Practical learnings from an epidemiology study on TDI-related occupational asthma. Part I - Cumulative exposure is not a good indicator of risk.

Supplemental Information - 5

Sensitivity analyses

Potential shift overtime

Gross cumulative exposure has been calculated as described in the Methods section assuming that every participant worked a similar number of hours per year.

However, overtime is a common occurrence in shift work to cover for vacation and sick time. The relationship between asthma incidence and gross cumulative exposure was investigated assuming a high but not uncommon overtime rate of 30% for shift workers as a potential alternate data assumption.

Figure S5-1 shows the histogram of gross cumulative exposure values in the same format as Figure 1. Compared to Figure 1, gross cumulative exposure for shift workers has shifted to higher values in its entirety.

Table S5-1 provides the overview of incidence rates in the same format as Table 2.

The 178 data points were analyzed by logistic regression. The slope parameter was not significant (P=0.35 for a linear model), neither was the goodness-of-fit (P=0.37): both indicating no significant relationship between this potential alternate adjusted gross exposure and asthma incidence.
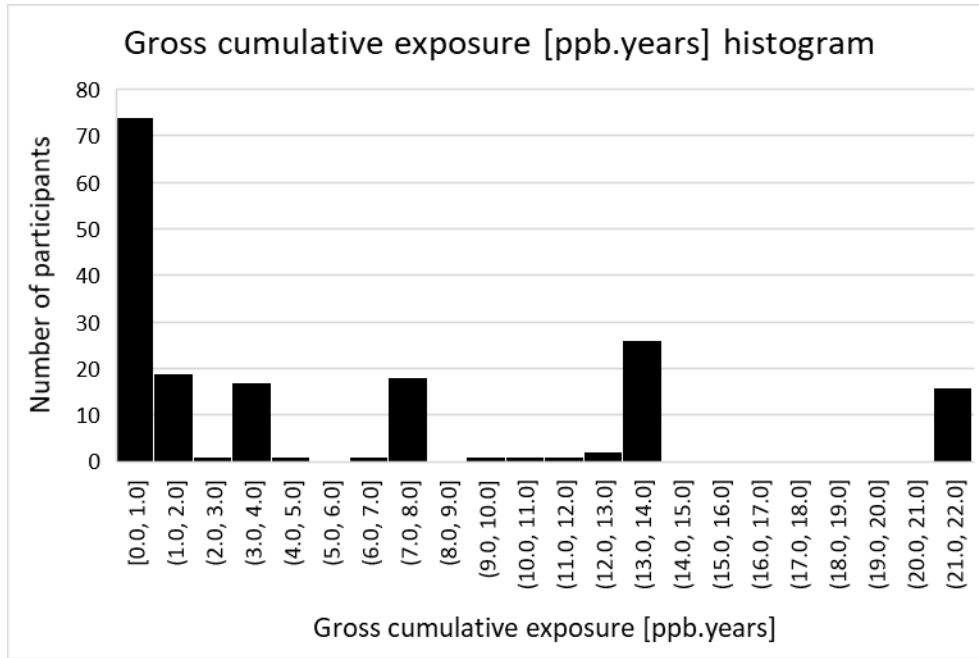
Figure S5-1 – *Histogram of calculated gross cumulative exposure values. X-axis: intervals of gross cumulative exposure values [ppb-years]; y-axis: number of participants. Sensitivity on gross cumulative exposure by assuming 30% overtime for shift work.*

Gross cumulative exposure [ppb-years]		<2		2-4	4-10	10-16	>16
SEG	Support		Others				
Number of participants		46	47	18	21	30	16
Number of asthma cases		0	2	1	1	2	1
Participant-years		190	201	83	87	144	80
Incidence per hundred person-years		0	1.00	1.21	1.15	1.39	1.25

Table S5-1 – *Incidence of TDI-related asthma as a function of gross cumulative exposure categories derived from **Figure S5-1**. Sensitivity on gross cumulative exposure by assuming 30% overtime for shift work. Incidence per hundred person-years of study participation. The overall incidence is 0.9 per hundred person-years.*

Use of μ_T instead of μ_A as an average

Gross cumulative exposure has been calculated as described in the Methods section based upon the average of TWA-values as measured (μ_A).

It was investigated whether replacing the average TWA-values (μ_A) with the reconstituted value calculated from the log-transformed TWA-distributions (μ_T), which assumes that the TWA-values would be log-normally distributed (as described by Middendorf et al., 2017), would affect the outcome.

Figure S5-2 shows the histogram of gross cumulative exposure values in the same format as Figure 1. Compared to Figure 1, gross cumulative exposure for this alternate case has generally shifted to lower values.

Table S5-2 provides the overview of incidence rates in the same format as Table 2.

The 178 data points were analyzed by logistic regression. The slope parameter was not significant (P=0.34 for a linear model), neither was the goodness-of-fit (P=0.38): both indicating no significant relationship between the adjusted gross exposure and asthma incidence for this potential alternate data assumption.
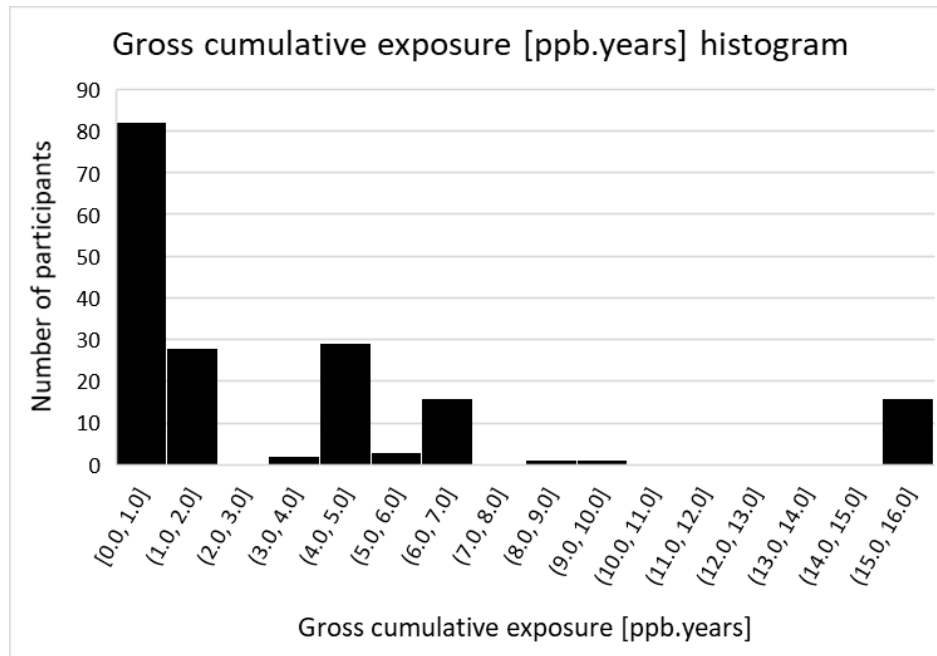
Figure S5-2 – *Histogram of calculated gross cumulative exposure values. X-axis: intervals of gross cumulative exposure values [ppb-years]; y-axis: number of participants. Sensitivity on use of μ_T instead of μ_A.*

Gross cumulative exposure [ppb-years]		<1	1-3	3-6	6-10	>10
SEG	Support	Others				
Number of participants	46	30	34	34	18	16
Number of asthma cases	0	2	1	2	1	1
Participant-years	190	122	159	151	83	80
Incidence per hundred person-years	0	1.64	0.63	1.33	1.21	1.25

Table S5-2 – *Incidence of TDI-related asthma as a function of gross cumulative exposure categories derived from **Figure S5-2**. Sensitivity on use of μ_T instead of μ_A. Incidence per hundred person-years of study participation. The overall incidence is 0.9 per hundred person-years.*