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

Supplemental Information - 1

Criteria for selection of papers for comparison to Collins et al. (2017)

A literature search of both publicly available studies and internal International Isocyanate Institute studies that included respiratory effects and isocyanate exposure was conducted. In addition, citations contained in several key reviews and recent authoritative publications were also considered (Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail (ANSES), 2019; American Conference of Governmental and Industrial Hygienists (ACGIH), 2016; Daniels, 2018; European Chemicals Agency (ECHA), 2019; Greim and Deutsche Forschungsgemeinschaft (DFG), 2003; Health Council of the Netherlands, 2018; Lynch et al., 2018; Ott et al., 2003).

From this list, the following criteria were applied:

- Studies were included that reported (or gave sufficient information to allow the calculation of) asthma incidence rates. Studies that only reported changes in lung function were excluded, as were studies that only assessed immune status (e.g. IgG, IgE levels).
- Studies that included more than one diisocyanate were excluded; only studies in TDI workers were included to minimize potential confounding.
- Studies where diisocyanates were generated from thermal decomposition of polyurethane were excluded, as this does not solely represent exposure to the intact diisocyanate moiety.
- Cross-sectional studies were excluded because of a lack of continuous industrial hygiene measurements and follow-up of the population.

This process resulted in the studies in **Table S1-1** being selected as relevant for comparison to Collins et al. (2017). **Table S1-2** gives as overview of all studies screened.

Reference	Study Type	Study Size	Reported TDI Concentrations	Asthma
Bodner et al. (2001)	Longitudinal	N=305	8-hr TWA TDI values of 2.3 ± 1 ppb After 1980, mean TWA concentrations were below 5 ppb for all job categories. Mean cumulative dose 97 ± 111 ppb.months	10 asthma cases identified between 1971 - 1997.
Bugler et al. (1991)	Longitudinal	N=1,462	8-hr TWA TDI values reported by job Production: 1.6-2.6 ppb Finishing: 0.9-1.6 ppb 22 % and 10 % of 8-hr TWA samples exceeded 20 ppb and 40 ppb, respectively.	81 cases of respiratory sensitization diagnosed, of those 41 diagnosed between 1981-1986.
Diem et al. (1982); Weill et al. (1981)	Longitudinal	N=277	8-hr TWA TDI values reported by job Mean 8-hr TWA: 2 ppb Low-High: 1.6-6.8 ppb In high exposure jobs, 8-hr TWA values exceeded 5 ppb and 20 ppb during 15 % and 10 % of the time, respectively.	12 cases of respiratory sensitization diagnosed between 1973-1978 Yearly incidence rate: 1.0 %
Jones et al. (1992)	Longitudinal	N=386	8-hr TWA TDI values reported by job Production: 2.9-4.5 ppb Finishing: 1.4-1.5 ppb In production jobs, 8-hr TWA values exceeded 20 ppb for 3 % of the time.	12 cases diagnosed between 1982-1986
Ott et al. (2000)	Longitudinal	N=297	8-hr TWA TDI values reported by period and job 1967-1980 - low-high: 3.4-10.1 ppb 1980-1997 - low-high: 0.3-2.7 ppb Between 1976-1988, 36 % and 59 % of 8-hr TWA values exceeded 20 ppb in moderate and high exposure jobs, respectively.	19 cases of respiratory sensitization diagnosed between 1967 - 1976. Yearly incidence rates: 1967-1979: 1.8 % 1980-1996: 0.7 %

Table S1-1 *- Results of a literature search criteria-screened to identify studies relevant for comparison to Collins et al. (2017).*

Citation	Unable to report asthma incidence or prevalence	Cross sectional study design	Exposed to multiple diisocyanates or decomposition products
Adams (1975)	✓		
Belin et al. (1983)	✓		
Bruckner et al. (1968)	✓		
Butcher et al. (1977)	✓		
Clark et al. (1998); Allport (1994)	✓		
Clark et al. (2003)	✓		
Daftarian et al. (2000)		✓	
Daftarian et al. (2002)		✓	
Franzinelli et al. (1978)		✓	
Gee and Morgan (1985)	✓		MDI and TDI exposures
Gui et al. (2014)	✓		
Holness et al. (1984)	✓		
Huang et al. (1991)	✓		
Kim et al. (1997)	✓		
Lee and Phoon (1992)	✓		
Meredith et al. (2000)		✓	
Musk et al. (1982)	✓		
Musk et al. (1985)	✓		
Olsen et al. (1989)	✓		
Omae (1984)	✓		
Omae et al. (1992)	✓		
Omae (1994)	✓		
Peters et al. (1968)	✓		
Peters and Wegman (1975)	✓		
Porter et al. (1975)	✓		
Venables et al. (1985)		✓	
Wang et al. (1988)		✓	
Wegman et al. (1977)	✓		
Wegman et al. (1974)	✓		
Wegman et al. (1982)	✓		
White et al. (1980)			PU degradation products
Williamson (1964)	✓		
Woodbury (1956)	✓		

Table S1-2 *- Studies from a literature search which were eliminated from consideration for comparison to Collins et al. (2017) based on screening criteria.*

References

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