

The effect of workplace smoking bans on heart rate variability and pulse wave velocity of non-smoking hospitality workers

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ABSTRACT

Objectives

To investigate the effect of a change in second hand smoke (SHS) exposure on heart rate variability (HRV) and pulse wave velocity (PWV), this study utilized a quasi-experimental setting when a smoking ban was introduced.

Methods

HRV, a quantitative marker of autonomic activity of the nervous system, and PWV, a marker of arterial stiffness, were measured in 55 non-smoking hospitality workers before and 3 to 12 months after a smoking ban and compared to a control group that did not experience an exposure change. SHS exposure was determined with a nicotine specific badge and expressed as inhaled cigarette equivalents per day (CE/d).

Results

PWV and HRV parameters significantly changed in a dose dependent manner in the intervention group compared to the control group. A one CE/d decrease was associated with a 2.3% (95% CI: 0.2, 4.4; $p=0.031$) higher root mean square of successive differences (RMSSD), a 5.7 % (95% CI: 0.9, 10.2; $p=0.02$) higher high frequency component and a 0.72% (95 % CI: 0.40-1.05; $p<0.001$) lower PWV.

Conclusions

PWV and HRV significantly improved after introducing smoke-free workplaces indicating a decreased cardiovascular risk.

INTRODUCTION

Several epidemiological studies from various countries have shown the beneficial effects of a public indoor smoking ban on cardiovascular health, especially acute myocardial infarction (AMI). In Indiana, USA, hospital admission rates for AMI declined by 50% primarily among non-smokers (Seo and Torabi 2007). In Helena, Montana rates decreased by 40%, but returned to former levels after ban suspension (Sargent et al. 2004), while decreased levels stayed low in Pueblo County after a longer enforcement period (Bartecchi et al. 2006). Studies in European cities suggest less pronounced decreases (Goodman et al. 2009). In Scotland, AMI rates decreased by 17% after the ban compared to a 4% decrease in England that did not have a ban (Pell et al. 2008). A recent meta-analysis including 45 studies calculated significantly lower hospital admission rates for both coronary events (RR: 0.848; 95% CI: 0.816-0.881) as well as for other heart diseases (RR: 0.610; 95% CI: 0.440-0.847) after introducing a comprehensive smoking ban (Tan and Glantz 2012). However, most studies lack a control group as well as exact information on smoking status and exposure because they were conducted on a population level only. To assess the mechanistic public health impact of public smoking bans, population-based, sensitive measures beyond AMI are needed.

Heart rate variability (HRV) is a quantitative marker of autonomic activity of the nervous system and lower HRV is associated with higher cardiovascular morbidity and mortality (Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. 1996). The main influencing factors are sex, age, physical activity, blood pressure and smoking status (Felber Dietrich et al. 2006). In

a study by Pope et al., acute exposure to SHS alternating with non-exposed periods led to consistently lower HRV measures during exposure (Pope et al. 2001). A cross-sectional analysis showed that long-term SHS exposed persons for >2h/day have higher High Frequency (HF), lower total power (TP), Low Frequency (LF) and a lower LF/HF ratio than unexposed people (Felber Dietrich et al. 2007) . These are important frequency-domain HRV measures providing further insight on fluctuations of HR (Bilchick and Berger 2006). Chen et al. showed that HRV was lower in mice during and after exposure to second-hand smoke (SHS) (Chen et al. 2008). No longitudinal study on long-term SHS exposure and HRV has been conducted so far.

Pulse wave velocity (PWV) provides a measure of arterial stiffness (Vlachopoulos et al. 2010) which is an important indicator of cardiovascular risk and atherosclerosis (McEniery and Cockcroft 2007). In addition arterial stiffness is a powerful predictor of all-cause mortality (Vlachopoulos et al. 2010; Vlachopoulos et al. 2012). An increase of PWV was observed after acute exposure to SHS (Barnoya and Glantz 2005) and after smoking one cigarette (Kubozono et al. 2011). Arteries such as the aorta and the femoral artery are composed of different amounts of smooth muscle cell layers and acute changes in arterial stiffness may reflect changes in arterial tone due to autonomic innervation or changes in endothelial function (Hill 2013).

In another study PWV was found to be higher among smokers than non-smokers but smoking cessation did not lead to any significant changes (Yu-Jie et al. 2013). A prospective cohort study found a significant relationship between the number of cigarettes smoked per day and the annual rate of change in PWV (Tomiyama et al. 2010).

Long-term exposure to SHS and its impact on arterial stiffness have not been examined as yet.

When Switzerland introduced a smoking ban in May 2010, the national law left room for exceptions (Roosli and Rajkumar 2013). While several cantons – administrative zones in Switzerland - completely banned smoking venues and rooms, in other cantons either small smoking venues or separated smoking rooms were still allowed. This unique situation served as a quasi-experimental setting for our prospective study. The aim was to directly relate SHS exposure in non-smoking hospitality workers before and after introduction of the smoking ban to HRV and arterial stiffness. We further compared possible changes in the intervention group which was subject to the introduction of smoke free workplaces to the control group that did not experience any changes in SHS exposure at the work place.

METHODS

Study population

This is a quasi-experimental study comparing non-smoking employees for whom second hand smoke exposure at work was eliminated as a result of the new smoking regulations (intervention group) with non-smoking employees that did not undergo any change in exposure (control groups). The intervention group consisted of participants who had worked for at least 1 year in venues where smoking was either partially or completely allowed prior to the introduction of the smoking ban (n=55). After introduction of the smoking ban, the intervention group was no longer exposed to SHS at work. The control group consisted of individuals who were exposed to SHS both before and after the

implementation of the smoking ban because of the exceptional rules described above (n=7) and non-smokers that were regularly exposed to SHS at work or in private without being employed in the hospitality sector (n=16). Due to difficulties in recruitment of non-smoking hospitality workers, we additionally included a supplementary group of 14 non-smoking hospitality workers at baseline, who worked in a smoke-free environment at all times (labelled supplementary group).

In the intervention group, a baseline examination was conducted within the 3 months prior to the introduction of the smoking ban. Subsequently, two follow-up examinations were conducted at 3-6 months and 9-12 months after the smoking ban introduction. The unexposed study participants constituting the supplementary group were examined once; all others were invited for examinations three times. Intervals between examinations were also about six months.

Recruitment procedure

A list of hospitality venues in the cantons of Zurich, Basel City and Basel County was created using the digital Swiss phonebook from 2009. Each venue received a letter that was followed-up by a phone call and a visit two weeks later.

Screening questionnaires were distributed to the waiting staff, for providing information on the eligibility criteria which were being between 18 and 65 years of age, working at least half-time, having worked for at least one year in the hospitality sector and having been a non-smoker for at least 5 years. Eligible study participants were invited to a health examination, which was carried out in one of the two study centres in Basel City and Zurich.

The non-hospitality workers were recruited by means of an online advertisement looking for non-smokers that were exposed to SHS on a regular basis, either privately or at work.

Health examinations

The health examinations comprised cardiovascular and respiratory tests as well as a computer-based interview. About 20 minutes into the health examination, electrocardiograms (ECG) were continuously recorded for 10 minutes with a 7-lead digital recorder (SEER Light, GE Healthcare, Freiburg, Germany) with participants in the supine position. ECGs were stored and subsequently analysed on a PC MARS workstation (GE Healthcare). Beat annotations were automatically assigned by the GE software and manually reviewed by an investigator blinded to the exposure status of participants to ensure proper annotation of non-sinus beats and artefacts. Only normal sinus beats were used in the calculation of HRV metrics. The duration between the R waves of consecutive normal sinus beats (N-N intervals) was identified and only beats with an N-N interval between 0.4 and 2.0 s and ratio between 0.8 and 1.2 were included in the analysis.

Calculations for time domain [standard deviation of N-N intervals (SDNN); square root of the mean squared differences of successive N-N intervals (rMSSD)] and frequency domain [low-frequency (LF) power (0.04-0.15 Hz), high-frequency (HF) power (0.04-0.15 Hz), and their ratio (LF/HF)] HRV parameters were evaluated on non-overlapping 5-min intervals of ECG data using standard techniques (Task Force of the European Society of Cardiology 1996). Only 5 minute intervals with a ratio of N-N/R-R intervals >90% were included in our analyses.

Subsequently, PWV and blood pressure were measured using a VaSera VS-1500N device (Fukuda Denshi Co., Tokyo, Japan). Participants were in supine position and at rest for at least 10 minutes beforehand. If the first two measures were more than 0.5 m/s apart, a third measurement was taken. For analysis the average of the two more similar measurements was used.

Exposure measurements

SHS was measured using newly developed MONIC passive sampling badges made of glass fibre. The amount of nicotine on a badge was determined by gas chromatography and used to calculate the number of passively smoked cigarettes (CEs)/day assuming a nicotine content of 0.2 mg/cigarette and an average ventilation rate of 10 L/min (Huynh et al. 2008), (Durham et al. 2011).

In the hospitality venues that agreed to participate, at least one MoNIC badge was placed for one week, often near the bar where waiting personnel spend much of their working time. We calculated for each hospitality worker a time-weighted average workplace exposure (Rajkumar et al. 2013) by multiplying their average workplace concentration by their workload (in percentage of full time equivalent) and by 0.6, which represents presence time at the work place including holidays and considering the fact that nicotine levels decrease when a venue is unattended (Rajkumar et al. 2013). For non-hospitality workers average SHS exposure was obtained from a personal badge that participants wore on themselves at work and in private on a typical day.

Statistical Analysis

Longitudinal analyses were conducted with two statistical approaches. First, for the intervention group and the control group a pre/post ban exposure variable was derived by defining baseline data of both groups as pre-ban and the two follow-up examinations as post ban although in the control group no ban was introduced. In order to increase statistical power we did not differentiate between the follow-up examinations and calculated an overall effect. For each outcome a linear mixed effects model with a random subject intercept was fit including a study group by pre/post ban interaction term. HRV analyses were adjusted for age, sex, BMI and season, PWV additionally for time of day and systolic blood pressure as continuous variables. Systolic blood pressure was adjusted for age, sex, BMI, season and self-reported asthma. Finally, we calculated crude and adjusted values of the health outcomes prior and after the ban for both groups. Secondly, covariate-adjusted exposure response associations were calculated with a random intercept model using the estimated work place SHS exposure at the time of each health examination as explanatory variable using data from all study participants, including the unexposed supplementary group.

Data were analysed using Stata 10.1 (StataCorp LP, College Station, TX).

RESULTS

Exposure of the study population

Our study sample comprised 92 participants, 55 in the intervention group, 23 in the control group and 14 in the supplementary group. Groups did not differ in terms of sociodemographic factors or health status, except for age, self-reported asthma and physical activity (Table 1). There were no diabetics in our sample. Average exposure in

the intervention group at baseline was 2.56 (95% CI: 1.70 to 3.44) cigarette equivalents per day (CE/day) and 0.16 (95% CI: 0.13 to 0.20) CE/day at follow-up resulting in an exposure reduction of 2.40 CE/day (Table 1). In the exposed control group exposure at baseline was 2.07 (95% CI: 0.96-3.18) CE/day and 1.59 (95% CI: 0.67-2.50) CE/day at follow-up.

Heart Rate Variability

From the HRV analyses 2 observations from the intervention group and 5 from the control group were excluded due to missing data (n=1) or insufficient quality (n=6). At baseline, adjusted HRV parameters did not differ between the intervention and the exposed control group (Table 2). After the introduction of the smoking ban, SDNN, RMSSD, HF, LF/HF and Total Power significantly diverge between the two groups (Figure 1). All these parameters increase in the intervention group while decreasing in the control group except the LF/HF ratio which goes in the opposite direction, leading to a significant change in the intervention group relative to the exposed control group after implementation of the smoking ban. The exposure-response model (Table 3) shows significant increases of 2.3% (95% CI: 0.2 to 4.4; p=0.031) and 5.7 % (95% CI: 0.9 to 10.2; p=0.02) per decrease in CE/day for RMSSD and HF, respectively. SDNN and Total Power are associated with an increase of 1.8 % (95% CI: -0.1 to 3.8; p=0.069) and 4.1% (95% CI: 0.0 to 8.0; p=0.51), while the LF/HF ratio significantly decreases by -5.7% (95% CI: -9.1 to -2.4); p=0.001) per decrease in CE/day. LF does not change materially. For comparison, age-dependent changes in HRV parameters obtained from the same model are shown in table 3.

Pulse Wave Velocity

For the arterial stiffness analyses two participants had missing data and technical problems resulted in the loss of five observations for the PWV measurements (4 intervention, 1 control). Table 2 shows crude and adjusted values of PWV for the intervention and control group. Figure 2 illustrates the changes in adjusted values comparing the intervention and control groups. Differences in PWV are not significant although the intervention group shows a steady decrease over the year, an effect not observed in the control group. Systolic blood pressure decreases in the intervention group and increases in the control group.

According to the exposure-response model (Table 3) PWV declines with each CE/day decrease by 0.72% (95% CI: 0.40 to 1.05; $p < 0.001$) whereas the decrease for systolic blood pressure is not statistically significant.

DISCUSSION

The smoking ban implementation led to statistically significant improvements in HRV parameters in non-smoking hospitality workers within 12 months. HRV increased in the intervention group and PWV decreased compared to the control group that did not experience any changes in SHS exposure.

This study addresses several research gaps that the Institute of Medicine 2010 report on SHS exposure and cardiovascular effects identified (Secondhand Smoke Exposure and Cardiovascular Effects: Making Sense of the Evidence 2010): It directly examines the exposure-response relationship of individual-level SHS exposure to HRV and arterial stiffness and accounts for potential confounders, including other risk factors for

cardiovascular events. It also compares possible changes in an intervention group where smoke free workplaces were introduced to a control group that did not experience a change in SHS exposure.

Comparison with the literature

Our results on HRV are in line with the only other study looking into long-term effects of SHS on HRV reporting trends of lower levels in SDNN, Total Power and HF in subjects that were exposed to SHS for >2h/d compared to unexposed subjects in a cross-sectional setting (Felber Dietrich et al. 2007). Our findings are also supported by other studies that looked at acute effects of SHS on HRV and found consistent decreases in SDNN as soon as subjects were exposed (Pope et al. 2001) or right after exposure (Zhang et al. 2013; Wilson et al. 2010). The effect of active smoking on heart rate variability has been studied extensively. While several studies found diminished HRV in heavy smokers (Barutcu et al. 2005; Levin et al. 1992; Hayano et al. 1990), others did not confirm this (Kageyama et al. 1997; Murata et al. 1992). A study examining the effect of smoking cessation on HRV recorded a significant increase one day after cessation in heavy smokers, that although diminished, persisted one month after cessation (Yotsukura et al. 1998). This effect is in line with another study looking at regular smokers (Minami et al. 1999).

Interpretation of our results

No significant difference in HRV parameters between the intervention and the exposed control group could be detected at baseline. SDNN, reflecting the overall variability of

HRV, increased by 1.8% per decrease in CE/day, which is more than the 1.5% decrease of SDNN per year of life according to the same exposure-response model. Applying the average exposure reduction of 2.4 CEs/day that we estimated in this study, this effect corresponds to a delay of roughly three years in HRV reduction. RMSSD and HF describing parasympathetic activity both increased significantly. LF did not change measurably while the LF/HF ratio significantly decreased. These alterations support former published evidence suggesting that passive smoking increases the sympathetic drive and reduces parasympathetic modulation as well as overall HRV (Dinas et al. 2013).

PWV was higher at baseline in the intervention group than in the exposed control group. During the study the two groups drew closer together although the ban effect was not significant. In the exposure-response model, PWV significantly declined by 0.72% per decrease in CE/day, which corresponds to a ban effect of about 2.5 years of life. The somewhat discordant result of the exposure-response model compared to the pre/post model means that PWV was strongly correlated with SHS exposure at the workplace but changes within 1 year were small. This pattern would be consistent with a more chronic effect of SHS assuming that measured exposure at the workplace at baseline is representative for chronic exposure.

Strengths and limitations

To the best of our knowledge this is the first study to prospectively measure the effect of a smoking ban on subclinical outcomes related to cardiovascular physiology. A major asset of this study is the quasi experimental setting that allowed comparing the effects in

workers where a smoke free workplace was introduced to a control group without an exposure change. A further strength is that exposure data was collected at the same time as the health outcomes. A prospective study avoids the dangers of a possible recall bias and mixed linear models allow for within-subject clustering. By using the MoNIC badge, SHS exposure was directly quantified by measuring nicotine without using a surrogate measure such as airborne particulate matter.

Although exposure misclassification cannot be excluded, in particular for individuals of the control group without a workplace badge, the consistency of the results between the pre/post model with the exposure-response model suggests that exposure misclassification is unlikely to bias our results. Due to limited sample size we could not differentiate between the two follow-up examinations in our analysis but this should not have caused any bias. Recruitment of eligible participants was unexpectedly tedious as restaurant owners were worried about financial losses caused by the smoking ban, a concern that was shown to be baseless (Schulz et al. 2012). The exposed control group was younger, physically more active and reported more asthma. This might have influenced the results. However, they are unlikely to explain the full pattern, since we have considered these factors in the exposure-response model. The pre/post model is mainly a within-subject comparison where group differences are less relevant.

Conclusions

This study indicates that introduction of smoke-free workplaces in hospitality venues substantially lowers cardiovascular risk factors in non-smoking hospitality workers and

emphasizes the need for authorities worldwide to implement comprehensive policies in order to prevent adverse health effects.

Conflict of interest

The authors declare that they have no conflict of interest.

Ethics Statement

Ethical approval was obtained from the EKBB (Ethics committee of both cantons of Basel) and all participants signed an informed consent before every examination (Ref. No. EK 317/09).

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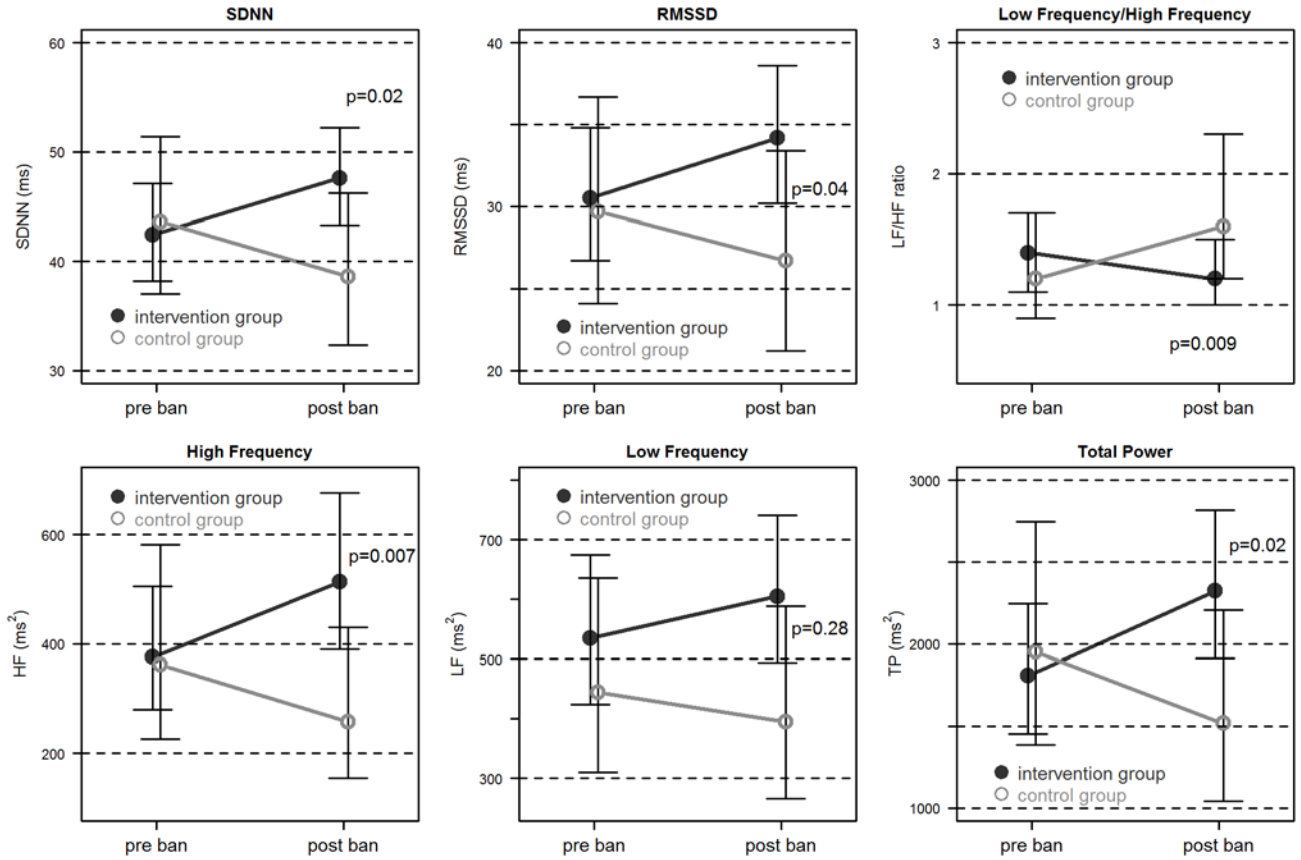


Figure 1: Covariate-adjusted Heart Rate Variability parameters at baseline and follow-up, Switzerland 2010/2011

P-values refer to the change in the intervention group relative to the control group.

SDNN= standard deviation of NN intervals; RMSSD=root mean square of successive difference

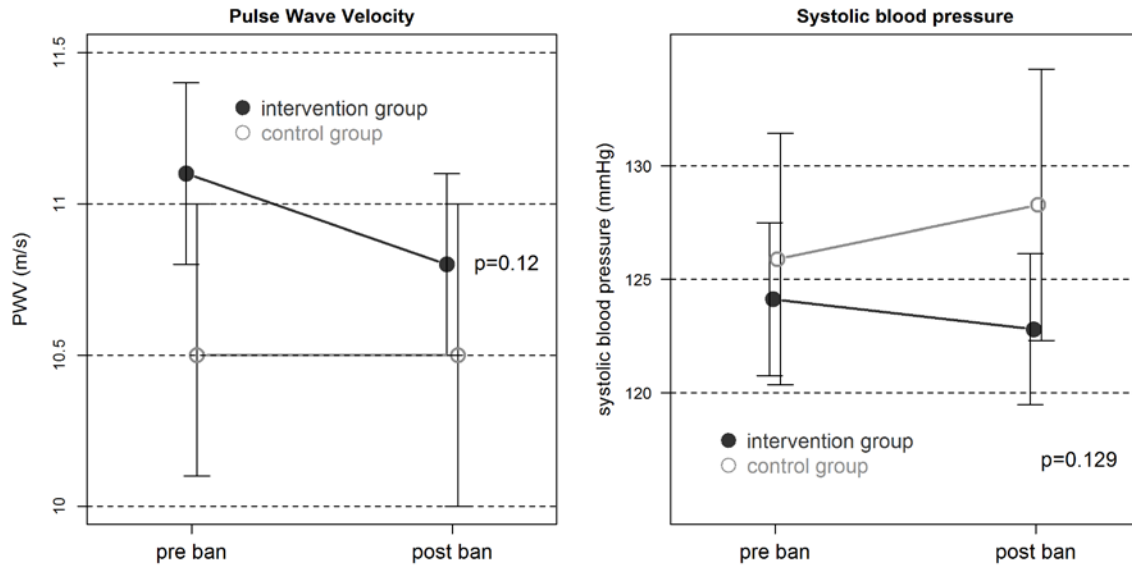


Figure 2: Covariate-adjusted Pulse Wave Velocity and systolic blood pressure at baseline and follow-up, Switzerland 2010/2011

P-values refer to the change in the intervention group relative to the control group

Table 1: Study population, Switzerland 2010/2011

| | Intervention group (n=55) | Control group (n=23) | Supplementary group (n=14) | p-Value‡ |
|---------------------------------|--------------------------------------|---------------------------------|---------------------------------------|-----------------|
| Female sex | 33 (60%) | 13 (57%) | 11 (79%) | 0.37 |
| Age (years) | 42.2 (95% CI: 39.0- 45.4) | 31.8 (95% CI: 26.4- 37.2) | 46.8 (95% CI: 41.1- 52.5) | 0.001 |
| BMI (kg/m ²) | 26.0 (95% CI: 24.9- 27.2) | 25.0 (95% CI: 22.7- 27.2) | 25.0 (95% CI: 23.3- 26.7) | 0.23 |
| Overweight (BMI>25) | 28 (50.1 %) | 11 (47.8 %) | 5 (35.7 %) | 0.60 |
| Smoking status | Never-smokers | 21 (91.3 %) | 12 (85.7 %) | 0.15 |
| | Ex-smokers | 2 (8.7 %) | 2 (14.3 %) | |
| Self-reported asthma | 4 (7.3 %) | 8 (34.8 %) | 1 (7.1) | 0.01 |
| Systolic blood pressure (mmHg) | 125.0 (95% CI: 121.2- 128.7) | 122.3 (95% CI: 115.6- 129.1) | 128.6 (95% CI: 122.7-134.4) | 0.16 |
| Diastolic blood pressure (mmHg) | 81.5 (95% CI: 78.8- 84.1) | 77.8 (95% CI: 73.3- 82.3) | 82.3 (95% CI: 77.9- 86.6) | 0.24 |
| Hypertension# | 15 (27.3 %) | 11 (4.4 %) | 4 (28.6 %) | 0.07 |

| | | | | | |
|---|--------------------------|--------------------------|--------------------------|------------|-------|
| Self-reported diabetes mellitus | 0 (0 %) | 0 (0 %) | 0 (0 %) | | |
| Coronary disease§ | 1 (1.8 %) | 0 (0 %) | 1 (7.1 %) | 0.34 | |
| Betablocker intake | 6 (10.9 %) | 1 (4.4 %) | 2 (14.3 %) | 0.56 | |
| Allergic* | 38 (69.1 %) | 16 (69.6 %) | 6 (42.9 %) | 0.30 | |
| Self-reported physical activity† | 19 (34.6 %) | 16 (69.6 %) | 10 (71.4 %) | 0.02 | |
| Average workload (%) | 93.8 (n=55) | 100.0 (n=7) | 84.3 (n=14) | 0.20 | |
| Type of workplace | bar | 5 (9.1 %) | 2 (88.7 %) | 0 (0 %) | 0.007 |
| | café | 18 (32.7 %) | 0 (0 %) | 0 (0 %) | |
| | restaurant | 32 (58.2 %) | 5 (21.7 %) | 14 (100 %) | |
| | other | 0 (0 %) | 16 (69.6 %) | 0 (0 %) | |
| Pre-ban workplace exposure (cigarette equivalents/day) | 2.56 (95% CI: 1.70-3.44) | 2.07 (95% CI: 0.96-3.18) | 0.12 (95% CI: 0.03-0.21) | | |
| Post-ban workplace exposure (cigarette equivalents/day) | 0.16 (95% CI: 0.13-0.20) | 1.59 (95% CI: 0.67-2.50) | NA | | |

Values shown are arithmetic means at baseline except where indicated

‡ Kruskal Wallis Test for numerical data, Chi square for proportion

defined as positive if diastolic blood pressure > 90 mmHg OR systolic blood pressure > 140 mmHg

§ defined as: has taken medication for coronary heart disease during the past 7d

*reacted positively to at least one skin prick test

† defined as: answered yes to: do you sweat at least once/week due to physical activity?

Table 2: Heart Rate Variability and Pulse Wave Velocity: pre/post model, Switzerland 2010/2011

| | | Pre-Ban | | | | | Post-Ban | | | | |
|-----------------------------|------------|--------------------|-------------------------|---------------|-------------------------|-----------|--------------------|-------------------------|---------------|-------------------------|-----------|
| | | Intervention Group | | Control Group | | p-Value # | Intervention Group | | Control Group | | p-Value ‡ |
| | | n | Geometric Mean (95% CI) | n | Geometric Mean (95% CI) | | n | Geometric Mean (95% CI) | n | Geometric Mean (95% CI) | |
| SDNN [ms]* | unadjusted | 53 | 42.1 (37.8-47.0) | 21 | 48.0 (37.5-61.5) | | 84 | 46.2 (42.3-50.4) | 19 | 41.4 (33.4-51.3) | |
| | adjusted | 53 | 42.4 (38.2-47.1) | 21 | 43.6 (37.0-51.4) | 0.79 | 84 | 47.6 (43.3-52.2) | 19 | 38.6 (32.3-46.2) | 0.02 |
| RMSSD [ms]* | unadjusted | 53 | 28.9 (24.9-33.5) | 21 | 36.2 (25.8-50.8) | | 84 | 32.5 (28.8-36.7) | 19 | 31.1 (22.2-43.6) | |
| | adjusted | 53 | 30.5 (26.7-34.8) | 21 | 29.7 (24.1-36.7) | 0.86 | 84 | 34.2 (30.2-38.6) | 19 | 26.7 (21.2-33.4) | 0.04 |
| LF/HF* | unadjusted | 53 | 1.5 (1.2-1.9) | 21 | 1.0 (0.6-1.6) | | 84 | 1.3 (1.1-1.5) | 19 | 1.3 (0.8-2.0) | |
| | adjusted | 53 | 1.4 (1.1-1.7) | 21 | 1.2 (0.9-1.7) | 0.48 | 84 | 1.2 (1.0-1.5) | 19 | 1.6 (1.2-2.3) | 0.01 |
| HF [ms²]* | unadjusted | 53 | 341.4 (240.8-483.8) | 21 | 556.3 (265.3-1166.3) | | 84 | 450.4 (342.7-591.9) | 19 | 377.8 (179.3-796.2) | |
| | adjusted | 53 | 376 (280-505) | 21 | 362 (226-582) | 0.92 | 84 | 514 (390-677) | 19 | 258 (155-430) | 0.01 |
| LF [ms²]* | unadjusted | 53 | 522.6 (408.7-668.2) | 21 | 555.9 (336.5-918.2) | | 84 | 558.1 (461.7-674.7) | 19 | 458.8 (287.2-732.7) | |

| | | | | | | | | | | | |
|--|------------|----|------------------------|----|------------------------|------|----|------------------------|----|------------------------|------|
| | adjusted | 53 | 535 (424-674) | 21 | 444 (310-636) | 0.39 | 84 | 605 (494-741) | 19 | 395 (266-588) | 0.28 |
| Total Power [ms²]* | unadjusted | 53 | 1797.2 (1439.4-2243.9) | 21 | 2348.0 (1399.6-3939.0) | | 84 | 2188.8 (1832.1-2614.9) | 19 | 1739.1 (1118.8-2703.2) | |
| | adjusted | 53 | 1807 (1454-2247) | 21 | 1951 (1387-2745) | 0.73 | 84 | 2323 (1915-2819) | 19 | 1517 (1042-2207) | 0.02 |
| PWV [m/s]** | unadjusted | 52 | 11.2 (10.8-11.6) | 19 | 9.8 (8.9-10.8) | | 83 | 10.8 (10.5-11.1) | 18 | 9.8 (9.2-10.5) | |
| | adjusted | 52 | 11.1 (10.8-11.4) | 19 | 10.5 (10.1-11.0) | 0.03 | 83 | 10.8 (10.5-11.1) | 18 | 10.5 (10.0-11.0) | 0.12 |
| Systolic blood pressure [mmHg]§ | unadjusted | 55 | 124.3 (120.7-127.9) | 23 | 121.3 (114.7-128.4) | | 85 | 123.4 (120.5-126.4) | 19 | 124.3 (119.8-128.9) | |
| | adjusted | 55 | 124.1 (120.7-127.5) | 23 | 125.9 (120.4-131.4) | 0.90 | 85 | 122.8 (119.5-126.1) | 19 | 128.3 (122.3-134.3) | 0.13 |

*Adjusted for age, sex, bmi and season

**Adjusted for age, sex, bmi, systolic blood pressure, circadian rhythm and season

§Adjusted for age, sex, bmi, season and asthma

#Covariate adjusted p-value for the baseline difference according to the mixed linear model

‡Covariate adjusted p-value for the intervention effect based on the interaction term of the mixed linear model

Table 3: Heart Rate Variability and Pulse Wave Velocity: Exposure-Response model, Switzerland 2010/2011

| | Coefficient# (95% CI) | p-Value | Age coefficient‡ (95% CI) | p-Value |
|----------------------------|------------------------|---------|---------------------------|---------|
| SDNN* | 1.8 (-0.1 to 3.8) | 0.069 | -1.5 (-2.1 to -0.9) | <0.001 |
| RMSSD* | 2.3 (0.2 to 4.4) | 0.031 | -2.6 (-3.4 to -1.9) | <0.001 |
| LF/HF* | -5.7 (-9.1 to -2.4) | 0.001 | 3.2 (2.1 to 4.4) | <0.001 |
| HF* | 5.7 (0.9 to 10.2) | 0.020 | -5.9 (-7.5 to -4.2) | <0.001 |
| LF* | 0.6 (-4.1 to 5.1) | 0.802 | -2.9 (-4.2 to -1.7) | <0.001 |
| Total Power* | 4.1 (0.0 to 8.0) | 0.051 | -3.0 (-4.1 to -1.8) | <0.001 |
| PWV** | -0.72 (-0.40 to -1.05) | <0.001 | 0.69 (0.54 to 0.85) | <0.001 |
| Systolic blood pressure*** | -0.07 (-0.32 to 0.47) | 0.722 | 0.28 (0.13 to 0.43) | <0.001 |

#change in % per unit decrease in cigarette equivalents

‡change in % per 1y increase in age

*adjusted for age, sex, bmi and season

**adjusted for age, sex, bmi, season, systolic blood pressure and circadian rhythm

***Adjusted for age, sex, bmi, season and asthma