.881** | 0.004 | 0.064 | 0.78371 |
| PNN50 | 0.218 | 0.822** | –0.056 | 0.321 | –0.051 | 0.83206 |
| QTc | 0.021 | 0.195 | 0.158 | 0.059 | 0.925** | 0.92250 |
| QTp_sd | –0.046 | 0.083 | 0.898** | –0.085 | 0.003 | 0.82287 |
| RMSSD | 0.211 | 0.820** | –0.065 | 0.363 | 0.015 | 0.85376 |
| SDNN | 0.869** | 0.324 | –0.085 | 0.237 | 0.012 | 0.92339 |
| Tamp | 0.333 | 0.298 | –0.638** | 0.072 | –0.278 | 0.68903 |

** = factor loading ≥ 0.60.

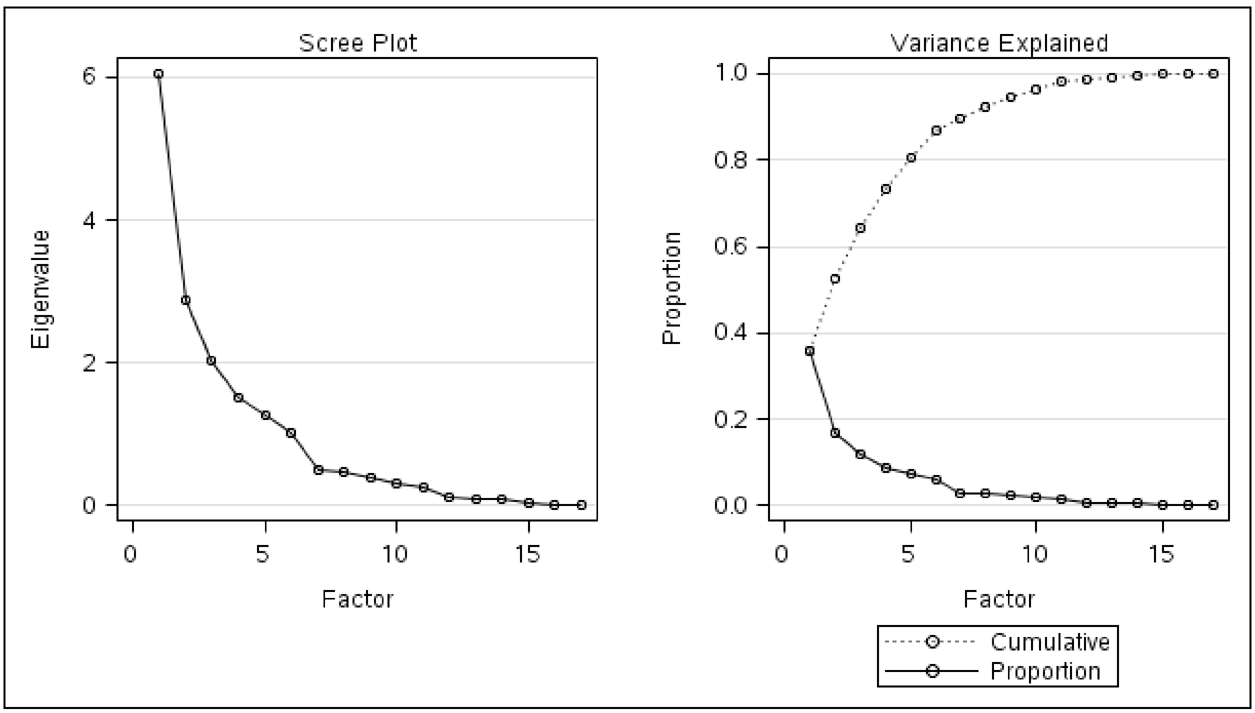



**Figure B.2: Scree plot and a plot of the variance explained by each additional factor in the UPDIABETES 1 hour study.**

**Table B.3:** Factor loadings for 4 factor orthogonal model in the REHAB study

| Variable | Parasympathetic Regulation | Overall HRV | Heart Rate | T-wave Morphology | Communalities |
|---|---|---|---|---|---|
| HF | 0.816** | 0.224 | 0.307 | 0.020 | 0.81097 |
| LF | 0.561 | 0.284 | 0.463 | –0.010 | 0.60951 |
| Tcomp | 0.060 | –0.076 | –0.058 | 0.985** | 0.98342 |
| DC | –0.063 | 0.107 | 0.858** | –0.164 | 0.77773 |
| TP | 0.243 | 0.924** | 0.185 | –0.026 | 0.94761 |
| VLF | 0.310 | 0.882** | 0.239 | –0.017 | 0.93085 |
| NN | 0.225 | 0.073 | 0.776** | 0.088 | 0.66563 |
| PNN50 | 0.893** | 0.091 | –0.100 | 0.005 | 0.81588 |
| RMSSD | 0.918** | 0.206 | 0.079 | 0.095 | 0.89945 |
| SDNN | 0.067 | 0.902** | –0.042 | –0.071 | 0.82458 |

** = factor loading ≥ 0.60.

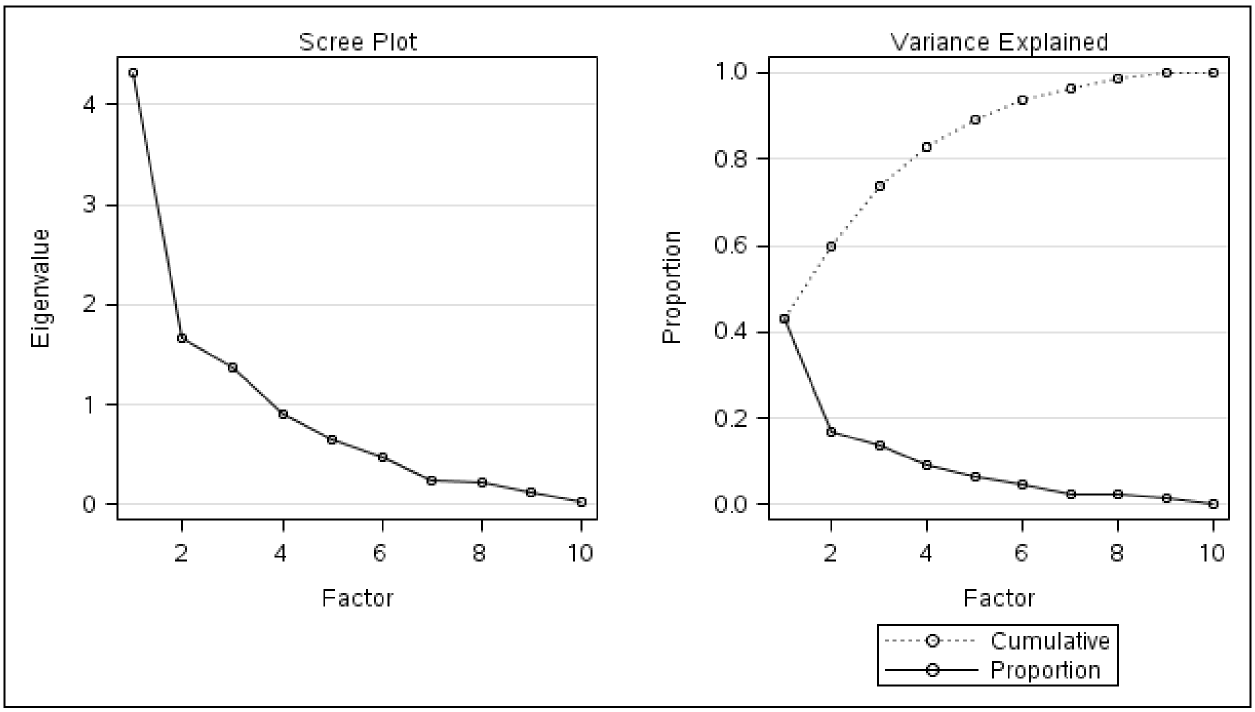



**Figure B.3: Scree plot and a plot of the variance explained by each additional factor in the REHAB study associated with Table 5 of the main report.**

**Table B.4:** Factor loadings for 4 factor orthogonal model in the Augsburg 1 hour Study

| Variable | Overall HRV | Parasympathetic | T-wave Morphology | Baroflex Sensitivity | Communality |
|---|---|---|---|---|---|
| **DC** | 0.260 | –0.381 | –0.267 | 0.748** | 0.844 |
| **HF** | –0.107 | 0.899** | –0.017 | 0.182 | 0.852 |
| **HR** | –0.367 | –0.340 | 0.502 | –0.019 | 0.503 |
| **LF** | –0.247 | 0.307 | –0.066 | 0.836** | 0.858 |
| **TP** | 0.968** | –0.024 | –0.081 | –0.073 | 0.950 |
| **VLF** | 0.956** | –0.007 | –0.149 | 0.059 | 0.940 |
| **Tcomp** | 0.017 | 0.089 | 0.743** | –0.076 | 0.566 |
| **QTc** | –0.077 | –0.017 | 0.715** | 0.018 | 0.517 |
| **RMSSD** | 0.226 | 0.918** | 0.036 | –0.149 | 0.917 |
| **SDNN** | 0.959** | 0.128 | –0.115 | –0.033 | 0.951 |
| **Tamp** | 0.183 | –0.017 | –0.733** | 0.276 | 0.647 |

** = factor loading ≥ 0.60.

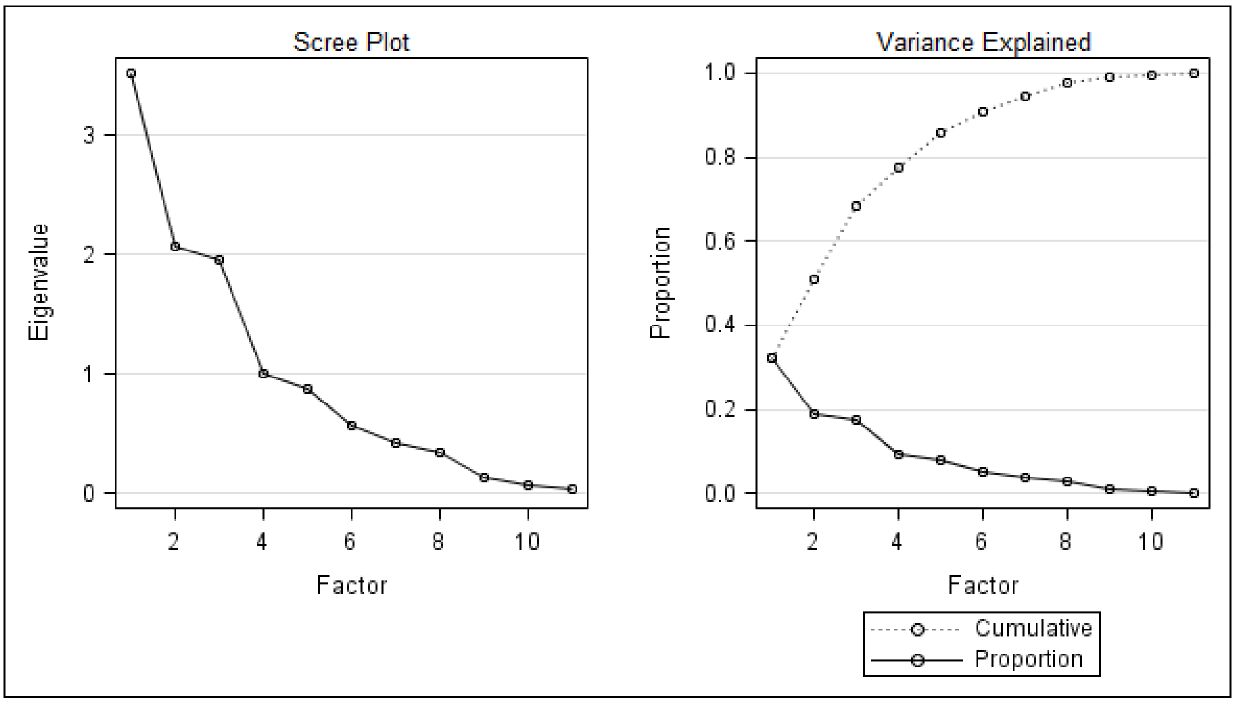


**Figure B.4: Scree Plot for Augsburg Study.**

**APPENDIX C. Meta-Analyses**

**Methods**: We combined study-specific effect estimates using meta-analysis methodology (van Houwelingen et al. 2002) to provide a single estimate of the percent change in SDNN associated with a standard incremental increase in pollutant concentration (percent change associated with each 1000 particles/$cm^3$ increase in UFP or AMP and with each 10 µg/$m^3$ increase in $PM_{2.5}$ concentrations). In a first step, we pooled the effect estimates of UFP for all studies (Augsburg Panel study – Individuals with type-2 diabetes or impaired glucose tolerance (Diabetes + IGT), Augsburg Panel study – Individuals with a potential genetic predisposition (Genetic Susceptibility), Rochester REHAB study, Rochester UPCON study, and Rochester UPDIABETES study). Further, we combined effects estimates of UFP, AMP and $PM_{2.5}$ for the two sub-groups of the Augsburg Panel study and the Rochester REHAB study. For each meta-analytical estimate, a test for heterogeneity was performed and the corresponding $I^2$ statistic reported, which represents the proportion of total variation in effect estimates that is due to between-study heterogeneity.

**Results:** Table 1 shows the percent changes associated with each 1000 particles/$cm^3$ increase in UFP or AMP and with each 10 µg/$m^3$ increase in $PM_{2.5}$ concentrations. When combining all studies (both panel studies and both controlled exposure studies, Table 1A), each 1000 particles/$cm^3$ increase in UFP concentration lagged 1 to 3 hours was associated with decreases in SDNN, although not statistically significantly. However, the $I^2$ statistic and the test for heterogeneity both pointed to a considerable amount of between-study heterogeneity (Table 1A).

Combined effects estimates of UFP, AMP and $PM_{2.5}$ in only pooling the two sub-groups of the Augsburg Panel study and the Rochester REHAB study are shown in Table 1B. Increases in UFP and AMP concentrations lagged 1 to 3 hours were each associated with significant decreases in SDNN, and there was no or only moderate between-study heterogeneity. Moreover, a 10 µg/$m^3$ increase in $PM_{2.5}$ concentrations resulted in consistent, significant decreases in SDNN for all lags, with the largest reduction associated with increased $PM_{2.5}$ concentration lagged 1 hour (–2.57% [95% confidence interval = –3.84%, –1.31%]) and no between-study heterogeneity.

**Table C.1.** Combined percent changes in SDNN (ms) associated with a standard incremental increase in concurrent and 1h to 6h lagged air pollutant concentrations.

**A.** Combined percent changes associated with a 1000 particles/$cm^3$ increase in UFP using effect estimates from the following panels: Augsburg study – Individuals with type-2 diabetes or impaired glucose tolerance (Diab + IGT), Augsburg study – Individuals with a potential genetic predisposition on the detoxifying and inflammatory pathways (Gen susc), Rochester REHAB study, Rochester UPCON study, and Rochester UPDIABETES study.

| | UFP | | |
|---|---|---|---|
| **Pollutant averaging time** | **% Change** | **95% confidence interval** | $I^2$ |
| **SDNN (ms)** | | | |
| Concurrent | 0.09% | –0.05%, 0.23% | 57.9% ° |
| Lag 1h | -0.01% | –0.24%, 0.22% | 84.2% ° |
| Lag 2h | -0.10% | –0.26%, 0.06% | 68.6% ° |
| Lag 3h | -0.14% | –0.33%, 0.05% | 79.3% ° |
| Lag 4h | -0.12% | –0.26%, 0.03% | 79.3% ° |
| Lag 5h | 0.02% | –0.18%, 0.22% | 78.3% ° |
| Lag 6h | 0.06% | –0.06%, 0.18% | 35.1% |

# *P*<0.10; * *P*<0.05; ***P*<0.01; ° *P*-value of χ-square test for heterogeneity < 0.1

**B.** Combined percent changes associated with each 1000 particles/$cm^3$ increase in UFP or AMP and with a 10 µg/$m^3$ increase in $PM_{2.5}$ using effect estimates from the following panels: Augsburg study – Individuals with type-2 diabetes or impaired glucose tolerance (Diab + IGT), Augsburg study – Individuals with a potential genetic predisposition on the detoxifying and inflammatory pathways (Gen susc), and Rochester REHAB study.

| | UFP | | | AMP | | | $PM_{2.5}$ | | |
|---|---|---|---|---|---|---|---|---|---|
| **Pollutant averaging time** | **% Change** | **95% confidence interval** | **$I^2$ (%)** | **% Change** | **95% confidence interval** | **$I^2$ (%)** | **% Change** | **95% confidence interval** | **$I^2$ (%)** |
| **SDNN (ms)** | | | | | | | | | |
| Concurrent | 0.13 | -0.06, 0.31 | 41.5 | -0.23 | -1.63, 1.18 | 65. ° | -1.62 | -2.83, -0.41** | 0.0 |
| Lag 1h | -0.07 | -0.26, 0.12 | 46.1 | -0.61 | -1.52, 0.30 | 29.0 | -2.26 | -3.48, -1.03** | 0.0 |
| Lag 2h | -0.21 | -0.34, -0.09** | 0.0 | -1.17 | -1.88, -0.47** | 0.2 | -2.57 | -3.84, -1.31** | 0.0 |
| Lag 3h | -0.22 | -0.34, -0.10** | 0.0 | -1.12 | -1.83, -0.41** | 0.0 | -2.35 | -3.66, -1.03** | 0.0 |
| Lag 4h | -0.22 | -0.34, -0.09** | 0.0 | -1.28 | -1.99, -0.56** | 0.0 | -2.26 | -3.60, -0.92** | 0.0 |
| Lag 5h | -0.09 | -0.24, 0.05 | 0.0 | -0.73 | -1.54, 0.08# | 11.9 | -2.05 | -3.42, -0.67** | 0.0 |
| Lag 6h | 0.12 | -0.05, 0.28 | 0.0 | -0.36 | -1.27, 0.54 | 21.7 | -1.91 | -3.58, -0.24* | 29.0 |

# *P* < 0.10; * *P* < 0.05; ** *P* < 0.01; ° *P*-value of $\chi$-square test for heterogeneity < 0.1

**APPENDIX D.** Distribution of **(a.)** 5-minute and **(b.)** 1-hour ECG parameters in Augsburg study

***(a.) 5-minute ECG recordings***

| | **Panel** | ***N*** | **Mean** | **SD** | **Min** | **P5** | **Q1** | **Median** | **Q3** | **P95** | **Max** | **IQR** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **SDNN** | All | 25,216 | 51.3 | 26.8 | 4.6 | 18.0 | 31.4 | 46.2 | 65.7 | 103.1 | 196.4 | 34.4 |
| (ms) | Diabetes+IGT | 14,815 | 47.1 | 25.1 | 4.6 | 16.1 | 28.4 | 41.6 | 60.6 | 96.1 | 190.1 | 32.2 |
| | Gen.Susc. | 10,401 | 57.4 | 27.9 | 5.2 | 22.4 | 36.6 | 52.5 | 72.1 | 111.2 | 196.4 | 35.4 |
| **RMSSD** | All | 25,219 | 28.9 | 25.7 | 1.0 | 7.8 | 14.3 | 21.6 | 32.5 | 82.3 | 281.7 | 18.3 |
| (ms) | Diabetes+IGT | 14,815 | 30.9 | 30.1 | 1.0 | 7.0 | 13.3 | 20.6 | 34.4 | 100.8 | 281.7 | 21.1 |
| | Gen.Susc. | 10,404 | 26.1 | 17.4 | 4.7 | 8.9 | 15.7 | 22.7 | 31.3 | 52.9 | 264.5 | 15.6 |
| **T-wave** | All | 25,042 | 18.2 | 9.1 | 5.0 | 8.1 | 11.9 | 15.9 | 21.9 | 37.4 | 60.0 | 10.1 |
| **complexity** | Diabetes+IGT | 14,691 | 17.7 | 8.1 | 5.3 | 8.1 | 12.0 | 16.0 | 21.2 | 34.9 | 57.3 | 9.2 |
| (%) | Gen.Susc. | 10,351 | 18.9 | 10.2 | 5.0 | 8.1 | 11.7 | 15.8 | 23.3 | 41.3 | 60.0 | 11.6 |
| **HR** | All | 25,219 | 78.6 | 14.6 | 44.6 | 56.9 | 68.2 | 77.4 | 87.5 | 104.3 | 143.4 | 19.2 |
| (beats/min) | Diabetes+IGT | 14,815 | 79.3 | 15.6 | 44.6 | 55.6 | 68.5 | 78.1 | 88.5 | 107.8 | 142.5 | 19.9 |
| | Gen.Susc. | 10,404 | 77.5 | 13.0 | 47.3 | 58.5 | 67.9 | 76.5 | 86.1 | 99.7 | 143.4 | 18.2 |
| **QTc** | All | 25,219 | 440.0 | 26.1 | 324.9 | 397.5 | 424.7 | 440.5 | 456.6 | 480.9 | 544.6 | 31.9 |
| (ms) | Diabetes+IGT | 14,815 | 443.1 | 26.4 | 324.9 | 402.9 | 428.1 | 444.2 | 459.8 | 483.0 | 535.5 | 31.7 |
| | Gen.Susc. | 10,404 | 435.6 | 25.1 | 351.3 | 393.3 | 420.2 | 435.8 | 451.3 | 475.0 | 544.6 | 31.0 |
| **HF** | All | 21,871 | 15.2 | 15.4 | 0.0 | 0.8 | 4.4 | 10.3 | 20.3 | 49.6 | 80.0 | 15.9 |
| (normalized | Diabetes+IGT | 12,567 | 16.5 | 16.6 | 0.0 | 0.7 | 4.4 | 11.0 | 22.5 | 54.2 | 80.0 | 18.1 |
| units) | Gen.Susc. | 9,304 | 13.5 | 13.3 | 0.0 | 0.8 | 4.4 | 9.5 | 18.0 | 40.9 | 79.1 | 13.6 |
| **LF** | All | 21,871 | 43.3 | 28.0 | 0.0 | 2.7 | 17.4 | 42.7 | 68.3 | 86.7 | 97.4 | 50.9 |
| (normalized | Diabetes+IGT | 12,567 | 39.8 | 27.3 | 0.0 | 2.2 | 14.9 | 37.0 | 63.7 | 84.6 | 97.1 | 48.8 |
| units) | Gen.Susc. | 9,304 | 48.1 | 28.3 | 0.0 | 3.7 | 21.9 | 50.6 | 73.4 | 88.6 | 97.4 | 51.5 |
| **LF/HF** | All | 21,871 | 5.2 | 4.9 | 0.0 | 0.5 | 2.0 | 3.9 | 6.9 | 14.8 | 39.7 | 4.9 |
| (normalized | Diabetes+IGT | 12,567 | 4.5 | 4.3 | 0.0 | 0.4 | 1.6 | 3.3 | 5.9 | 12.7 | 39.5 | 4.2 |
| units) | Gen.Susc. | 9,304 | 6.2 | 5.4 | 0.0 | 0.7 | 2.6 | 4.7 | 8.2 | 17.0 | 39.7 | 5.6 |
| **T-wave** | All | 24,815 | 330.3 | 135.1 | 100.0 | 142.7 | 223.3 | 313.0 | 418.7 | 580.6 | 798.5 | 195.5 |
| **amplitude** | Diabetes+IGT | 14,514 | 305.5 | 129.6 | 100.1 | 133.7 | 207.6 | 284.6 | 377.5 | 558.0 | 798.5 | 169.9 |
| (μV) | Gen.Susc. | 10,301 | 365.1 | 135.0 | 100.0 | 163.7 | 252.8 | 357.2 | 462.8 | 603.2 | 787.7 | 210.1 |
| **DC** | All | 25,664 | 5.0 | 4.1 | -85.1 | 0.3 | 3.2 | 5.0 | 7.2 | 10.4 | 25.7 | 4.0 |
| (ms) | Diabetes+IGT | 15,102 | 4.0 | 4.3 | -85.1 | -1.8 | 2.6 | 4.2 | 6.0 | 9.1 | 25.7 | 3.4 |
| | Gen.Susc. | 10,562 | 6.5 | 3.2 | -31.1 | 2.1 | 4.5 | 6.4 | 8.5 | 11.4 | 20.8 | 4.0 |

HR: heart rate, SDNN: standard deviation of normal-to-normal (NN) beats, RMSSD: root mean square of successive differences, HF: high frequency power, LF: low frequency power, QTc: Bazett-corrected QT-interval, DC: deceleration capacity, IGT: impaired glucose tolerance, Gen. Susc.: participants with a genetic susceptibility, SD: standard deviation, P5: 5$^{th}$ percentile, Q1: 1$^{st}$ quartile, Q3: 3$^{rd}$ quartile, P95: 95$^{th}$ percentile, IQR: interquartile range.

***(b) 1 hour ECG-parameters.***

| | Panel | *N* | Mean | SD | Min | P5 | Q1 | Median | Q3 | P95 | Max | IQR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **SDNN** | All | 2,041 | 80.2 | 28.5 | 11.8 | 39.0 | 60.1 | 77.0 | 97.5 | 132.2 | 198.8 | 37.4 |
| (ms) | Diabetes+IGT | 1,198 | 76.7 | 27.2 | 11.8 | 36.9 | 56.2 | 74.3 | 94.9 | 124.2 | 161.2 | 38.7 |
| | Gen.Susc. | 843 | 85.2 | 29.7 | 22.6 | 43.3 | 65.1 | 80.4 | 101.6 | 142.9 | 198.8 | 36.5 |
| **RMSSD** | All | 2,042 | 31.3 | 26.6 | 1.3 | 10.1 | 17.3 | 23.7 | 33.1 | 89.4 | 227.3 | 15.8 |
| (ms) | Diabetes+IGT | 1,198 | 34.0 | 31.8 | 1.3 | 8.3 | 16.6 | 23.0 | 35.7 | 109.8 | 227.3 | 19.1 |
| | Gen.Susc. | 844 | 27.5 | 16.2 | 7.2 | 11.9 | 18.3 | 24.5 | 31.8 | 51.6 | 159.8 | 13.5 |
| **T-wave** | All | 2,042 | 18.0 | 8.6 | 5.3 | 8.5 | 12.1 | 15.8 | 21.5 | 36.5 | 55.5 | 9.4 |
| **complexity** | Diabetes+IGT | 1,198 | 17.5 | 7.5 | 5.6 | 8.5 | 12.2 | 15.9 | 20.7 | 33.9 | 46.0 | 8.5 |
| (%) | Gen.Susc. | 844 | 18.8 | 9.9 | 5.3 | 8.5 | 11.9 | 15.6 | 22.9 | 41.2 | 55.5 | 11.0 |
| **HR** | All | 2,042 | 78.4 | 13.1 | 46.5 | 58.3 | 69.4 | 78.0 | 86.3 | 100.4 | 132.9 | 16.9 |
| (beats/min) | Diabetes+IGT | 1,198 | 79.1 | 14.4 | 46.5 | 55.9 | 69.2 | 78.5 | 87.4 | 104.1 | 132.9 | 18.2 |
| | Gen.Susc. | 844 | 77.4 | 11.0 | 50.0 | 60.6 | 69.5 | 77.0 | 85.1 | 95.6 | 117.9 | 15.6 |
| **QTc** | All | 2,042 | 440.4 | 24.3 | 340.8 | 400.5 | 425.9 | 441.2 | 456.3 | 478.4 | 527.6 | 30.4 |
| (ms) | Diabetes+IGT | 1,198 | 443.5 | 24.3 | 340.8 | 406.0 | 429.7 | 444.9 | 459.0 | 481.7 | 507.5 | 29.3 |
| | Gen.Susc. | 844 | 435.9 | 23.5 | 360.4 | 395.8 | 422.2 | 435.6 | 449.6 | 471.6 | 527.6 | 27.5 |
| **HF** | All | 2,038 | 4.3 | 7.5 | 0.0 | 0.3 | 0.9 | 2.0 | 4.4 | 15.1 | 77.5 | 3.5 |
| (normalized | Diabetes+IGT | 1,195 | 4.8 | 9.1 | 0.0 | 0.2 | 0.8 | 1.8 | 4.4 | 19.3 | 77.5 | 3.6 |
| units) | Gen.Susc. | 843 | 3.6 | 4.3 | 0.2 | 0.4 | 1.1 | 2.1 | 4.5 | 11.0 | 36.0 | 3.3 |
| **LF** | All | 2,038 | 9.9 | 10.9 | 0.1 | 0.9 | 2.7 | 5.8 | 13.0 | 33.7 | 73.5 | 10.3 |
| (normalized | Diabetes+IGT | 1,195 | 7.8 | 9.2 | 0.1 | 0.7 | 2.2 | 4.6 | 9.9 | 25.7 | 73.5 | 7.8 |
| units) | Gen.Susc. | 843 | 12.8 | 12.2 | 0.5 | 1.5 | 3.8 | 8.3 | 18.3 | 37.8 | 67.4 | 14.5 |
| **LF/HF** | All | 2,038 | 3.8 | 2.9 | 0.0 | 0.5 | 1.7 | 3.2 | 5.1 | 9.7 | 24.0 | 3.4 |
| (normalized | Diabetes+IGT | 1,195 | 3.2 | 2.4 | 0.0 | 0.5 | 1.3 | 2.8 | 4.3 | 7.8 | 16.0 | 3.0 |
| units) | Gen.Susc. | 843 | 4.7 | 3.2 | 0.1 | 0.8 | 2.3 | 3.9 | 6.3 | 11.4 | 24.0 | 4.0 |
| **T-wave** | All | 2,019 | 330.0 | 133.7 | 100.4 | 144.5 | 225.6 | 315.2 | 417.5 | 574.4 | 758.3 | 191.9 |
| **amplitude** | Diabetes+IGT | 1,180 | 305.0 | 127.6 | 102.1 | 137.1 | 207.9 | 283.6 | 378.0 | 558.2 | 758.3 | 170.2 |
| (µV) | Gen.Susc. | 839 | 365.1 | 134.2 | 100.4 | 166.8 | 253.4 | 363.1 | 462.1 | 603.5 | 745.8 | 208.7 |
| **DC** | All | 2,033 | 5.0 | 3.4 | -34.7 | 0.6 | 3.4 | 5.0 | 7.0 | 9.5 | 14.2 | 3.6 |
| (ms) | Diabetes+IGT | 1,196 | 4.0 | 3.5 | -34.7 | -1.0 | 2.8 | 4.2 | 5.7 | 8.1 | 12.7 | 2.8 |
| | Gen.Susc. | 837 | 6.4 | 2.6 | -5.4 | 2.2 | 4.7 | 6.4 | 8.2 | 10.6 | 14.2 | 3.4 |

HR: heart rate, SDNN: standard deviation of normal-to-normal (NN) beats, RMSSD: root mean square of successive differences, PNN50: percentage of NN-intervals with difference>50ms, HF: high frequency power, LF: low frequency power, QTc: Bazett-corrected QT-interval, DC: deceleration capacity, IGT: impaired glucose tolerance, Gen. Susc.: participants with a genetic susceptibility, SD: standard deviation, P5: 5$^{th}$ percentile, Q1: 1$^{st}$ quartile, Q3: 3$^{rd}$ quartile, P95: 95$^{th}$ percentile, IQR: interquartile range

**APPENDIX E.** Distribution of 1-hour ECG parameters in REHAB study

| | *N* | Mean | SD | Min | P5 | Q1 | Median | Q3 | P95 | Max | IQR |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **SDNN** (ms) | 2,794 | 104.9 | 44.9 | 10.1 | 40.9 | 71.9 | 98.9 | 131.1 | 190.6 | 249.6 | 59.2 |
| **RMSSD** (ms) | 2,802 | 60.8 | 34.9 | 6.0 | 16.6 | 33.6 | 55.7 | 80.0 | 125.5 | 230.3 | 46.5 |
| **T-wave complexity** (%) | 2,793 | 0.079 | 0.085 | 0.007 | 0.017 | 0.031 | 0.050 | 0.094 | 0.243 | 0.666 | 0.062 |
| NN (ms) | 2,909 | 66 | 11 | 33 | 50 | 59 | 65 | 72 | 86 | 112 | 13 |
| PNN50 (%) | 2,806 | 4.60 | 5.66 | 0 | 0 | 1 | 3 | 6 | 14 | 48 | 5 |
| HF (normalized) | 2,795 | 3.6 | 7.2 | 0.0 | 0.2 | 0.7 | 1.6 | 3.5 | 13.7 | 81.5 | 2.8 |
| LF (normalized) | 2,795 | 5.7 | 11.2 | 0.1 | 0.5 | 1.3 | 2.5 | 4.9 | 21.4 | 93.9 | 3.5 |
| LF/HF | 2,795 | 2.2 | 2.1 | 0.1 | 0.5 | 1.1 | 1.7 | 2.6 | 5.7 | 25.6 | 1.5 |
| DC (ms) | 2,701 | 4.0 | 1.9 | 0.0 | 1.7 | 2.8 | 3.8 | 4.9 | 7.1 | 27.3 | 2.1 |
| TP ($ms^2$) | 2,795 | 27,389 | 25,918 | 53 | 1,969 | 8,959 | 19,125 | 37,656 | 80,684 | 20,418 | 28,698 |
| VLF ($ms^2$) | 2,795 | 6,790 | 6,317 | 25 | 643 | 2,291 | 4,761 | 9,259 | 20,091 | 45,678 | 6,968 |

**APPENDIX F.** Distribution of (a) 5 minute and (b) 1 hour ECG parameters in UPDIABETES study.

***(a.) 5 minute***

| | ***N*** | **Mean** | **SD** | **Min** | **P5** | **Q1** | **Median** | **Q3** | **P95** | **Max** | **IQR** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **SDNN** (ms) | 408 | 49.3 | 25.2 | 13.4 | 18.7 | 33.8 | 46.1 | 59.5 | 94.7 | 222.5 | 25.6 |
| **RMSSD** (ms) | 407 | 32.5 | 18.2 | 6.5 | 9.0 | 18.0 | 29.3 | 42.7 | 68.9 | 102.2 | 24.6 |
| **T-wave complexity** (%) | 377 | 13.6 | 8.8 | 4.3 | 6.2 | 8.2 | 10.5 | 18.5 | 24.6 | 78.4 | 10.2 |
| QTc (ms) | 408 | 413.3 | 22.3 | 360.3 | 377.1 | 397.0 | 413.6 | 423.2 | 457.3 | 470.3 | 26.2 |
| DC (ms) | 403 | 9.1 | 3.9 | 0.2 | 4.0 | 6.2 | 8.5 | 11.8 | 16.2 | 20.0 | 5.6 |
| QTp_sd (ms) | 396 | 16.7 | 17.8 | 2.9 | 4.1 | 5.9 | 8.7 | 19.2 | 62.4 | 84.0 | 13.4 |
| TAMP (μV) | 408 | 284.6 | 97.2 | 95.8 | 129.8 | 225.7 | 268.1 | 315.0 | 478.4 | 534.4 | 89.3 |
| PNN50 (%) | 407 | 4.71 | 5.76 | 0 | 0 | 0 | 3 | 8 | 16 | 27 | 8 |
| TP ($ms^2$) | 408 | 3039 | 4282 | 114 | 310 | 950 | 2046 | 3328 | 9170 | 43866 | 2378 |
| VLF ($ms^2$) | 408 | 1362 | 2327 | 33 | 110 | 333 | 761 | 1461 | 3884 | 23806 | 1128 |
| LF ($ms^2$) | 408 | 737 | 977 | 27 | 61 | 197 | 440 | 877 | 2044 | 8181 | 680 |
| HF ($ms^2$) | 408 | 511 | 595 | 11 | 31 | 88 | 290 | 775 | 1580 | 4521 | 687 |
| LF/HF | 408 | 2.5 | 2.5 | 0.1 | 0.3 | 0.9 | 1.8 | 3.2 | 8.2 | 17.2 | 2.3 |
| LF (normalized) | 408 | 50.2 | 21.2 | 0.9 | 11.7 | 35.1 | 52.6 | 66.5 | 83.0 | 92.7 | 31.3 |
| HF (normalized) | 408 | 33.9 | 20.4 | 0.3 | 7.3 | 17.4 | 30.8 | 47.3 | 72.0 | 94.8 | 29.9 |

***(b.) 1 hour***

| | *N* | Mean | SD | Min | P5 | Q1 | Median | Q3 | P95 | Max | IQR |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **SDNN** (ms) | 256 | 75.5 | 27.9 | 21.7 | 37.6 | 57.7 | 71.6 | 89.1 | 124.6 | 207.9 | 31.4 |
| **RMSSD** (ms) | 256 | 34.2 | 20.2 | 7.2 | 10.9 | 19.3 | 28.9 | 44.9 | 70.5 | 130.9 | 25.6 |
| **T-wave complexity** (%) | 256 | 16.6 | 10.0 | 5.1 | 7.0 | 9.8 | 12.9 | 21.8 | 35.2 | 74.0 | 11.9 |
| QTc (ms) | 256 | 414.7 | 21.5 | 353.5 | 378.1 | 399.2 | 417.2 | 425.2 | 456.5 | 468.0 | 25.9 |
| DC (ms) | 256 | 8.0 | 2.9 | 1.8 | 4.0 | 5.9 | 7.8 | 9.6 | 13.0 | 15.5 | 3.7 |
| QTp_sd (ms) | 256 | 19.3 | 16.0 | 3.4 | 4.7 | 8.1 | 13.9 | 23.8 | 53.8 | 81.5 | 15.7 |
| TAMP (μV) | 256 | 265.7 | 99.0 | 95.6 | 117.5 | 202.5 | 247.6 | 297.7 | 475.1 | 522.0 | 95.2 |
| PNN50 (ms) | 256 | 4.68 | 6.03 | 0 | 0 | 0 | 3 | 7 | 16 | 32 | 7 |
| TP ($ms^2$) | 256 | 8329 | 6958 | 377 | 1777 | 4122 | 6603 | 10355 | 19722 | 61422 | 6233 |
| VLF ($ms^2$) | 256 | 2864 | 2432 | 192 | 622 | 1275 | 2347 | 3506 | 7095 | 18620 | 2231 |
| LF ($ms^2$) | 256 | 777 | 751 | 67 | 128 | 289 | 484 | 960 | 2179 | 4796 | 671 |
| HF ($ms^2$) | 256 | 531 | 687 | 18 | 29 | 86 | 255 | 669 | 2070 | 4627 | 582 |
| LF/HF | 256 | 3.1 | 2.6 | 0.1 | 0.5 | 1.1 | 2.3 | 4.2 | 9.1 | 13.6 | 3.1 |
| LF (normalized) | 256 | 16.7 | 11.2 | 1.7 | 3.2 | 7.8 | 13.2 | 23.8 | 36.2 | 66.0 | 16.0 |
| HF (normalized) | 256 | 10.1 | 11.0 | 0.3 | 1.0 | 2.6 | 7.1 | 13.2 | 33.0 | 80.5 | 10.6 |

**APPENDIX G.** Distribution of (a) 5-minute and (b) 1-hour ECG parameters in UPCON study.

***(a.) 5 minute***

| | *N* | Mean | SD | Min | P5 | Q1 | Median | Q3 | P95 | Max | IQR |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **SDNN (ms)** | 17,687 | 60.7 | 34.0 | 0.0 | 20.8 | 36.0 | 52.8 | 77.4 | 126.8 | 246.2 | 41.4 |
| **RMSSD (ms)** | 17,644 | 30.9 | 23.3 | 4.5 | 9.1 | 15.0 | 23.7 | 38.2 | 81.7 | 249.8 | 23.2 |
| **T-wave complexity(%)** | 17,108 | 18.1 | 12.1 | 3.0 | 5.5 | 9.1 | 14.4 | 24.0 | 41.0 | 79.3 | 15.0 |
| NN (ms) | 17,720 | 820.7 | 155.0 | 404.0 | 577.3 | 704.3 | 811.5 | 932.5 | 1084.9 | 1537.1 | 228.2 |
| QTc (ms) | 17,632 | 417.7 | 23.1 | 335.4 | 383.8 | 402.7 | 416.0 | 431.8 | 461.4 | 499.9 | 29.1 |
| DC (ms) | 17,450 | 8.2 | 3.3 | 0.0 | 3.2 | 5.9 | 8.0 | 10.1 | 13.9 | 30.0 | 4.1 |
| QTp_sd (ms) | 17,304 | 23.4 | 22.6 | 1.8 | 4.5 | 7.6 | 13.3 | 32.1 | 75.7 | 100.0 | 24.5 |
| TAMP (μV) | 17,726 | 305.2 | 158.1 | 64.5 | 102.1 | 159.5 | 293.6 | 416.8 | 592.7 | 770.0 | 257.3 |
| PNN50 (ms) | 17,645 | 4.3 | 6.8 | 0.0 | 0.0 | 0.0 | 1.0 | 6.0 | 20.0 | 43.0 | 6.0 |
| TP ($ms^2$) | 17,680 | 5,080 | 14,785 | 24 | 342 | 1,086 | 2,468 | 5,696 | 17,188 | 1,222,793 | 4,610 |
| VLF ($ms^2$) | 17,680 | 2,585 | 5,109 | 5 | 114 | 428 | 1,026 | 2,604 | 10,268 | 188,019 | 2,176 |
| LF ($ms^2$) | 17,680 | 1,143 | 5,575 | 2 | 67 | 225 | 524 | 1,238 | 3,771 | 446,292 | 1,013 |
| HF ($ms^2$) | 17,680 | 606 | 6152 | 1 | 15 | 60 | 172 | 501 | 2274 | 673603 | 442 |
| LF/HF | 17,680 | 4.7 | 4.8 | 0.0 | 0.5 | 1.6 | 3.3 | 6.1 | 13.6 | 66.9 | 4.5 |
| LF (normalized) | 17,680 | 52.8 | 24.0 | 0.1 | 9.4 | 34.7 | 55.9 | 72.5 | 87.0 | 97.3 | 37.8 |
| HF (normalized) | 17,680 | 22.6 | 18.7 | 0.0 | 2.0 | 8.4 | 17.3 | 31.8 | 62.4 | 96.7 | 23.4 |

***(b.) 1 hour***

| | *N* | Mean | SD | Min | P5 | Q1 | Median | Q3 | P95 | Max | IQR |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **SDNN (ms)** | 1453 | 82.4 | 35.2 | 17.3 | 36.3 | 57.4 | 76.6 | 99.7 | 149.3 | 248.2 | 42.3 |
| **RMSSD (ms)** | 1457 | 31.8 | 21.2 | 6.2 | 10.4 | 16.8 | 25.3 | 39.2 | 80.7 | 121.9 | 22.4 |
| **T-wave complexity (%)** | 1432 | 18.1 | 11.5 | 3.8 | 5.6 | 9.3 | 14.6 | 24.1 | 40.4 | 79.1 | 14.9 |
| NN (ms) | 1457 | 816.7 | 145.1 | 439.8 | 593.0 | 708.1 | 807.1 | 921.6 | 1065.5 | 1220.8 | 213.5 |
| QTc (ms) | 1450 | 417.5 | 22.0 | 346.7 | 384.9 | 402.8 | 415.4 | 430.7 | 459.8 | 495.2 | 27.9 |
| DC (ms) | 1456 | 8.1 | 2.8 | 0.4 | 3.8 | 6.2 | 8.1 | 9.7 | 12.9 | 19.7 | 3.5 |
| QTp_sd (ms) | 1433 | 24.1 | 22.3 | 2.9 | 4.9 | 8.3 | 14.3 | 33.0 | 74.2 | 100.0 | 24.6 |
| TAMP (μV) | 1457 | 304.4 | 156.3 | 74.0 | 103.8 | 158.4 | 296.5 | 415.9 | 589.0 | 718.6 | 257.4 |
| PNN50 (ms) | 1457 | 4.2 | 6.2 | 0.0 | 0.0 | 0.0 | 1.0 | 6.0 | 18.0 | 32.0 | 6.0 |
| TP ($ms^2$) | 1457 | 10673 | 14456 | 356 | 1550 | 3885 | 7255 | 13238 | 29527 | 388092 | 9353 |
| VLF ($ms^2$) | 1457 | 3792 | 8138 | 127 | 612 | 1441 | 2586 | 4452 | 10281 | 286118 | 3012 |
| LF ($ms^2$) | 1457 | 1109 | 1687 | 47 | 132 | 331 | 647 | 1288 | 3574 | 34791 | 957 |
| HF ($ms^2$) | 1457 | 570 | 1533 | 7 | 25 | 85 | 213 | 550 | 2298 | 47066 | 465 |
| LF/HF | 1457 | 3.9 | 2.8 | 0.1 | 0.7 | 1.9 | 3.3 | 5.2 | 9.3 | 23.6 | 3.4 |
| LF (normalized) | 1457 | 20.6 | 14.8 | 0.6 | 3.2 | 8.6 | 16.8 | 30.0 | 49.6 | 76.9 | 21.4 |
| HF (normalized) | 1457 | 9.3 | 10.5 | 0.1 | 0.6 | 2.3 | 5.6 | 12.0 | 32.3 | 70.5 | 9.7 |

**APPENDIX H.** Percent change in ECG outcomes associated with each IQR increase in concurrent and 1- to 6-hour lagged air pollutant concentrations (taken from the stationary site) in participants in the Augsburg study.

**Subjects with type-2 diabetes or impaired glucose tolerance (Diabetes + IGT)**

| | UFP IQR = 7157 particles/cm$^3$ | | | AMP IQR = 1595 particles/cm$^3$ | | | $PM_{2.5}$ IQR = 12.3 μg/m$^3$ | | | Black Carbon IQR = 1.2 μg/m$^3$ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Pollutant averaging time** | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** |
| **SDNN (ms)** | | | | | | | | | | | | |
| Concurrent | 1158 | 1.44%# | -0.22%, 3.10% | 1158 | -0.10% | -2.07%, 1.87% | 1185 | -3.03%* | -5.68%, -0.37% | 957 | -0.42% | -2.47%, 1.64% |
| Lag 1h | 1160 | 0.04% | -1.56%, 1.65% | 1160 | -1.04% | -2.89%, 0.81% | 1185 | -4.49%** | -7.18%, -1.80% | 953 | -1.93%* | -3.82%, -0.04% |
| Lag 2h | 1162 | -2.11%** | -3.65%, -0.58% | 1162 | -2.47%** | -4.27%, -0.68% | 1185 | -4.59%** | -7.44%, -1.75% | 954 | -3.96%** | -5.77%, -2.16% |
| Lag 3h | 1167 | -1.98%** | -3.47%, -0.50% | 1167 | -1.74%# | -3.58%, 0.11% | 1186 | -3.74%* | -6.77%, -0.72% | 960 | -3.36%** | -5.16%, -1.55% |
| Lag 4h | 1166 | -1.95%* | -3.45%, -0.45% | 1166 | -2.54%** | -4.42%, -0.65% | 1186 | -4.19%** | -7.32%, -1.07% | 966 | -3.38%** | -5.23%, -1.53% |
| Lag 5h | 1166 | -0.58% | -2.27%, 1.12% | 1166 | -1.49% | -3.47%, 0.50% | 1186 | -3.92%* | -7.17%, -0.67% | 974 | -2.14%* | -4.20%, -0.09% |
| Lag 6h | 1168 | 1.15% | -0.89%, 3.19% | 1168 | -0.73% | -2.89%, 1.44% | 1186 | -4.42%* | -7.79%, -1.05% | 980 | -1.34% | -3.68%, 1.01% |
| **RMSSD (ms)** | | | | | | | | | | | | |
| Concurrent | 1158 | -0.06% | -2.41%, 2.36% | 1158 | -1.60% | -5.32%, 2.26% | 1185 | -7.20%** | -12.11%, -2.02% | 957 | -2.95%# | -6.32%, 0.54% |
| Lag 1h | 1160 | -0.60% | -2.94%, 1.80% | 1160 | -1.22% | -4.79%, 2.47% | 1185 | -4.90%# | -9.90%, 0.38% | 953 | -3.45%* | -6.57%, -0.22% |
| Lag 2h | 1162 | 0.52% | -1.72%, 2.82% | 1162 | 0.44% | -2.89%, 3.88% | 1185 | -2.27% | -7.66%, 3.43% | 954 | -1.02% | -4.05%, 2.10% |
| Lag 3h | 1167 | -1.14% | -3.30%, 1.07% | 1167 | -1.58% | -4.85%, 1.80% | 1186 | -0.41% | -6.32%, 5.87% | 960 | -1.05% | -4.13%, 2.12% |
| Lag 4h | 1166 | -0.86% | -3.05%, 1.39% | 1166 | -1.25% | -4.61%, 2.22% | 1186 | -2.54% | -8.58%, 3.91% | 966 | -1.12% | -4.34%, 2.22% |
| Lag 5h | 1166 | 0.00% | -2.47%, 2.53% | 1166 | -0.24% | -3.85%, 3.51% | 1186 | -5.02% | -11.19%, 1.57% | 974 | -2.63% | -6.29%, 1.18% |
| Lag 6h | 1168 | -2.11% | -4.98%, 0.86% | 1168 | -0.27% | -4.51%, 4.17% | 1186 | -6.01%# | -12.40%, 0.85% | 980 | -5.95%** | -10.20%, -1.50% |
| **T-wave complexity (%)** | | | | | | | | | | | | |
| Concurrent | 1157 | 0.34% | -0.88%, 1.57% | 1157 | 0.74% | -1.07%, 2.57% | 1184 | 1.25% | -1.28%, 3.84% | 956 | 0.72% | -0.98%, 2.45% |
| Lag 1h | 1159 | -0.29% | -1.50%, 0.93% | 1159 | -0.06% | -1.76%, 1.67% | 1184 | 0.37% | -2.13%, 2.94% | 952 | 0.24% | -1.36%, 1.86% |
| Lag 2h | 1161 | 0.49% | -0.67%, 1.66% | 1161 | 0.18% | -1.41%, 1.80% | 1184 | -0.41% | -3.03%, 2.27% | 953 | 0.69% | -0.82%, 2.22% |
| Lag 3h | 1166 | 0.16% | -0.96%, 1.30% | 1166 | -0.26% | -1.87%, 1.38% | 1185 | 0.43% | -2.40%, 3.34% | 960 | -0.23% | -1.75%, 1.32% |
| Lag 4h | 1165 | -0.44% | -1.57%, 0.70% | 1165 | -0.24% | -1.88%, 1.43% | 1185 | -0.99% | -3.89%, 2.00% | 965 | -0.24% | -1.81%, 1.36% |
| Lag 5h | 1165 | -0.51% | -1.76%, 0.76% | 1165 | 0.22% | -1.53%, 1.99% | 1185 | 2.60% | -0.52%, 5.83% | 973 | 1.25% | -0.55%, 3.09% |
| Lag 6h | 1167 | 2.03% ** | 0.52%, 3.57% | 1167 | 1.77%# | -0.23%, 3.81%# | 1185 | 2.38% | -0.90%, 5.76% | 979 | 3.46%** | 1.29%, 5.69% |
| **HR (beats/min)** | | | | | | | | | | | | |
| Concurrent | 1157 | 0.50%# | -0.04%, 1.05% | 1157 | 0.92%* | 0.18%, 1.66% | 1184 | 0.83% | -0.21%, 1.88% | 956 | 0.71%# | -0.01%, 1.42% |
| Lag 1h | 1159 | -0.05% | -0.60%, 0.49% | 1159 | 0.50% | -0.21%, 1.21% | 1184 | 0.55% | -0.50%, 1.60% | 952 | 0.25% | -0.42%, 0.93% |
| Lag 2h | 1161 | 0.09% | -0.44%, 0.62% | 1161 | 0.19% | -0.49%, 0.86% | 1184 | 0.25% | -0.86%, 1.36% | 953 | 0.32% | -0.32%, 0.96% |
| Lag 3h | 1166 | 0.36% | -0.15%, 0.86% | 1166 | 0.46% | -0.23%, 1.15% | 1185 | 0.56% | -0.62%, 1.75% | 959 | 0.53% | -0.11%, 1.18% |
| Lag 4h | 1165 | -0.26% | -0.77%, 0.25% | 1165 | 0.08% | -0.62%, 0.78% | 1185 | -0.13% | -1.36%, 1.10% | 965 | -0.10% | -0.77%, 0.56% |
| Lag 5h | 1165 | -0.39% | -0.96%, 0.17% | 1165 | 0.10% | -0.64%, 0.84% | 1185 | 1.26%# | -0.02%, 2.54% | 973 | 0.22% | -0.52%, 0.96% |
| Lag 6h | 1167 | 0.02% | -0.65%, 0.69% | 1167 | 0.27% | -0.54%, 1.09% | 1185 | 1.04% | -0.29%, 2.38% | 979 | 1.10%* | 0.24%, 1.96% |

**Subjects with a potential genetic predisposition on the detoxifying and inflammatory pathways (Gen susc).**

| | UFP IQR = 7157 particles/cm$^3$ | | | AMP IQR = 1595 particles/cm$^3$ | | | $PM_{2.5}$ IQR = 12.3 μg/m$^3$ | | | Black Carbon IQR = 1.2 μg/m$^3$ | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Pollutant averaging time** | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** | ***N*** | **% Change** | **95% confidence interval** |
| **SDNN (ms)** | | | | | | | | | | | | |
| Concurrent | 782 | 1.92%* | 0.19%, 3.65% | 782 | 1.88% | -0.69%, 4.44% | 823 | -1.10% | -4.25%, 2.05% | 796 | 1.23% | -0.85%, 3.32% |
| Lag 1h | 778 | 0.17% | -1.59%, 1.92% | 778 | 0.29% | -2.14%, 2.72% | 823 | -2.92%# | -6.08%, 0.25% | 794 | -0.81% | -2.78%, 1.15% |
| Lag 2h | 772 | -1.49%# | -3.24%, 0.26% | 772 | -0.85% | -3.28%, 1.58% | 823 | -3.34%* | -6.57%, -0.12% | 794 | -2.15%* | -4.01%, -0.29% |
| Lag 3h | 764 | -2.26%* | -3.98%, -0.53% | 764 | -1.89% | -4.29%, 0.51% | 823 | -2.72% | -5.97%, 0.54% | 796 | -2.69%** | -4.45%, -0.92% |
| Lag 4h | 756 | -1.57%# | -3.35%, 0.22% | 756 | -1.31% | -3.72%, 1.11% | 823 | -1.76% | -5.08%, 1.55% | 803 | -1.87%* | -3.68%, -0.06% |
| Lag 5h | 753 | -1.21% | -3.29%, 0.88% | 753 | 0.27% | -2.28%, 2.82% | 823 | -0.46% | -3.86%, 2.94% | 804 | -0.76% | -2.77%, 1.25% |
| Lag 6h | 752 | 1.66% | -0.90%, 4.22% | 752 | 1.12% | -1.53%, 3.77% | 823 | 0.41% | 3.05%, 3.88% | 811 | 1.01% | -1.19%, 3.20% |
| **RMSSD (ms)** | | | | | | | | | | | | |
| Concurrent | 783 | -1.86% | -3.98%, 0.31%# | 783 | -1.53% | -5.21%, 2.30% | 824 | -2.47% | -6.78%, 2.04% | 797 | -1.46% | -4.17%, 1.31% |
| Lag 1h | 779 | -1.06% | -3.28%, 1.21% | 779 | -1.50% | -5.03%, 2.17% | 824 | -3.09% | -7.33%, 1.35% | 795 | 0.10% | -2.45%, 2.71% |
| Lag 2h | 773 | 0.15% | -2.05%, 2.40% | 773 | -1.83% | -5.31%, 1.77% | 824 | -2.42% | -6.80%, 2.16% | 795 | 0.47% | -1.98%, 2.98% |
| Lag 3h | 765 | -0.40% | -2.59%, 1.85% | 765 | -1.25% | -4.73%, 2.35% | 824 | -1.65% | -6.16%, 3.08% | 797 | -2.13%# | -4.46%, 0.26% |
| Lag 4h | 757 | -0.31% | -2.62%, 2.05% | 757 | -2.89% | -6.33%, 0.68% | 824 | -1.50% | -6.15%, 3.37% | 804 | 0.72% | -1.71%, 3.21% |
| Lag 5h | 754 | -0.44% | -3.20%, 2.41% | 754 | -0.38% | -4.24%, 3.65% | 824 | 1.83% | -3.19%, 7.11% | 806 | -0.15% | -2.93%, 2.71% |
| Lag 6h | 753 | -1.76% | -5.05%, 1.64% | 753 | -2.51% | -6.51%, 1.68% | 824 | 0.59% | -4.54%, 6.01% | 812 | -0.70% | -3.79%, 2.49% |
| **T-wave complexity (%)** | | | | | | | | | | | | |
| Concurrent | 783 | -0.47% | -1.64%, 0.71% | 783 | -0.63% | -2.57%, 1.35% | 824 | 0.19% | -2.13%, 2.56% | 797 | -0.72% | -2.17%. 0.74% |
| Lag 1h | 779 | -0.06% | -1.27%, 1.17% | 779 | 0.09% | -1.78%, 1.99% | 824 | -0.46% | -2.76%, 1.89% | 795 | -0.13% | -1.48%. 1.24% |
| Lag 2h | 773 | -1.24%* | -2.41%, -0.06% | 773 | -1.39% | -3.20%, 0.45% | 824 | -0.59% | -2.94%, 1.82% | 795 | -1.09% | -2.38%. 0.22% |
| Lag 3h | 765 | 0.01% | -1.17%, 1.21% | 765 | 0.17% | -1.66%, 2.02% | 824 | 1.35% | -1.08%, 3.84% | 797 | 0.02% | -1.26%. 1.32% |
| Lag 4h | 757 | 0.05% | -1.18%, 1.29% | 757 | 1.00% | -0.83%, 2.87% | 824 | 1.89% | -0.61%, 4.46% | 804 | 0.01% | -1.29%. 1.33% |
| Lag 5h | 754 | 0.52% | -0.95%, 2.01% | 754 | 0.28% | -1.68%, 2.28% | 824 | 1.08% | -1.48%, 3.71% | 806 | 0.76% | -0.74%. 2.28% |
| Lag 6h | 753 | 0.96% | -0.83%, 2.79% | 753 | 0.59% | -1.49%, 2.72% | 824 | 2.58%# | -0.11%, 5.34% | 812 | 1.14% | -0.53%. 2.84% |
| **HR (beats/min)** | | | | | | | | | | | | |
| Concurrent | 783 | -0.02% | -0.65%, 0.61% | 783 | 0.11% | -0.91%, 1.14% | 824 | 0.81% | -0.40%, 2.03% | 797 | 0.19% | -0.58%, 0.96 |
| Lag 1h | 779 | 0.43% | -0.23%, 1.08% | 779 | 0.34% | -0.65%, 1.32% | 824 | 0.50% | -0.72%, 1.72% | 795 | -0.03% | -0.75%, 0.70 |
| Lag 2h | 773 | -0.33% | -0.98%, 0.31% | 773 | -0.07% | -1.04%, 0.91% | 824 | 0.17% | -1.08%, 1.42% | 795 | -0.02% | -0.71%, 0.68 |
| Lag 3h | 765 | -0.14% | -0.77%, 0.49% | 765 | -0.07% | -1.02%, 0.88% | 824 | 0.21% | -1.06%, 1.48% | 797 | 0.40% | -0.28%, 1.07 |
| Lag 4h | 757 | -0.14% | -0.80%, 0.52% | 757 | 0.26% | -0.69%, 1.21% | 824 | 0.56% | -0.74%, 1.85% | 804 | -0.15% | -0.83%, 0.52 |
| Lag 5h | 754 | 0.29% | -0.48%, 1.06% | 754 | 0.27% | -0.74%, 1.29% | 824 | 0.21% | -1.12%, 1.55% | 806 | 0.36% | -0.42%, 1.13 |
| Lag 6h | 753 | 1.00%* | 0.07%, 1.93% | 753 | 0.70% | -0.37%, 1.78% | 824 | 0.69% | -0.68%, 2.06% | 812 | 0.48% | -0.37%, 1.32 |

# $P < 0.10$; * $P < 0.05$; ** $P < 0.01$

**APPENDIX I.** Percent change in ECG outcomes associated with each IQR increase in concurrent and 1- to 6-hour lagged air pollutant concentrations in participants in the REHAB study.

| | **UFP IQR = 3058 particles/cm$^3$** | | | **AMP IQR = 902 particles/cm$^3$** | | | **PM $_{2.5}$ IQR = 7.6 μg/m$^3$** | | | **Black Carbon IQR = 0.73 μg/m$^3$** | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ***N*** | **% Change** | **95% CI** | ***N*** | **% Change** | **95% CI** | ***N*** | **% Change** | **95% CI** | ***N*** | **% Change** | **95% CI** |
| **SDNN (ms)** | | | | | | | | | | | | |
| Concurrent | 2536 | -0.61% | -1.70%,0.47% | 2536 | -1.79%* | -3.41%,-0.17% | 2251 | -1.23% | -2.89%,0.44% | 2326 | -0.21% | -2.64%, 2.21% |
| Lag 1h | 2536 | -1.15%* | -2.19%,-0.11% | 2536 | -1.78%* | -3.37%,-0.19% | 2259 | -0.71% | -2.39%,0.97% | 2314 | 0.10% | -1.97%, 2.17% |
| Lag 2h | 2537 | -0.49% | -1.38%,0.40% | 2537 | -1.75%* | -3.30%,-0.20% | 2265 | -1.30% | -3.01%,0.42% | 2302 | -0.66% | -2.55%, 1.22% |
| Lag 3h | 2539 | -0.25% | -1.07%,0.56% | 2539 | -1.71%* | -3.19%,-0.24% | 2271 | -1.74%# | -3.49%,0.00% | 2298 | -0.42% | -2.22%, 1.38% |
| Lag 4h | 2540 | -0.71% | -1.73%,0.32% | 2540 | -1.75%* | -3.19%,-0.31% | 2275 | -1.75%# | -3.51%,0.00% | 2296 | -1.03% | -2.81%, 0.74% |
| Lag 5h | 2540 | -0.24% | -1.30%,0.83% | 2540 | -1.57%* | -2.97%,-0.16% | 2280 | -2.13%* | -3.91%,-0.35% | 2293 | -0.96% | -2.81%, 0.89% |
| Lag 6h | 2540 | -0.02% | -0.92%,0.87% | 2540 | -1.28%# | -2.66%,0.09% | 2283 | -2.00%* | -3.77%,-0.23% | 2289 | -1.27% | -3.30%, 0.76% |
| **RMSSD (ms)** | | | | | | | | | | | | |
| Concurrent | 2545 | -0.18% | -1.80%,1.44% | 2545 | -0.65% | -3.06%,1.76% | 2260 | -2.18%# | -4.65%,0.30% | 2336 | -1.45% | -5.05%, 2.15% |
| Lag 1h | 2545 | -0.76% | -2.31%,0.79% | 2545 | -0.96% | -3.32%,1.40% | 2268 | -1.35% | -3.84%,1.14% | 2324 | -1.31% | -4.42%, 1.80% |
| Lag 2h | 2546 | -0.94% | -2.27%,0.39% | 2546 | -1.26% | -3.56%,1.05% | 2274 | -1.94% | -4.48%,0.61% | 2312 | -0.82% | -3.65%, 2.02% |
| Lag 3h | 2548 | -1.05%# | -2.27%,0.17% | 2548 | -1.43% | -3.62%,0.76% | 2280 | -2.48%# | -5.06%,0.10% | 2308 | -1.10% | -3.81%, 1.62% |
| Lag 4h | 2549 | -2.51%** | -4.04%,-0.98% | 2549 | -2.04%# | -4.19%,0.10% | 2284 | -2.98%* | -5.58%,-0.38% | 2306 | -1.92% | -4.58%, 0.74% |
| Lag 5h | 2549 | -1.02% | -2.60%,0.56% | 2549 | -1.07% | -3.16%,1.03% | 2289 | -3.49%** | -6.13%,-0.84% | 2303 | -0.94% | -3.72%, 1.83% |
| Lag 6h | 2549 | -0.81% | -2.15%,0.52% | 2549 | -1.23% | -3.27%,0.81% | 2292 | -2.75%* | -5.38%,-0.12% | 2299 | -1.56% | -4.62%, 1.50% |
| **T-wave complexity (%)** | | | | | | | | | | | | |
| Concurrent | 2565 | -0.82% | -3.07%, 1.42% | 2565 | -0.06% | -3.43%,3.31% | 2286 | -0.84% | -4.28%,2.60% | 2354 | -0.73% | -5.80%,4.35% |
| Lag 1h | 2565 | -1.39% | -3.53%, 0.75% | 2565 | -0.18% | -3.49%,3.13% | 2293 | 0.50% | -2.97%,3.98% | 2343 | -0.98% | -5.36%,3.39% |
| Lag 2h | 2566 | -0.20% | -2.05%, 1.65% | 2566 | -0.70% | -3.92%,2.53% | 2299 | -0.05% | -3.59%,3.50% | 2332 | -0.66% | -4.60%,3.29% |
| Lag 3h | 2568 | 0.03% | -1.67%, 1.73% | 2568 | -0.37% | -3.46%,2.72% | 2304 | -0.38% | -3.99%,3.24% | 2327 | 0.22% | -3.52%,3.96% |
| Lag 4h | 2569 | -0.29% | -2.42%, 1.85% | 2569 | -0.47% | -3.47%,2.54% | 2308 | 0.30% | -3.33%,3.92% | 2325 | 0.42% | -3.31%,4.15% |
| Lag 5h | 2569 | -2.11%# | -4.32%, 0.10% | 2569 | -1.71% | -4.65%,1.22% | 2313 | 0.53% | -3.15%,4.22% | 2323 | 0.29% | -3.63%,4.21% |
| Lag 6h | 2569 | -2.02%* | -3.88%, -0.16% | 2569 | -1.82% | -4.68%,1.05% | 2316 | 0.27% | -3.37%,3.91% | 2319 | -1.10% | -5.40%,3.19% |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **NN (ms)** | | | | | | | | | | | | |
| Concurrent | 2548 | 0.26% | -0.14%,0.65% | 2548 | 0.26% | -0.33%,0.84% | 2263 | 0.25% | -0.34%,0.85% | 2338 | 0.56% | -0.31%, 1.43% |
| Lag 1h | 2548 | 0.51%** | 0.14%,0.89% | 2548 | 0.24% | -0.33%,0.81% | 2271 | 0.17% | -0.43%,0.77% | 2326 | 0.59% | -0.16%, 1.34% |
| Lag 2h | 2549 | 0.34%* | 0.02%,0.66% | 2549 | 0.35% | -0.21%,0.91% | 2277 | 0.14% | -0.47%,0.76% | 2314 | 0.41% | -0.27%, 1.09% |
| Lag 3h | 2551 | 0.11% | -0.19%,0.40% | 2551 | 0.30% | -0.24%,0.83% | 2283 | 0.07% | -0.55%,0.70% | 2310 | 0.25% | -0.40%, 0.90% |
| Lag 4h | 2552 | 0.01% | -0.36%,0.38% | 2552 | 0.13% | -0.39%,0.65% | 2287 | -0.15% | -0.78%,0.48% | 2308 | 0.37% | -0.26%, 1.00% |
| Lag 5h | 2552 | -0.05% | -0.44%,0.33% | 2552 | 0.01% | -0.50%,0.52% | 2292 | -0.17% | -0.81%,0.47% | 2305 | 0.55% | -0.11%, 1.20% |
| Lag 6h | 2552 | 0.06% | -0.27%,0.38% | 2552 | 0.18% | -0.32%,0.67% | 2295 | -0.10% | -0.73%,0.54% | 2301 | -0.05% | -0.77%, 0.67% |

# $P < 0.10$; * $P < 0.05$; ** $P < 0.01$

**Appendix J.** Percent change in REHAB ECG outcomes associated with each Augsburg IQR increase in concurrent and lagged air pollutant concentrations in participants of the REHAB study

| | **UFP IQR = 7157 particles/cm$^3$** | | | **AMP IQR = 1595 particles/cm$^3$** | | | **$PM_{2.5}$ IQR = 12.3 μg/m$^3$** | | | **Black Carbon IQR = 1.2 μg/m$^3$** | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | ***N*** | **% Change** | **95% CI** | ***N*** | **% Change** | **95% CI** | ***N*** | **% Change** | **95% CI** | ***N*** | **% Change** | **95% CI** |
| **SDNN (ms)** | | | | | | | | | | | | |
| Concurrent | 2536 | -1.43% | -3.98%, 1.10% | 2536 | -3.17%* | -6.03%, -0.30% | 2251 | -1.99% | -4.68%, 0.71% | 2326 | -0.35% | -4.34%, 3.63% |
| Lag 1h | 2536 | -2.69%* | -5.13%, -0.26% | 2536 | -3.15%* | -5.96%, -0.34% | 2259 | -1.15% | -3.87%, 1.57% | 2314 | 0.16% | -3.24%, 3.57% |
| Lag 2h | 2537 | -1.15% | -3.23%, 0.94% | 2537 | -3.09%* | -5.84%, -0.35% | 2265 | -2.10% | -4.87%, 0.68% | 2302 | -1.08% | -4.19%, 2.01% |
| Lag 3h | 2539 | -0.59% | -2.50%, 1.31% | 2539 | -3.02%* | -5.64%, -0.42% | 2271 | -2.82%# | -5.65%, 0.00% | 2298 | -0.69% | -3.65%, 2.27% |
| Lag 4h | 2540 | -1.66% | -4.05%, 0.75% | 2540 | -3.09%* | -5.64%, -0.55% | 2275 | -2.83%# | -5.68%, 0.00% | 2296 | -1.69% | -4.62%, 1.22% |
| Lag 5h | 2540 | -0.56% | -3.04%, 1.94% | 2540 | -2.78%* | -5.25%, -0.28% | 2280 | -3.45%* | -6.33%, -0.57% | 2293 | -1.58% | -4.62%, 1.46% |
| Lag 6h | 2540 | -0.05% | -2.15%, 2.04% | 2540 | -2.26%# | -4.70%, 0.16% | 2283 | -3.24%* | -6.10%, -0.37% | 2289 | -2.09% | -5.42%, 1.25% |
| **RMSSD (ms)** | | | | | | | | | | | | |
| Concurrent | 2545 | -0.42% | -4.21%, 3.37% | 2545 | -1.15% | -5.41%, 3.11% | 2260 | -3.53%# | -7.53%, 0.49% | 2336 | -2.38% | -8.30%, 3.53% |
| Lag 1h | 2545 | -1.78% | -5.41%, 1.85% | 2545 | -1.70% | -5.87%, 2.48% | 2268 | -2.18% | -6.21%, 1.85% | 2324 | -2.15% | -7.27%, 2.96% |
| Lag 2h | 2546 | -2.20% | -5.31%, 0.91% | 2546 | -2.23% | -6.3%, 1.86% | 2274 | -3.14% | -7.25%, 0.99% | 2312 | -1.35% | -6.00%, 3.32% |
| Lag 3h | 2548 | -2.46%# | -5.31%, 0.40% | 2548 | -2.53% | -6.4%, 1.34% | 2280 | -4.01%# | -8.19%, 0.16% | 2308 | -1.81% | -6.26%, 2.66% |
| Lag 4h | 2549 | -5.87%** | -9.46%, -2.29% | 2549 | -3.61%# | -7.41%, 0.18% | 2284 | -4.82%* | -9.03%, -0.62% | 2306 | -3.16% | -7.53%, 1.22% |
| Lag 5h | 2549 | -2.39% | -6.09%, 1.31% | 2549 | -1.89% | -5.59%, 1.82% | 2289 | -5.65%** | -9.92%, -1.36% | 2303 | -1.55% | -6.12%, 3.01% |
| Lag 6h | 2549 | -1.90% | -5.03%, 1.22% | 2549 | -2.18% | -5.78%, 1.43% | 2292 | -4.45%* | -8.71%, -0.19% | 2299 | -2.56% | -7.59%, 2.47% |
| **T-wave complexity (%)** | | | | | | | | | | | | |
| Concurrent | 2565 | -1.92% | -7.19%, 3.32% | 2565 | -0.11% | -6.07%, 5.85% | 2286 | -1.36% | -6.93%, 4.21% | 2354 | -1.20% | -9.53%, 7.15% |
| Lag 1h | 2565 | -3.25% | -8.26%, 1.76% | 2565 | -0.32% | -6.17%, 5.53% | 2293 | 0.81% | -4.81%, 6.44% | 2343 | -1.61% | -8.81%, 5.57% |
| Lag 2h | 2566 | -0.47% | -4.80%, 3.86% | 2566 | -1.24% | -6.93%, 4.47% | 2299 | -0.08% | -5.81%, 5.66% | 2332 | -1.08% | -7.56%, 5.41% |
| Lag 3h | 2568 | 0.07% | -3.91%, 4.05% | 2568 | -0.65% | -6.12%, 4.81% | 2304 | -0.62% | -6.46%, 5.24% | 2327 | 0.36% | -5.79%, 6.51% |
| Lag 4h | 2569 | -0.68% | -5.66%, 4.33% | 2569 | -0.83% | -6.14%, 4.49% | 2308 | 0.49% | -5.39%, 6.34% | 2325 | 0.69% | -5.44%, 6.82% |
| Lag 5h | 2569 | -4.94%# | -10.11%, 0.23% | 2569 | -3.02% | -8.22%, 2.16% | 2313 | 0.86% | -5.10%, 6.83% | 2323 | 0.48% | -5.97%, 6.92% |
| Lag 6h | 2569 | -4.73%* | -9.08%, -0.37% | 2569 | -3.22% | -8.28%, 1.86% | 2316 | 0.44% | -5.45%, 6.33% | 2319 | -1.81% | -8.88%, 5.24% |

# $P < 0.10$; * $P < 0.05$; ** $P < 0.01$

**APPENDIX K.** Percent change in hourly UPDIABETES ECG outcomes associated with each 9,812,327 p/cm$^3$ increase in concurrent and lagged total PNCs

| Time of Total Particle Count Exposure | Time of Holter Monitor Recording | *N* | % Change | 95% CI |
|---|---|---|---|---|
| **SDNN (ms)** | | | | |
| Hour 1 | Hour 1 of Exposure | 34 | 0.60% | -8.02%,9.22% |
| Hours 1 & 2 | Hour 2 of Exposure | 34 | 0.69% | -7.82%,9.20% |
| Hours 1 & 2 | Lag 1h | 34 | -13.22%* | -24.11%,-2.33% |
| Hours 1 & 2 | Lag 2h | 33 | 11.67% | -3.84%,27.17% |
| Hours 1 & 2 | Lag 3h | 33 | -0.65% | -12.15%,10.85% |
| Hours 1 & 2 | Lag 4h | 33 | -13.75%# | -27.75%,0.25% |
| Hours 1 & 2 | Lag 5h | 33 | 0.93% | -9.23%,11.08% |
| Hours 1 & 2 | Lag 6h | 22 | 6.66% | -11.98%,25.29% |
| **RMSSD (ms)** | | | | |
| Hour 1 | Hour 1 of Exposure | 34 | 8.11% | -6.06%,22.27% |
| Hours 1 & 2 | Hour 2 of Exposure | 34 | 8.12% | -5.86%,22.10% |
| Hours 1 & 2 | Lag 1h | 34 | -1.44% | -15.58%,12.71% |
| Hours 1 & 2 | Lag 2h | 33 | -6.52% | -25.36%,12.32% |
| Hours 1 & 2 | Lag 3h | 33 | 12.36% | -7.50%,32.21% |
| Hours 1 & 2 | Lag 4h | 33 | 9.32% | -26.92%,45.55% |
| Hours 1 & 2 | Lag 5h | 33 | 7.19% | -8.32%,22.70% |
| Hours 1 & 2 | Lag 6h | 22 | 3.42% | -41.08%,47.92% |
| **T-wave complexity (%)** | | | | |
| Hour 1 | Hour 1 of Exposure | 34 | 17.59% | -10.63%,45.80% |
| Hours 1 & 2 | Hour 2 of Exposure | 34 | 17.21% | -10.70%,45.11% |
| Hours 1 & 2 | Lag 1h | 34 | 4.81% | -10.95%,20.57% |
| Hours 1 & 2 | Lag 2h | 33 | -12.14% | -28.70%,4.43% |
| Hours 1 & 2 | Lag 3h | 33 | -21.06% | -56.01%,13.89% |
| Hours 1 & 2 | Lag 4h | 33 | -0.32% | -29.24%,28.61% |
| Hours 1 & 2 | Lag 5h | 33 | -6.03% | -19.53%,7.47% |
| Hours 1 & 2 | Lag 6h | 22 | -0.44% | -15.19%,14.31% |
| **NN (ms)** | | | | |
| Hour 1 | Hour 1 of Exposure | 34 | -0.77% | -3.04%,1.49% |
| Hours 1 & 2 | Hour 2 of Exposure | 34 | -0.75% | -2.99%,1.49% |
| Hours 1 & 2 | Lag 1h | 34 | 0.75% | -1.35%,2.84% |
| Hours 1 & 2 | Lag 2h | 33 | -0.26% | -4.40%,3.89% |
| Hours 1 & 2 | Lag 3h | 33 | 1.18% | -3.63%,5.99% |
| Hours 1 & 2 | Lag 4h | 33 | -0.31% | -5.22%,4.60% |
| Hours 1 & 2 | Lag 5h | 33 | -0.32% | -2.10%,1.45% |
| Hours 1 & 2 | Lag 6h | 22 | -0.08% | -2.75%,2.60% |

# $P < 0.10$; * $P < 0.05$; ** $P < 0.01$

**APPENDIX L.** Percent change in hourly UPCON ECG outcomes associated with each 235,429 p/cm$^3$ increase in concurrent and lagged total PNCs

| Time of Total Particle Count Exposure | Time of Holter Monitor Recording | *N* | % Change | 95% CI |
|---|---|---|---|---|
| **SDNN (ms)** | | | | |
| Hour 1 | Hour 1 of Exposure | 30 | 0.16% | -10.09%,10.41% |
| Hours 1 & 2 | Hour 2 of Exposure | 30 | 12.90% | -17.04%,42.84% |
| Hours 1 & 2 | Lag 1h | 30 | 27.62% | -19.07%,74.32% |
| Hours 1 & 2 | Lag 2h | 28 | 17.34% | -22.36%,57.05% |
| Hours 1 & 2 | Lag 3h | 31 | 8.93% | -19.28%,37.15% |
| Hours 1 & 2 | Lag 4h | 32 | 2.28% | -23.02%,27.58% |
| Hours 1 & 2 | Lag 5h | 32 | 20.06%# | -1.63%,41.75% |
| Hours 1 & 2 | Lag 6h | 33 | 0.01% | -18.78%,18.81% |
| **RMSSD (ms)** | | | | |
| Hour 1 | Hour 1 of Exposure | 30 | 20.58% | -17.69%,58.85% |
| Hours 1 & 2 | Hour 2 of Exposure | 30 | -0.34% | -83.47%,82.79% |
| Hours 1 & 2 | Lag 1h | 30 | 76.22%# | -9.75%,162.18% |
| Hours 1 & 2 | Lag 2h | 28 | 18.18% | -53.11%,89.47% |
| Hours 1 & 2 | Lag 3h | 31 | 25.10% | -20.65%,70.86% |
| Hours 1 & 2 | Lag 4h | 32 | 13.28% | -11.85%,38.40% |
| Hours 1 & 2 | Lag 5h | 32 | 14.07% | -13.29%,41.42% |
| Hours 1 & 2 | Lag 6h | 33 | 8.24% | -13.52%,30.01% |
| **T-wave complexity (%)** | | | | |
| Hour 1 | Hour 1 of Exposure | 30 | -15.12% | -35.49%,5.26% |
| Hours 1 & 2 | Hour 2 of Exposure | 30 | -15.52% | -51.69%,20.65% |
| Hours 1 & 2 | Lag 1h | 30 | -9.47% | -53.00%,34.06% |
| Hours 1 & 2 | Lag 2h | 28 | -11.44% | -51.88%,29.00% |
| Hours 1 & 2 | Lag 3h | 31 | -23.14% | -60.41%,14.12% |
| Hours 1 & 2 | Lag 4h | 31 | -22.99%* | -44.07%,-1.91% |
| Hours 1 & 2 | Lag 5h | 31 | -12.47% | -35.96%,11.03% |
| Hours 1 & 2 | Lag 6h | 33 | -5.75% | -27.50%,16.00% |
| **NN (ms)** | | | | |
| Hour 1 | Hour 1 of Exposure | 30 | 2.24% | -3.40%,7.88% |
| Hours 1 & 2 | Hour 2 of Exposure | 30 | -3.12% | -15.50%,9.27% |
| Hours 1 & 2 | Lag 1h | 30 | 0.77% | -13.43%,14.96% |
| Hours 1 & 2 | Lag 2h | 28 | 1.92% | -8.42%,12.26% |
| Hours 1 & 2 | Lag 3h | 31 | 5.47% | -4.40%,15.35% |
| Hours 1 & 2 | Lag 4h | 32 | 5.31% | -2.85%,13.47% |
| Hours 1 & 2 | Lag 5h | 32 | 5.90% | -2.75%,14.54% |
| Hours 1 & 2 | Lag 6h | 33 | 0.58% | -7.78%,8.94% |

# $P < 0.10$; * $P < 0.05$; ** $P < 0.01$

**APPENDIX M.** Percent change in 5-minute mean ECG outcomes associated with each IQR increase in concurrent and lagged 5-minute personal UFP concentrations in the Augsburg study

| | Individuals with type-2 diabetes or impaired glucose tolerance (Diabetes + IGT) | | Individuals with potential genetic predisposition (Genetic Susceptibility) | |
|---|---|---|---|---|
| | Personal UFP IQR = 16,047 particles/cm$^3$ | | Personal UFP IQR = 16,047 particles/cm$^3$ | |
| **Pollutant averaging time** | **% Change** | **95% confidence interval** | **% Change** | **95% confidence interval** |
| **SDNN (ms)** | | | | |
| Concurrent 5-minutes | -0.62% | (-1.09%, -0.16%)** | -0.93% | (-1.40%, -0.46%)** |
| Minutes 0-4 | 0.31% | (-0.16%, 0.77%) | -0.21% | (-0.68%, 0.27%) |
| Minutes 5-9 | -0.03% | (-0.50%, 0.44%) | -0.45% | (-0.92%, 0.02%)# |
| Minutes 10-14 | -0.21% | -0.68%, 0.26%) | -0.50% | (-0.98%, -0.03%)* |
| Minutes 15-19 | 0.05% | (-0.43%, 0.52%) | -0.46% | (-0.93%, 0.01%)# |
| Minutes 20-24 | -0.02% | (-0.49%, 0.46%) | -0.49% | (-0.97%, -0.02%)* |
| Minutes 25-29 | 0.16% | (-0.32%, 0.63%) | -0.35% | (-0.82%, 0.13%) |
| **RMSSD (ms)** | | | | |
| Concurrent 5-minutes | -0.13% | (-0.74%, 0.49%) | -0.95% | (-1.48%, -0.43%)** |
| Minutes 0-4 | 0.07% | (-0.55%, 0.69%) | -0.05% | (-0.58%, 0.49%) |
| Minutes 5-9 | 0.16% | (-0.47%, 0.78%) | -0.50% | (-1.03%, 0.03%)# |
| Minutes 10-14 | -0.07% | (-0.69%, 0.55%) | -0.59% | (-1.12%, -0.06%)* |
| Minutes 15-19 | -0.16% | (-0.78%, 0.47%) | -0.46% | (-0.99%, 0.07%)* |
| Minutes 20-24 | 0.29% | (-0.34%, 0.92%) | -0.71% | (-1.23%, -0.18%)** |
| Minutes 25-29 | 0.58% | (-0.05%, 1.22%)# | -0.21% | (-0.74%, 0.32%) |
| **T-Wave complexity (%)** | | | | |
| Concurrent 5-minutes | -0.24% | (-0.48%, 0.01%)# | -0.18% | (-0.43%, 0.07%) |
| Minutes 0-4 | 0.28% | (0.03%, 0.52%)* | 0.14% | (-0.11%, 0.39%) |
| Minutes 5-9 | 0.32% | (0.07%, 0.56%)* | -0.17% | (-0.42%, 0.08%) |
| Minutes 10-14 | 0.29% | (0.04%, 0.54%)* | 0.15% | (-0.10%, 0.40%) |
| Minutes 15-19 | 0.08% | (-0.17%, 0.33%) | 0.18% | (-0.07%, 0.42%) |
| Minutes 20-24 | 0.01% | (-0.24%, 0.26%) | 0.13% | (-0.12%, 0.38%) |
| Minutes 25-29 | 0.40% | (0.14%, 0.65%)** | 0.04% | (-0.21%, 0.29%) |
| **HR (beats/min)** | | | | |
| Concurrent 5-minutes | -0.05% | (-0.17%, 0.08%) | 0.00% | (-0.14%, 0.14%) |
| Minutes 0-4 | 0.23% | (0.10%, 0.36%)** | 0.03% | (-0.11%, 0.17%) |
| Minutes 5-9 | 0.16% | (0.04%, 0.29%)* | 0.13% | (-0.01%, 0.27%)# |
| Minutes 10-14 | 0.00% | (-0.13%, 0.12%) | 0.13% | (0.00%, 0.27%)# |
| Minutes 15-19 | 0.02% | (-0.10%, 0.15%) | 0.08% | (-0.06%, 0.21%) |
| Minutes 20-24 | 0.08% | (-0.04%, 0.21%) | 0.09% | (-0.05%, 0.22%) |
| Minutes 25-29 | 0.10% | (-0.03%, 0.22%) | 0.09% | (-0.05%, 0.22%) |

# $P < 0.10$; * $P < 0.05$; ** $P < 0.01$

**APPENDIX N.** Percent change in 5-minute mean ECG outcomes associated with each IQR increase in 5-minute mean total PNCs in the UPDIABETES and UPCON studies

**(a) UPDIABETES Study**

| Outcome | *N* | % Change | 95% confidence interval |
|---|---|---|---|
| **SDNN (msec)** | | | |
| Minutes 0-4 | 363 | -3.38% | -10.24%,3.48% |
| Minutes 5-9 | 363 | 2.39% | -6.47%,11.25% |
| Minutes 10-14 | 363 | 5.13% | -3.99%,14.24% |
| Minutes 15-19 | 363 | 5.41% | -3.66%,14.48% |
| Minutes 20-24 | 363 | 5.57% | -3.36%,14.51% |
| Minutes 25-29 | 363 | 2.28% | -6.37%,10.94% |
| Minutes 30-34 | 363 | -5.83% | -13.60%,1.95% |
| Minutes 35-39 | 363 | -10.00%** | -17.20%,-2.81% |
| Minutes 40-44 | 363 | -5.29% | -13.08%,2.50% |
| Minutes 45-49 | 363 | 1.67% | -6.91%,10.24% |
| Minutes 50-54 | 363 | 3.09% | -5.49%,11.67% |
| Minutes 55-59 | 363 | 5.05% | -3.45%,13.56% |
| **RMSSD (msec)** | | | |
| Minutes 0-4 | 362 | 3.01% | -2.38%,8.41% |
| Minutes 5-9 | 362 | 3.41% | -2.34%,9.15% |
| Minutes 10-14 | 362 | 3.88% | -2.00%,9.76% |
| Minutes 15-19 | 362 | 5.81%# | -0.83%,12.46% |
| Minutes 20-24 | 362 | 7.57%* | 0.83%,14.30% |
| Minutes 25-29 | 362 | 8.59%* | 1.76%,15.41% |
| Minutes 30-34 | 362 | 10.05%** | 3.23%,16.86% |
| Minutes 35-39 | 362 | 12.82%** | 6.09%,19.54% |
| Minutes 40-44 | 362 | 13.24%** | 6.66%,19.82% |
| Minutes 45-49 | 362 | 10.35%** | 4.48%,16.22% |
| Minutes 50-54 | 362 | 6.63%* | 0.64%,12.61% |
| Minutes 55-59 | 363 | 5.70%# | -0.62%,12.02% |

| **T-wave complexity (%)** | | | |
|---|---|---|---|
| Minutes 0-4 | 363 | 18.31%** | 10.48%,26.15% |
| Minutes 5-9 | 363 | 20.68%** | 11.48%,29.89% |
| Minutes 10-14 | 363 | 21.11%** | 11.86%,30.36% |
| Minutes 15-19 | 363 | 20.47%** | 11.21%,29.74% |
| Minutes 20-24 | 363 | 19.38%** | 9.87%,28.89% |
| Minutes 25-29 | 363 | 20.86%** | 11.14%,30.59% |
| Minutes 30-34 | 363 | 19.86%** | 10.00%,29.73% |
| Minutes 35-39 | 363 | 12.96%** | 4.08%,21.83% |
| Minutes 40-44 | 363 | 14.28%** | 5.42%,23.14% |
| Minutes 45-49 | 363 | 18.77%** | 9.94%,27.60% |
| Minutes 50-54 | 363 | 18.94%** | 10.17%,27.72% |
| Minutes 55-59 | 363 | 17.46%** | 9.57%,25.36% |

| **NN (msec)** | N | % Change | 95% CI |
|---|---|---|---|
| Minutes 0-4 | 363 | -0.62% | -1.35%,0.12% |
| Minutes 5-9 | 363 | -0.84%# | -1.70%,0.01% |
| Minutes 10-14 | 363 | -1.16%* | -2.08%,-0.24% |
| Minutes 15-19 | 363 | -0.81% | -1.85%,0.24% |
| Minutes 20-24 | 363 | -0.44% | -1.56%,0.68% |
| Minutes 25-29 | 363 | -0.02% | -1.16%,1.12% |
| Minutes 30-34 | 363 | 0.63% | -0.49%,1.75% |
| Minutes 35-39 | 363 | 1.08%# | -0.02%,2.18% |
| Minutes 40-44 | 363 | 0.80% | -0.34%,1.94% |
| Minutes 45-49 | 363 | -0.07% | -1.22%,1.07% |
| Minutes 50-54 | 363 | -0.49% | -1.66%,0.68% |
| Minutes 55-59 | 363 | -0.47% | -1.63%,0.70% |

**(B) UPCON Study**

| Response | Number of minutes between exposure and response | *N* | % Change | 95% CI |
|---|---|---|---|---|
| **SDNN (msec)** Mean = 65 | 0-4 | 368 | 1.51% | -0.39%,3.41% |
| | 5-9 | 404 | 2.60%* | 0.53%,4.68% |
| | 10-14 | 404 | 2.22%* | 0.19%,4.25% |
| | 15-19 | 404 | 2.40%* | 0.41%,4.40% |
| | 20-24 | 404 | 3.05%** | 1.06%,5.05% |
| | 25-29 | 404 | 3.23%** | 1.30%,5.17% |
| | 30-34 | 404 | 3.38%** | 1.47%,5.28% |
| | 35-39 | 403 | 3.50%** | 1.54%,5.46% |
| | 40-44 | 402 | 4.25%** | 2.30%,6.20% |
| | 45-49 | 400 | 4.62%** | 2.70%,6.54% |
| | 50-54 | 398 | 4.23%** | 2.24%,6.23% |
| | 55-59 | 396 | 3.60%** | 1.58%,5.62% |
| **RMSSD (msec)** Mean = 34 | 0-4 | 368 | 0.70% | -1.72%,3.12% |
| | 5-9 | 404 | 1.57% | -0.72%,3.86% |
| | 10-14 | 404 | 1.14% | -1.13%,3.41% |
| | 15-19 | 404 | 1.48% | -0.74%,3.71% |
| | 20-24 | 404 | 2.35%* | 0.11%,4.58% |
| | 25-29 | 404 | 4.13%** | 1.65%,6.61% |
| | 30-34 | 404 | 3.61%** | 1.12%,6.11% |
| | 35-39 | 403 | 3.48%** | 1.00%,5.97% |
| | 40-44 | 401 | 3.06%* | 0.40%,5.72% |
| | 45-49 | 399 | 3.93%** | 1.29%,6.58% |
| | 50-54 | 397 | 3.57%* | 0.73%,6.41% |
| | 55-59 | 395 | 3.31%* | 0.27%,6.35% |
| **T-wave complexity (%)** Mean = 17 | 0-4 | 360 | -3.92%** | -5.70%,-2.13% |
| | 5-9 | 394 | -3.29%** | -5.18%,-1.41% |
| | 10-14 | 394 | -4.03%** | -5.88%,-2.18% |
| | 15-19 | 394 | -4.17%** | -6.02%,-2.33% |
| | 20-24 | 394 | -4.30%** | -6.15%,-2.45% |
| | 25-29 | 394 | -4.24%** | -6.07%,-2.41% |
| | 30-34 | 395 | -4.50%** | -6.35%,-2.65% |
| | 35-39 | 395 | -4.64%** | -6.51%,-2.77% |
| | 40-44 | 395 | -4.89%** | -6.86%,-2.91% |
| | 45-49 | 395 | -5.04%** | -7.10%,-2.97% |
| | 50-54 | 395 | -5.38%** | -7.43%,-3.33% |

| | | | | |
|---|---|---|---|---|
| | 55-59 | 394 | -5.48%** | -7.51%,-3.45% |
| **NN (msec)** Mean = 839 | 0-4 | 368 | -0.05% | -0.50%,0.41% |
| | 5-9 | 404 | 0.29% | -0.14%,0.72% |
| | 10-14 | 404 | 0.41%# | -0.02%,0.83% |
| | 15-19 | 404 | 0.36%# | -0.07%,0.78% |
| | 20-24 | 404 | 0.46%* | 0.04%,0.88% |
| | 25-29 | 404 | 0.80%** | 0.38%,1.22% |
| | 30-34 | 404 | 0.73%** | 0.31%,1.16% |
| | 35-39 | 403 | 0.75%** | 0.32%,1.18% |
| | 40-44 | 402 | 0.84%** | 0.40%,1.28% |
| | 45-49 | 400 | 0.78%** | 0.32%,1.25% |
| | 50-54 | 398 | 0.76%** | 0.28%,1.24% |
| | 55-59 | 396 | 0.71%** | 0.22%,1.20% |

# $P < 0.10$; * $P < 0.05$; ** $P < 0.01$

## APPENDIX O. Effect Modification by Total Antioxidant Capacity

**Results:** We hypothesized that the decrease in SDNN and RMSSD and the increase in T-wave complexity associated with increased $PM_{2.5}$ concentration would be larger for those subject-visits where the TAC levels are below the median compared with those subject-visits where the TAC levels are above the median. In the Augsburg Panel Study, we did not observe larger reductions in SDNN or RMSSD or larger increases in T-wave complexity associated with each IQR increase in $PM_{2.5}$ for those with TAC levels below the median compared with those with TAC levels above the median (Table O.1 below). Further, none were significantly different. Similarly, we did not find any significant effect modification of the change in outcome associated with increased $PM_{2.5}$ concentration by TAC level in the Rochester REHAB Study (Table O.1 below). Therefore, we concluded that there was “No association or agreement” and that this hypothesis was not confirmed (Table 9 in main report).

**Table O.1.** Percent change in each outcome associated with each IQR increase in mean $PM_{2.5}$ concentration (Augsburg; lagged 2h: 12.3 μg/$m^3$; Rochester; lagged 4 hours: 7.6 μg/$m^3$) by study/group

| Outcome | % Change | 95% Confidence Interval | % Change | 95% Confidence Interval | Interaction term *P*-value |
|---|---|---|---|---|---|
| | | **Effect modification by total antioxidant capacity** | | | |
| **AUGSBURG PANEL STUDY: DIABETES/IGT GROUP** | | | | | |
| | ***≤ Median (0.54 mmol/l)*** | | ***> Median (0.54 mmol/l)*** | | |
| SDNN | -3.95% | (-8.04%, 0.13%) | -5.06% | (-8.95%, -1.17%) | 0.70 |
| RMSSD | -1.88% | (-9.24%, 6.07%) | -2.73% | (-10.35%, 5.53%) | 0.88 |
| T-wave complexity | -1.24% | (-4.82%, 2.47%) | 0.44% | (-3.28%, 4.30%) | 0.53 |
| **AUGSBURG PANEL STUDY: GENETIC SUSCEPTIBILITY GROUP** | | | | | |
| | ***≤ Median (0.54 mmol/l)*** | | ***> Median (0.54 mmol/l)*** | | |
| SDNN | -3.82% | (-7.98%, 0.33%) | 3.25% | (-7.94%, 1.44%) | 0.85 |
| RMSSD | -4.14% | (-9.55%, 1.59%) | -0.17% | (7.10%, 7.28%) | 0.38 |
| T-wave complexity | -0.37% | (-3.38%, 2.74%) | -1.31% | (-4.85%, 2.36%) | 0.69 |
| **ROCHESTER REHAB STUDY** | | | | | |
| | ***≤ Median (0.62)*** | | ***> Median (0.62)*** | | |
| SDNN | -1.94% | (-6.65%, 2.76%) | -0.23% | (-5.26%, 4.81%) | 0.60 |
| RMSSD | 1.54% | (-5.26%, 8.34%) | -6.81%# | (-14.14%, 0.52%) | 0.08 |
| T-wave complexity | -3.00% | (-12.32%, 6.33%) | -4.55% | (-14.41%, 5.32%) | 0.81 |

**APPENDIX P.** Sensitivity analyses: Percent change in SDNN associated with each IQR increase in 2- and 3-hour lagged concentrations of UFP (IQR: 7157 particles/cm$^3$), $PM_{2.5}$ (IQR: 12.3 µg/m$^3$), or BC (IQR: 1.2 µg/m$^3$) in the Augsburg study.

**a)** Individuals with type-2 diabetes or impaired glucose tolerance (Diab + IGT)

| Pollutant and Lag | Main Model Fixed set of confounders, trend smooth, and AR(1) as covariance structure | | Model #1 Confounders chosen by AIC | | Model #2 Trend as polynomial of 4$^{th}$ degree | | Model #3 Fixed participant effect | | Model #4 Compound Symmetry as covariance structure | | Model #5 Lagged outcome and Compound Symmetry as covariance structure | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % Change | 95% confidence interval | % Change | 95% confidence interval | % Change | 95% confidence interval | % Change | 95% confidence interval | % Change | 95% confidence interval | % Change | 95% confidence interval |
| **UFP** Lag 2h | -2.11 | -3.65,-0.58** | -1.93 | -3.42,-0.43* | -2.18 | -3.71,-0.64** | -2.11 | -3.55,-0.66** | -2.33 | -3.88,-0.78** | -1.28 | -2.81,0.25 |
| **$PM_{2.5}$** Lag 2h | -4.59 | -7.44,-1.75** | -4.33 | -7.06,-1.59** | -4.77 | -7.64,-1.90** | -5.00 | -7.67,-2.33** | -4.64 | -7.62,-1.66** | -3.09 | -5.82,-0.37* |
| **BC** Lag 2h | -3.97 | -5.77,-2.16** | -3.73 | -5.48,-1.98** | -3.96 | -5.77,-2.15** | -4.07 | -5.75,-2.39** | -4.16 | -6.02,-2.29** | -2.50 | -4.36,-0.64** |

**b)** Individuals with a potential genetic predisposition (Gen susc)

| Pollutant and Lag | Main Model Fixed set of confounders, trend smooth, and AR(1) as covariance structure | | Model #1 Confounders chosen by AIC | | Model #2 Trend as polynomial of 4$^{th}$ degree | | Model #3 Fixed participant effect | | Model #4 Compound Symmetry as covariance structure | | Model #5 Lagged outcome and Compound Symmetry as covariance structure | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | % Change | 95% confidence interval | % Change | 95% confidence interval | % Change | 95% confidence interval | % Change | 95% confidence interval | % Change | 95% confidence interval | % Change | 95% confidence interval |
| **UFP** Lag 3h | -2.26 | -3.98,-0.53* | -1.71 | -3.45,0.03# | -2.34 | -4.07, -0.61** | -2.16 | -3.76, -0.55** | -2.71 | -4.36,-1.06** | 0.28 | -1.12,1.68 |
| **$PM_{2.5}$** Lag 2h | -3.34 | -6.57,-0.12* | -3.04 | -6.10,0.01# | -3.24 | -6.49,0.01# | -3.00 | -6.03,0.04# | -3.73 | -6.89,-0.56* | -1.07 | -3.59,1.45 |
| **BC** Lag 3h | -2.69 | -4.45, -0.92** | -2.01 | -3.76, -0.26* | -2.90 | -4.72, -1.08** | -2.53 | -4.19, -0.89** | -3.24 | -4.96,-1.52** | -0.52 | -1.98,0.94 |

# $P < 0.10$; * $P < 0.05$; ** $P < 0.01$

**APPENDIX Q**. Sensitivity Analyses

**Table 1.** Percent change in SDNN associated with each IQR increase in concurrent hour and 1- to 6-hour lagged air pollutant concentrations in the REHAB study for various model specifications.

| Pollutant and Lag | Model #1 | | Model #2 | | Model #3 | | Model #4 | | Main Analysis | |
|---|---|---|---|---|---|---|---|---|---|---|
| | β | 95% CI | β | 95% CI | β | 95% CI | β | 95% CI | β | 95% CI |
| **UFP** | | | | | | | | | | |
| Concurrent | -0.29 | -1.29,0.71 | -1.06 | -2.38,0.26 | -0.48 | -1.42,0.46 | -0.46 | -1.56,0.65 | -0.61 | -1.70,0.47 |
| Lag 1h | -0.89# | -1.86,0.09 | -2.63** | -4.02,-1.23 | -1.22** | -2.10,-0.33 | -1.15* | -2.21,-0.09 | -1.15* | -2.19,-0.11 |
| Lag 2h | -0.68 | -1.51,0.14 | -1.09* | -2.09,-0.09 | -0.65 | -1.46,0.16 | -0.62 | -1.52,0.28 | -0.49 | -1.38,0.40 |
| Lag 3h | -0.66# | -1.45,0.12 | -1.24* | -2.37,-0.12 | -0.44 | -1.11,0.23 | -0.41 | -1.22,0.40 | -0.25 | -1.07,0.56 |
| Lag 4h | -1.28** | -2.26,-0.31 | -1.80* | -3.57,-0.04 | -0.87** | -1.50,-0.25 | -0.83# | -1.76,0.11 | -0.71 | -1.73,0.32 |
| Lag 5h | -0.62 | -1.65,0.40 | -0.25 | -1.43,0.92 | -0.41 | -1.13,0.30 | -0.39 | -1.47,0.69 | -0.24 | -1.30,0.83 |
| Lag 6h | -0.11 | -0.98,0.77 | -0.04 | -1.20,1.12 | -0.04 | -0.79,0.71 | -0.04 | -0.95,0.88 | -0.02 | -0.92,0.87 |
| **AMP** | | | | | | | | | | |
| Concurrent | -1.49* | -2.90,-0.07 | -3.12** | -5.17,-1.07 | -2.03# | -4.14,0.08 | -1.95* | -3.59,-0.32 | -1.79* | -3.41,-0.17 |
| Lag 1h | -1.65* | -3.04,-0.27 | -3.49** | -5.53,-1.45 | -2.09* | -3.99,-0.19 | -2.01* | -3.62,-0.41 | -1.78* | -3.37,-0.19 |
| Lag 2h | -1.77** | -3.12,-0.42 | -3.50** | -5.44,-1.56 | -2.22* | -3.99,-0.45 | -2.14** | -3.69,-0.58 | -1.75* | -3.30,-0.20 |
| Lag 3h | -1.86** | -3.16,-0.57 | -3.62** | -5.47,-1.77 | -2.12** | -3.63,-0.60 | -2.04** | -3.52,-0.55 | -1.71* | -3.19,-0.24 |
| Lag 4h | -1.81** | -3.08,-0.54 | -3.14** | -4.99,-1.29 | -2.15** | -3.62,-0.69 | -2.07** | -3.51,-0.62 | -1.75* | -3.19,-0.31 |
| Lag 5h | -1.59* | -2.83,-0.35 | -2.69** | -4.45,-0.92 | -2.00** | -3.18,-0.82 | -1.92** | -3.34,-0.51 | -1.57* | -2.97,-0.16 |
| Lag 6h | -1.32* | -2.53,-0.10 | -2.27* | -4.03,-0.51 | -1.69** | -2.82,-0.55 | -1.62* | -3.01,-0.23 | -1.28# | -2.66,0.09 |
| **$PM_{2.5}$** | | | | | | | | | | |
| Concurrent | -0.89 | -2.34,0.57 | -1.00 | -3.15,1.16 | -1.35 | -3.07,0.36 | -1.30 | -2.97,0.37 | -1.23 | -2.89,0.44 |
| Lag 1h | -0.64 | -2.11,0.84 | -0.82 | -2.99,1.36 | -0.88 | -2.77,1.01 | -0.84 | -2.53,0.85 | -0.71 | -2.39,0.97 |
| Lag 2h | -1.17 | -2.68,0.33 | -1.97# | -4.22,0.28 | -1.52 | -3.35,0.30 | -1.46# | -3.19,0.27 | -1.30 | -3.01,0.42 |
| Lag 3h | -1.53* | -3.05,-0.01 | -1.70 | -3.94,0.54 | -1.98* | -3.96,-0.00 | -1.90* | -3.66,-0.14 | -1.74# | -3.49,0.00 |
| Lag 4h | -1.35# | -2.87,0.17 | -1.28 | -3.54,0.99 | -1.92# | -4.13,0.29 | -1.84* | -3.61,-0.07 | -1.75# | -3.51,0.00 |
| Lag 5h | -1.47# | -3.01,0.07 | -1.33 | -3.65,1.00 | -2.51* | -4.76,-0.25 | -2.40** | -4.20,-0.60 | -2.13* | -3.91,-0.35 |
| Lag 6h | -1.27 | -2.80,0.27 | -1.01 | -3.28,1.25 | -2.27* | -4.45,-0.09 | -2.17* | -3.96,-0.38 | -2.00* | -3.77,-0.23 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| **BC** | | | | | | | | | | |
| Concurrent | 2.19* | 0.09,4.29 | -0.15 | -3.05, 2.75 | -0.20 | -2.10,1.69 | -0.49 | -2.94,1.96 | -0.21 | -2.64,2.21 |
| Lag 1h | 2.18* | 0.40,3.96 | -0.38 | -2.87, 2.10 | 0.10 | -1.54,1.75 | -0.07 | -2.18,2.03 | 0.10 | -1.97,2.17 |
| Lag 2h | 0.94 | -0.67,2.55 | -2.02# | -4.38, 0.34 | -0.66 | -2.37,1.05 | -0.67 | -2.58,1.24 | -0.66 | -2.55,1.22 |
| Lag 3h | -0.23 | -1.77,1.30 | -1.80 | -4.04, 0.44 | -0.42 | -2.02,1.18 | -0.64 | -2.45,1.18 | -0.42 | -2.22,1.38 |
| Lag 4h | -1.53* | -3.04,-0.02 | -3.15** | -5.43, -0.88 | -1.03 | -2.42,0.36 | -1.36 | -3.16,0.43 | -1.03 | -2.81,0.74 |
| Lag 5h | -2.12** | -3.71,-0.53 | -3.45** | -5.82, -1.08 | -0.95 | -2.45,0.54 | -1.27 | -3.11,0.58 | -0.96 | -2.81,0.89 |
| Lag 6h | -2.04* | -3.81,-0.27 | -2.23 | -4.89, 0.43 | -1.27 | -3.10,0.57 | -1.25 | -3.30,0.80 | -1.27 | -3.30,0.76 |

# $P<0.10$; * $P<0.05$; **$P<0.01$

Model #1: Additional variance term added to estimate the variance across multiple measures within the same study subject
Model #2: First hour of clinic visit only
Model #3: Generalized estimating equations used
Model #4: Main analysis, but relative humidity modeled with just a linear term

**Table 2.** Percent change in ECG outcomes associated with each IQR increase in pollutant concentrations in the REHAB and Augsburg studies when using covariates in Model A and covariates in Model B.

| | **Rochester REHAB** | | | **Rochester REHAB** | | | **Augsburg Panel Study** *Type 2 diabetes or impaired glucose tolerance* | | | **Augsburg Panel Study** *Genetic susceptibility* | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | **MODEL A Covariates†** | | | **MODEL B Covariates‡** | | | **MODEL B Covariates‡** | | | **MODEL B Covariates‡** | | |
| | ***N*** | **% Change** | **95% CI** | ***N*** | **% Change** | **95% CI** | ***N*** | **% Change** | **95% CI** | ***N*** | **% Change** | **95% CI** |
| **SDNN (ms) and UFP** | **UFP IQR = 3058 particles/cm$^3$** | | | **UFP IQR = 3058 particles/cm$^3$** | | | **UFP IQR = 7157 particles/cm$^3$** | | | **UFP IQR = 7157 particles/cm$^3$** | | |
| Concurrent | 2536 | -0.61% | -1.70%,0.47% | 2536 | -0.05% | -1.21%, 1.11% | 1158 | 1.44%# | -0.22%, 3.10% | 782 | 1.92%* | 0.19%, 3.65% |
| Lag 1h | 2536 | -1.15%* | -2.19%,-0.11% | 2536 | -0.74% | -1.85%, 0.38% | 1160 | 0.04% | -1.56%, 1.65% | 778 | 0.17% | -1.59%, 1.92% |
| Lag 2h | 2537 | -0.49% | -1.38%,0.40% | 2537 | -0.60% | -1.55%, 0.36% | 1162 | -2.11%** | -3.65%, -0.58% | 772 | -1.49%# | -3.24%, 0.26% |
| Lag 3h | 2539 | -0.25% | -1.07%,0.56% | 2539 | -0.52% | -1.39%, 0.36% | 1167 | -1.98%** | -3.47%, -0.50% | 764 | -2.26%* | -3.98%, -0.53% |
| Lag 4h | 2540 | -0.71% | -1.73%,0.32% | 2540 | -1.19%* | -2.29%, -0.10% | 1166 | -1.95%* | -3.45%, -0.45% | 756 | -1.57%# | -3.35%, 0.22% |
| Lag 5h | 2540 | -0.24% | -1.30%,0.83% | 2540 | -0.34% | -1.47%, 0.79% | 1166 | -0.58% | -2.27%, 1.12% | 753 | -1.21% | -3.29%, 0.88% |
| Lag 6h | 2540 | -0.02% | -0.92%,0.87% | 2540 | -0.04% | -1.00%, 0.91% | 1168 | 1.15% | -0.89%, 3.19% | 752 | 1.66% | -0.90%, 4.22% |
| **SDNN (ms) and PM$_{2.5}$** | **PM$_{2.5}$ IQR = 7.6 µg/m$^3$** | | | **PM$_{2.5}$ IQR = 7.6 µg/m$^3$** | | | **PM$_{2.5}$ IQR = 12.3 µg/m$^3$** | | | **PM$_{2.5}$ IQR = 12.3 µg/m$^3$** | | |
| Concurrent | 2251 | -1.23% | -2.89%,0.44% | 2251 | -0.79% | -2.51%, 0.93% | 1185 | -3.03%* | -5.68%, -0.37% | 823 | -1.10% | -4.25%, 2.05% |
| Lag 1h | 2259 | -0.71% | -2.39%,0.97% | 2259 | -0.32% | -2.04%, 1.40% | 1185 | -4.49%** | -7.18%, -1.80% | 823 | -2.92%# | -6.08%, 0.25% |
| Lag 2h | 2265 | -1.30% | -3.01%,0.42% | 2265 | -0.97% | -2.70%, 0.77% | 1185 | -4.59%** | -7.44%, -1.75% | 823 | -3.34%* | -6.57%, -0.12% |
| Lag 3h | 2271 | -1.74%# | -3.49%,0.00% | 2271 | -1.26% | -3.02%, 0.49% | 1186 | -3.74%* | -6.77%, -0.lag72% | 823 | -2.72% | -5.97%, 0.54% |
| Lag 4h | 2275 | -1.75%# | -3.51%,0.00% | 2275 | -1.03% | -2.77%, 0.71% | 1186 | -4.19%** | -7.32%, -1.07% | 823 | -1.76% | -5.08%, 1.55% |
| Lag 5h | 2280 | -2.13%* | -3.91%,-0.35% | 2280 | -1.13% | -2.89%, 0.64% | 1186 | -3.92%* | -7.17%, -0.67% | 823 | -0.46% | -3.86%, 2.94% |
| Lag 6h | 2283 | -2.00%* | -3.77%,-0.23% | 2283 | -0.96% | -2.73%, 0.81% | 1186 | -4.42%* | -7.79%, -1.05% | 823 | 0.41% | 3.05%, 3.88% |
| **RMSSD (ms) and PM$_{2.5}$** | **PM$_{2.5}$ IQR = 7.6 µg/m$^3$** | | | **PM$_{2.5}$ IQR = 7.6 µg/m$^3$** | | | **PM$_{2.5}$ IQR = 12.3 µg/m$^3$** | | | **PM$_{2.5}$ IQR = 12.3 µg/m$^3$** | | |
| Concurrent | 2260 | -2.18%# | -4.65%,0.30% | 2260 | -1.71% | -4.09%, 0.67% | 1185 | -7.20%** | -12.11%, -2.02% | 824 | -2.47% | -6.78%, 2.04% |
| Lag 1h | 2268 | -1.35% | -3.84%,1.14% | 2268 | -1.25% | -3.63%, 1.13% | 1185 | -4.90%# | -9.90%, 0.38% | 824 | -3.09% | -7.33%, 1.35% |
| Lag 2h | 2274 | -1.94% | -4.48%,0.61% | 2274 | -2.06%# | -4.47%, 0.36% | 1185 | -2.27% | -7.66%, 3.43% | 824 | -2.42% | -6.80%, 2.16% |
| Lag 3h | 2280 | -2.48%# | -5.06%,0.10% | 2280 | -2.40%# | -4.83%, 0.02% | 1186 | -0.41% | -6.32%, 5.87% | 824 | -1.65% | -6.16%, 3.08% |
| Lag 4h | 2284 | -2.98%* | -5.58%,-0.38% | 2284 | -2.30%# | -4.71%, 0.12% | 1186 | -2.54% | -8.58%, 3.91% | 824 | -1.50% | -6.15%, 3.37% |
| Lag 5h | 2289 | -3.49%** | -6.13%,-0.84% | 2289 | -2.35%# | -4.80%, 0.09% | 1186 | -5.02% | -11.19%, 1.57% | 824 | 1.83% | -3.19%, 7.11% |
| Lag 6h | 2292 | -2.75%* | -5.38%,-0.12% | 2292 | -1.62% | -4.08%, 0.83% | 1186 | -6.01%# | -12.40%, 0.85% | 824 | 0.59% | -4.54%, 6.01% |

# $P < 0.10$; * $P < 0.05$; ** $P < 0.01$

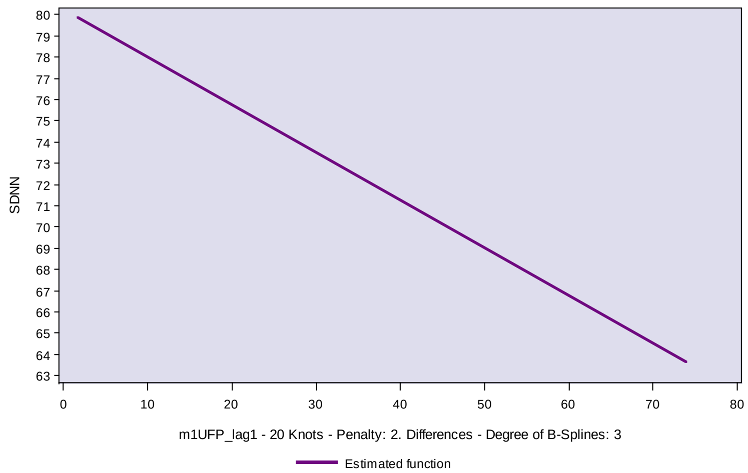
† Covariates included in the model were rehabilitation visit number, hour of the day, month of the visit, weekday, mean ambient temperature in the past 6 hours, mean ambient relative humidity in the past 5 hours modeled using a penalized spline (3 df), and mean hourly carbon monoxide concentration lagged 4 hours.

‡ Covariates included in the model were the mean ambient temperature in the past 6 hours, mean ambient relative humidity in the past 6 hours, long-term time trend as a penalized spline, time of the day (morning versus afternoon).

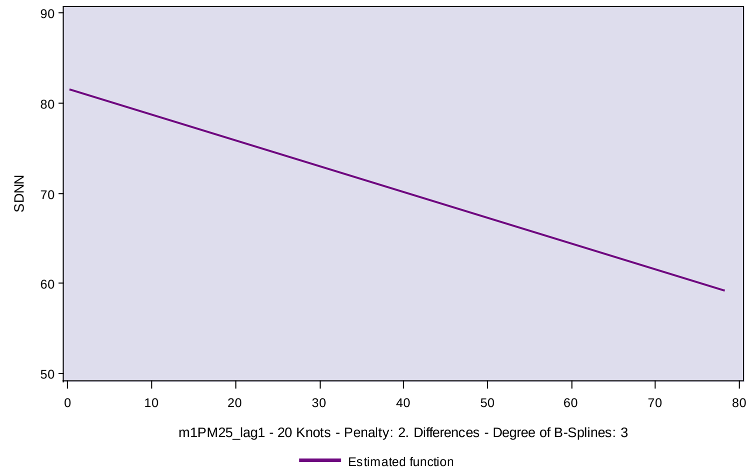
**Appendix R.** Additional analysis: Linear exposure–response functions for SDNN and air pollutant concentrations in the Augsburg study.

**a) Individuals with type-2 diabetes or impaired glucose tolerance Diab + IGT)**

UFP, lag 2h

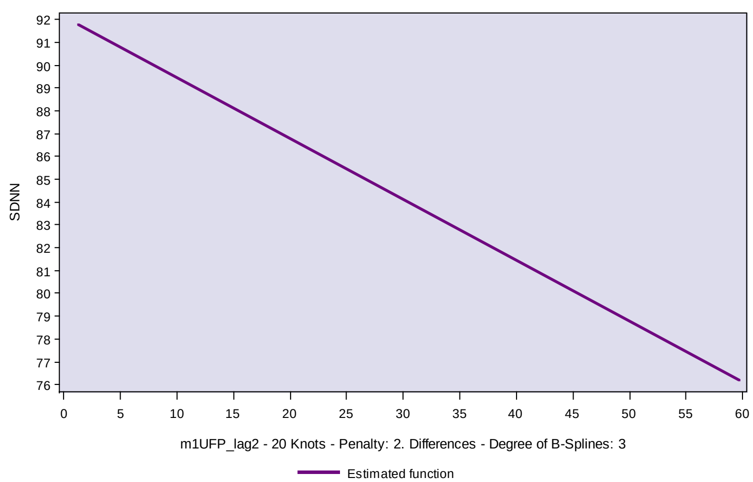



$PM_{2.5}$, lag 2h

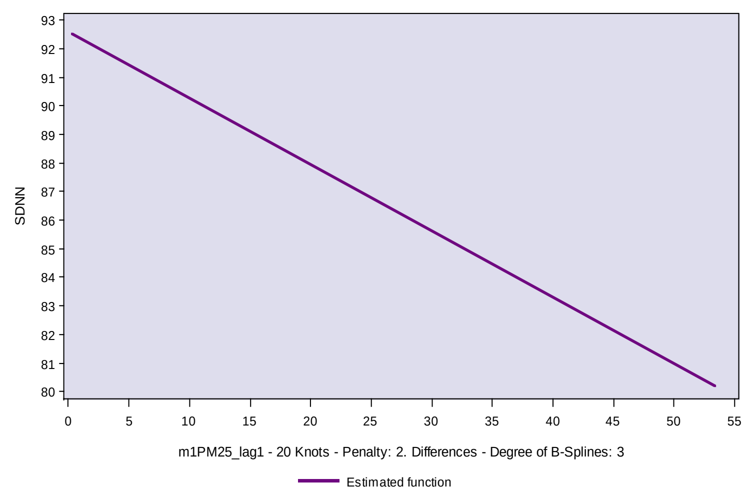



**b) Individuals with a potential genetic predisposition (Gen susc)**

UFP, lag 3h



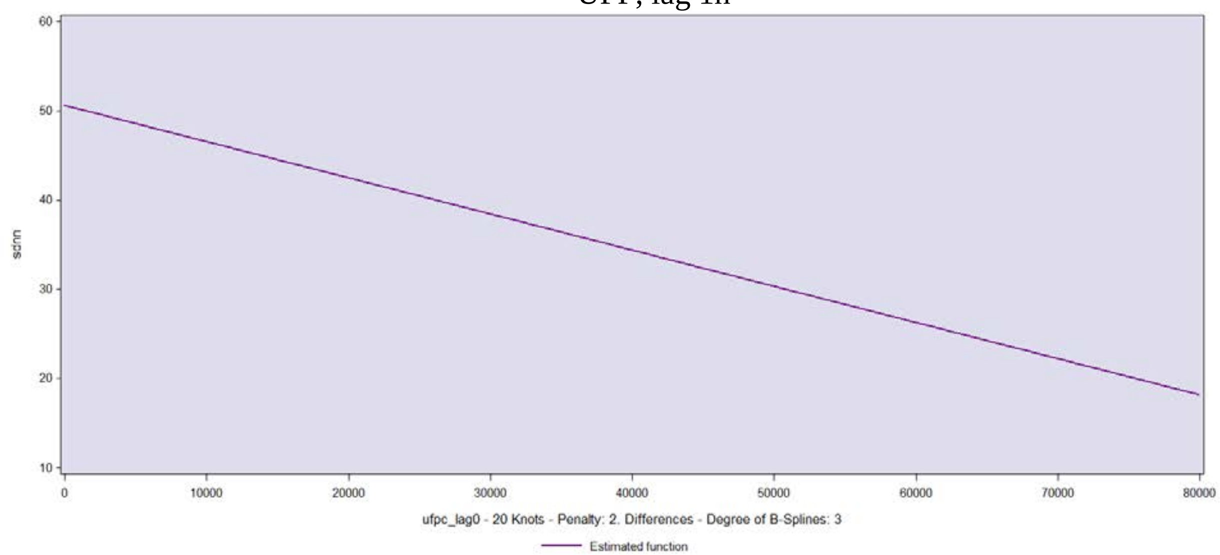

$PM_{2.5}$, lag 2h



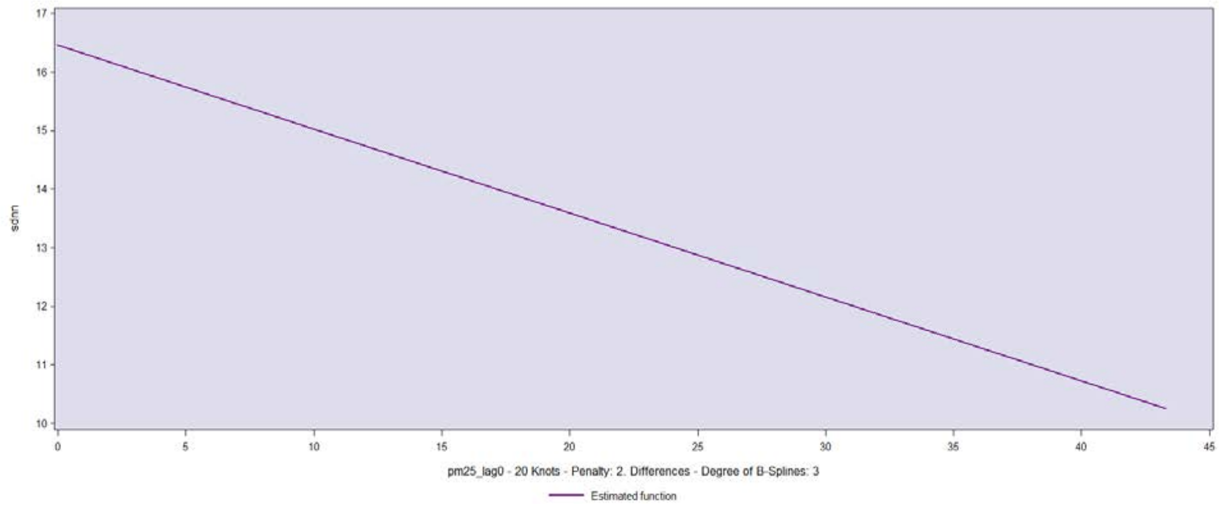
# Appendix S. Additional Analysis

**Appendix S**. Additional analysis: Linear exposure–response functions for SDNN and air pollutant concentrations in the REHAB study.

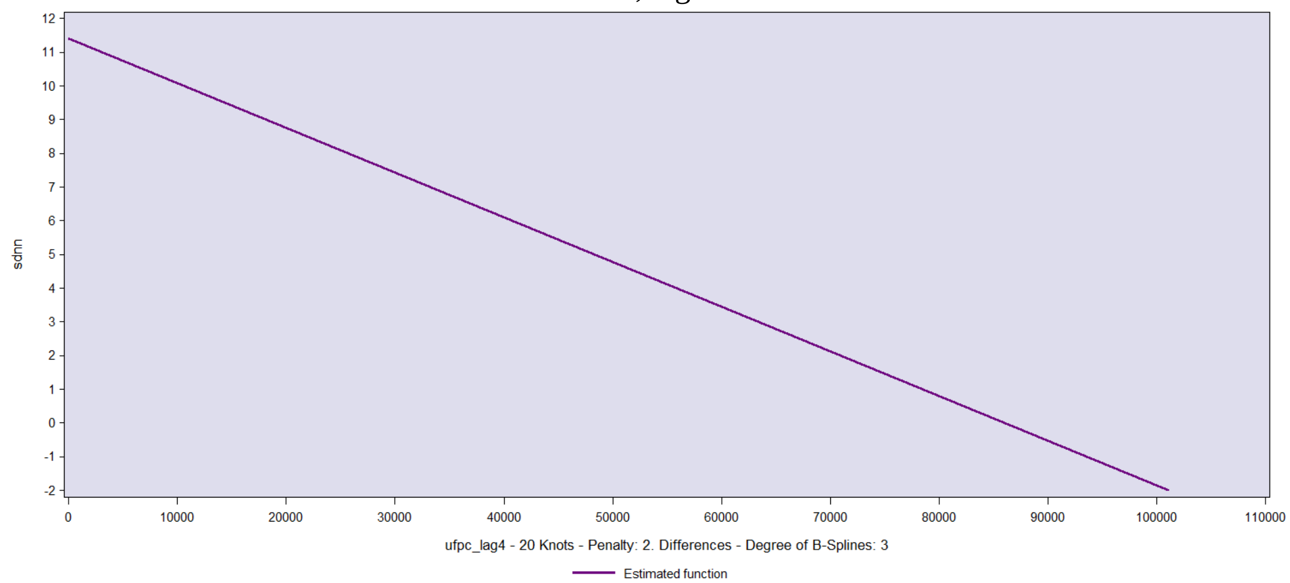
UFP, lag 1h



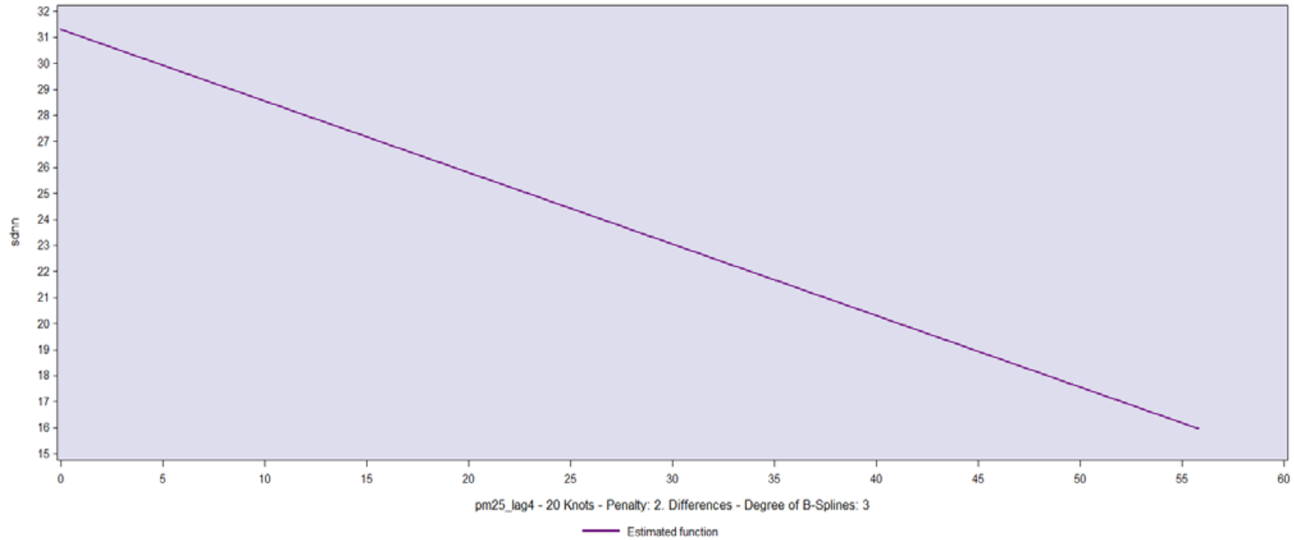
PM$_{2.5}$, lag 1h




UFP, lag 5h



PM$_{2.5}$, lag 5h


sdnn
pm25_lag4 - 20 Knots - Penalty: 2. Differences - Degree of B-Splines: 3
Estimated function

**Appendix T. Comparative Exposure Assessment in Augsburg, Germany, and Rochester, New York**

In Rochester, characterizations of the ambient aerosol have focused on $PM_{2.5}$ and particle number concentrations in several size ranges, whereas the work in Augsburg has focused on $PM_{10}$ and PNCs. In addition, there are various time intervals over which measurements were made and reported. Thus, there are difficulties in directly comparing the ambient aerosol compositions between Rochester and Augsburg. However, source apportionment studies, described below, have been conducted and thus, a better basis of comparison may be to examine the sources and relative source contributions of the major source types in each location.

Gu and colleagues (2011) reported particle compositions and size distribution data for winter 2006/07 at three sites in Augsburg. Qadir and colleagues (2014) presented results for measurements made during a 1-month sampling campaign from February 13 to March 12, 2008, at eight different sampling sites. The data from each of these studies were then used in source apportionment analyses using positive matrix factorization. In addition to the normal suite of elements, ions, and organic and elemental carbon used as the basis of the apportionments, organic markers have also been employed. The results from Gu and colleagus (2011) and Qadir and colleagues (2014) are presented in Tables T.1 to T.3. Elsasser and colleagues (2012) used organic molecular markers to assess wood smoke contributions to the $PM_{10}$ in Augsburg during a six-week winter period from 31 January 31 to March 12, 2010. They found that wood combustion organic aerosol (WCOA) contributed 23% of the organic matter (OM) on average and 27% in the evening and night time.

Using Principal Matrix Factorization (PMF), Kasumba and colleagues (2009) estimated the source contribution to the submicron particles (100–470 nm), measured between January 2002 and December 2007 at two New York State Department of Environmental Conservation (NYS DEC) sites in Rochester. Ten sources were identified at both sites, including traffic, nucleation, residential/commercial heating, industrial emissions, secondary nitrate, ozone-rich secondary aerosol, secondary sulfate, regionally transported aerosol, and a mixed source of nucleation and traffic. These results are summarized in Table T.4. Wang and colleagues (2011a) used PNCs in several size bins, along with gaseous pollutants measured at the NYS DEC site, to assess the impacts of the 2008 shutdown of a 260-megawatt coal-fired power plant in Rochester. They found that on average, 10–50 nm, 50–100 nm, and 100–500 nm PNCs decreased 49.8%, 51.9%, and 52.9% from 2007 to 2008, respectively. The annual average $SO_2$, CO, and $PM_{2.5}$ concentrations also decreased by 64.1%, 39.6%, and 45.6% from 2007 to 2008, respectively.

Wang and colleagues (2012a; 2012b) used $PM_{2.5}$ composition data collected between January 2007 and December 2010 to perform PMF analyses. In one study, the usual chemical speciation data (elements, ions, organic and elemental carbon) was augmented with a BC measurement that is the difference between BC measured at 370 nm and that measured at 880 nm (Delta-C). These results are presented in Table T.5. In the other study, these data were further augmented with molecular marker data although the time period of the study was reduced to October 2009 and October 2010. These results are also shown in Table T.5. There was good agreement in the apportionment between these studies and with the Kasumba and colleagues (2009) results as well with respect to sources such as wood smoke having an average contribution to $PM_{2.5}$ concentrations of about 7%. This value is in good agreement with the emissions inventory for the area. However, if the wood smoke contribution is examined on a seasonal basis, it contributed 17% of the winter $PM_{2.5}$ over the 2007 to 2010 period and 30% of the winter $PM_{2.5}$ in 2009–2010.

Both groups have also assessed spatial and temporal variations in particulate matter and particle concentrations within their respective communities. Gu and colleagues (2013) examined the variability of source contributions over the eight sites listed in Table T.3 based on data from winter 2006–07 and winter 2007–08. They performed separate PMF analyses for each winter seasonal data that identified six sources. Although the source profiles were generally similar, there were year-to-year differences suggesting the changing nature of residential and commercial combustion (including wood smoke) and traffic factors. Secondary sulfate and nitrate were relatively uniform across the area, whereas other source types like traffic and road salting were quite variable. Qadir and colleagues (2014) also looked at spatial variability over these same eight sites and again found that the secondary material was relatively uniform, but the local sources such as traffic, wood combustion, and road salting were heterogeneous. All of the published studies have focused on winter sampling campaigns, with the result that wood smoke was an important component of the ambient aerosol mass.

Wang and colleagues (2011b and c) explored the temporal and spatial variability of PNCs, BC, and Delta-C over Rochester using mobile monitoring for limited periods over four seasons. They observed considerable heterogeneity in the concentrations of particle sizes and Delta-C that would be indicative of traffic and wood smoke. Lagudu and colleagues (2011) used passive samplers to examine the heterogeneity of coarse particle mass ($PM_{2.5–10}$). They reported variations in both particle type and concentrations depending on both location and season.

Thus, comparing the exposures in Rochester and Augsburg suggests that wood smoke is an important component of the winter aerosol in both cities. There are significant amounts of secondary inorganic species in both areas, with high nitrate in the winter and sulfate in the summer. Although similar source types like motor vehicles were identified in both cities, there will be differences in the emitted materials. For example, traffic is important but there is a much larger fraction of diesel light-duty vehicles in Augsburg compared with Rochester. Both locations had impacts from coal combustion, but that impact diminished in Rochester after the shutdown of the local coal-fired power plant in spring 2008.

**Table T.1.** $PM_{10}$ mass apportionment based on particle compositions measured in 2008 (Gu et al. 2011).

| | Mass contribution ($\mu g\ m^{-3}$) | Fractional contribution |
|---|---|---|
| Road salting | 2.1 | 6.70% |
| Secondary sulfate | 4.1 | 13.0% |
| Residential & commercial combustion including wood smoke | 4.2 | 13.5% |
| Secondary nitrate | 9.5 | 30.4% |
| Motor vehicles | 5.2 | 16.6% |
| Resuspended dust | 6.2 | 20.0% |

**Table T.2.** Average number and volume concentration and proportion of each source in comparison with the total concentration (Gu et al. 2011).

| | Number ($cm^{-3}$) | Number ratio (%) | Volume ($\mu m^3\ cm^{-3}$) | Volume ratio (%) |
|---|---|---|---|---|
| Resuspended dust | 340 | 2.6 | 1.5 | 8.7 |
| Fresh traffic emissions | 3201 | 24.9 | 0.1 | 0.5 |
| Aged traffic emissions | 5182 | 40.3 | 1.7 | 10.1 |
| Stationary combustion | 3358 | 26.1 | 7.1 | 41.8 |
| Long-range transported dust | 136 | 1.1 | 1.5 | 8.9 |
| Nucleation particles | 471 | 3.7 | 0.2 | 0.9 |
| Secondary aerosols | 157 | 1.2 | 4.9 | 29.1 |

**Table T.3.** Percentage of factor source contributions and average of measured $PM_{10}$ mass at the eight sampling sites in Augsburg (Qadir et al. 2014).

| | Sampling site | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | KP | BP | LSW | LfU | HT | WE | Bifa | KI |
| Mean PM concentration ($\mu g/m^3$) | 43 | 28 | - | 25 | - | 18 | 26 | 19 |
| Coal & wood combustion | 6% | 14% | 17% | 18% | 5% | 12% | 13% | 12% |
| Wood combustion | 5% | 10% | 19% | 15% | 9% | 21% | 10% | 14% |
| Diesel & fuel oil | 8% | 18% | 5% | 8% | 6% | 8% | 20% | 14% |
| Road dust & tram | 20% | 15% | 5% | 11% | 5% | 3% | 9% | 7% |
| Hopanes | 5% | 14% | 11% | 13% | 11% | 9% | 15% | 16% |
| De-icing NaCl | 15% | 11% | 10% | 11% | 14% | 12% | 11% | 6% |
| Secondary sulfate | 5% | 9% | 10% | 13% | 12% | 11% | 10% | 9% |
| Secondary nitrate | 4% | 9% | 10% | 11% | 24% | 18% | 12% | 18% |
| Mixed sources | 32% | 0% | 13% | 0% | 14% | 14% | 0% | 4% |

**Table T.4.** Source apportionment based on particle size distributions measured between 2004 and 2007 (Kasumba et al. 2009).

| | Winter | | Summer | | Spring and fall | |
|---|---|---|---|---|---|---|
| | Number (# $cm^{-3}$) | Fractional contribution (%) | Number (# $cm^{-3}$) | Fractional contribution (%) | Number (# $cm^{-3}$) | Fractional contribution (%) |
| Nucleation 1 | 1345 | 16 | 905 | 11.4 | 831 | 11.1 |
| Mixed source | N/A | N/A | 1629 | 20.5 | 1673 | 22.3 |
| Traffic 1 | 2493 | 29.7 | 1694 | 21.3 | 1427 | 19 |
| Traffic 2 | 1599 | 19.1 | 1275 | 16 | 1125 | 15 |
| Resid./comm heating | 598 | 7.1 | N/A | | 703 | 9.4 |
| Industrial emissions | 2128 | 25.4 | 1545 | 19.4 | 1389 | 18.5 |
| Secondary nitrate | 166 | 2 | N/A | | 112 | 1.5 |
| $O_3$-rich secondary | 60 | 0.7 | 162 | 2 | 56 | 0.7 |
| Secondary sulfate | N/A | N/A | 666 | 8.4 | 182 | 2.4 |
| Regional transport | N/A | N/A | 87 | 1.1 | N/A | N/A |
| Sum | 8389 | 100 | 7963 | 100 | 7498 | 100 |

**Table T.5.** Comparison of source apportionments based on

| Source | Speciation data (Wang et al. 2012a) Mean contribution (µg $m^{-3}$) | Speciation and molecular marker data (Wang et al. 2012b) Mean contribution (µg $m^{-3}$) |
|---|---|---|
| Soil | 0.45 | 1.02 |
| Wood combustion | 0.84 | 0.72 |
| Diesel emissions | 1.45 | 0.62 |
| Gasoline vehicles | 1.73 | 0.63 |
| Secondary nitrate | 1 | 0.5 |
| Secondary sulfate | 3.72 | 3.62 |
| Road salt | 0.12 | |
| Isoprene SOA | | 0.55 |
| Other SOA | | 0.29 |

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