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Research into Malignant and Non-malignant Respiratory Disease Prescriptions: Report for Cleaning Products and COPD

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Contents

1 Introduction 4

2 Methods 5

3 Results 6

3.1 Cohort studies 6

3.2 Case-control studies 7

4 Synthesis and Discussion 8

5 Conclusions 9

6 References 10

Appendix 1 – Data Extraction Spreadsheet and List of All the References Considered 11

Appendix 2- Current prescription for Cleaning Products and COPD 12

1 Introduction

Exposure to cleaning products and chronic obstructive pulmonary disease (COPD) is the third of 6 high-priority occupational exposure-disease combinations that were identified with IIAC as being of highest priority for more detailed investigation (see Report of Phase 1 of this project).

This document contains a commentary on the extracted data for relevant occupational epidemiological studies and is meant to be read in conjunction with the associated spreadsheets containing the data extraction from these studies.

2 Methods

Searches of Web of Science and NLM PubMed databases were undertaken in September/November 2022 using the following search string:

Exposure AND (COPD OR "chronic obstructive pulmonary disease" OR "chronic bronchitis" OR emphysema) AND (bleach OR disinfectants OR clean*) AND (job OR work* OR occupation* OR cleaner* OR nurse* OR health*) NOT (industrial AND solvents)

Bibliographies of the studies included in the cleaning products and COPD reviews found in our earlier literature searches (see below) were searched to identify any additional individual studies that should be screened for inclusion in the tables of evidence.

3 Results

A total of 153 papers were identified in the searches (including duplicates) (see Appendix 1). After screening on title and abstract 22 papers were identified for full text screening. Ten papers were identified as reviews, and a further paper was not accessible. Thus, ten papers were identified for data extraction. During data extraction one paper was excluded as it referred to acute illness (Medina-Ramon et al, 2006).

Overall, 128 relevant papers were identified from the literature searches and screened using title and abstract. No additional papers, not already identified in the searches, were identified from bibliographies of recent systematic reviews (Archangelidi et al 2020; Dumas 2021; Fazen et al 2020; Romero Starke et al 2021).

After exclusion of studies that were not cohort or case-control studies, the search resulted in 10 studies that were included for data extraction, of which 5 were cross-sectional, 4 were cohort, and 1 was a case-control study. To interpret the weight of the evidence, the following two subsections will summarise the results of only the (longitudinal) cohort and case-control studies in order of year of publication.

The full extracted data is contained in Appendix 1.

3.1 Cohort studies

Four relevant cohort studies were identified and had their data extracted (Mirabelli et al., 2012; Van der Borne & Deboosere, 2018; Dumas et al., 2019; Xie et al., 2021). Three of four studies were from the US, with the other from Belgium (Van der Borne & Deboosere, 2018). Two of the US studies examined female nurses (Dumas et al., 2019; Xie et al., 2021). The other US study included cleaners (as well as other occupations) (Mirabelli et al., 2012), as did the Belgian study (Van der Borne & Deboosere, 2018). (See accompanying spreadsheet).

A cohort using data from the ARIC (Atherosclerosis Risk in Communities) study in the US examined 8,967 participants aged 45-64 years (Mirabelli et al., 2012). The incidence of respiratory symptoms (chronic cough, chronic phlegm, and wheezing) and lung function change (annual changes in FEV_1 and FVC in mL) over three years in 'Cleaning and building service' workers (n=188) were compared to those employed in 'managerial and administrative support'. Occupations were self-reported and there was no information on specific cleaning products used, duration of employment or other exposure details. Relative risks (RR) for chronic cough (1.85 [95% CI: 1.01-3.37]) and chronic phlegm (2.28 [95% CI: 1.27-4.08]) were elevated, but not wheezing or airway obstruction. There was no evidence of a decline in lung function; by contrast, male FVC changes (in mL) were significantly less than the reference (22.96 [95% CI: 3.79-42.12]. Estimates were adjusted for age, height, race, sex, and smoking status. A doubling of risk was present in this study, but only for specific symptoms; COPD, specifically, was not included as an outcome in this study.

A cohort derived from the 1991 Belgian population census examined COPD mortality (i.e., underlying cause recorded on death certificates) in 150,054 cleaners, aged 30-60 years (Van der Borne & Deboosere, 2018). Workers were followed up over 20 years and were compared to non-manual workers. SMRs were in excess of 2.00 for both males (2.45 [95% CI: 2.20-2.73]) and females (2.20 [95% CI: 1.93-2.51]). SMRs were attenuated by adjustment for smoking, but estimates remained at or above 2. With separate adjustment for education (i.e., not smoking), SMR confidence intervals decreased below 2 for women (upper CI was still >2 for men). Similar to the Mirabelli study, exposure data was limited to occupation. While this was a large study, interpretation is limited by adjusting for education and smoking in separate models and the limited data assessing exposures to cleaning products. Further, COPD mortality (the outcome in this study) has previously been shown to be underreported (Drummond et al., 2010).

Dumas et al. (2019) investigated associations between disinfectant exposure and COPD risk in the Nurses' Health Study II, a female nurse cohort in the US. 73,262 nurses from 14 US states who were originally enrolled in 1989 were followed through in the present study from 2009 to 2015. COPD was defined as reported physician-diagnosed COPD, and exposure to seven common disinfectants (i.e., formaldehyde, glutaraldehyde, hypochlorite bleach, hydrogen peroxide, alcohol, quaternary ammonium compounds, and enzymatic cleaners) was evaluated by a nurse-specific job-task-exposure matrix) was characterised via a job task exposure matrix (JTEM). The JTEM was based on types of nursing jobs and general disinfection tasks. Cox proportional hazards models were adjusted by age, race, ethnicity, and body mass index. Hazard Ratios (HRs) were elevated for nurses using any disinfectant on a weekly basis (1.35 [95% CI: 1.14-1.59]), with similar estimates for cleaning surfaces or instruments only, and the use of sprays (borderline significant). The trend for frequency of use for each of these indicators was statistically significant. There was no evidence for a doubling of COPD risk.

The other nurse cohort study (Nurses' Health Study in the US [Xie et al., 2021]) included nurses who worked in the operating room (as a proxy for exposure to cleaning products, but also other substances such as surgical smoke) and were followed up from 1984 to 2000. COPD was defined as reported physician-diagnosed COPD. Cox proportional hazards models were adjusted by pack-years of smoking, age, race, ethnicity, and body mass index. The highest HR was apparent for those with the longest duration of operating room experience (>15 years): 1.69 (95% CI: 1.25-2.28), which overlapped with a doubling of COPD risk. A comparison of nurses who worked in inpatient care with no operating room experience (medium to high disinfectant exposure, no surgical smoke exposure) had a HR of 1.31 (95% CI: 1.07-1.59).

3.2 Case-control studies

One case-control study nested in a larger population-based survey examined the risks associated with various cleaning tasks in domestic cleaning women in Spain (Medina-Ramon et al., 2005). There were 40 cases with self-reported asthma/chronic bronchitis symptoms and 155 controls who no such symptoms in the previous 12 months and no history of asthma. There were only 3 COPD cases in this study. Subjects performed at least three acceptable spirometric measures and 'COPD was defined as both a FEV_1 less than 80% of its predicted value and a FEV_1 to FVC ratio less than 0.7'. Exposure was based on 23 cleaning tasks (groups of tasks included general, kitchen cleaning, bathroom cleaning, and laundry) and 22 different cleaning products (groups of products included irritant products, sprays or atomsiers, and other products), which was categorised via a job exposure matrix (JEM). Short-term personal exposures to airborne chlorine and ammonia were completed for 10 participants. ORs were adjusted for employment in non-domestic cleaning, smoking status, and age tertile, and were elevated beyond 2 for intermediate (3.3 [95% CI: 0.9-11]) and high (4.9 [95% CI: 1.5-15]) exposures to bleach. The use of multi-use cleaning products presented inverse risks for intermediate (0.3 [95% CI: 0.1-0.8]) and high (0.2 [95% CI: 0.1-0.6]) exposures.

4 Synthesis and Discussion

Exposure to cleaning products and COPD has not previously been assessed by IIAC. At present, the only occupation prescribed for COPD relates to work as a coalminer. Cadmium exposure is also included, but only for emphysema (as detailed in Appendix 1).

Four recent reviews on occupational exposure to cleaning products and respiratory disease were included in our phase 1 report, which had all been published since 2020 (Archangelidi et al., 2020; Fazen et al., 2020; Romero Starke et al., 2021; Dumas, 2021). The Archangelidi et al. (2020) review also included a meta-analysis of three studies that produced a meta-RR of 1.43 (95% CI: 1.31-1.56) for COPD risk in occupational cleaners. These authors note, importantly, that all studies lacked quantitative exposure estimates to cleaning products. To confirm, we have included in the present report the cohort/case-control studies discussed in these reviews. Some other population surveys may have included cleaners, but were out with the scope of the review (e.g., cross-sectional studies [De Matteis et al., 2016]).

Our search of the literature for relevant epidemiological evidence for cleaning products and COPD yielded four cohort studies and one case-control design. Two of the cohort studies examined risks in cleaners and the other two assessed risks in nurses. An important methodological limitation to the studies of cleaners was the comparison to the reference categories of managerial or non-manual occupations. While some risk excesses were observed in these studies, due to the limited exposure information, it is not possible to attribute these increases to cleaning products rather than other differences between occupational groups (e.g., socioeconomic position). Unadjusted SMRs for COPD were increased in the Van der Borne & Deboosere (2018) study, but were below 2.00 after adjustment for education, which would have been further attenuated with the addition of smoking adjustment. Another possible limitation of these studies is the challenge to differentiate COPD from asthma (Mekov et al., 2021).

One of the nurses studies (Dumas et al., 2019) used a JTEM to characterise frequency of use. A review of nurses' working time suggests <10% is spent on cleaning activities (Lavander et al., 2016). Importantly, trends of higher risks for more frequent use were significant. This internal comparison helps strengthen the interpretation of risks that are more difficult to assess between occupations. The other nurse study (Xie et al., 2021) did suggest a doubling of risk for the development of COPD in those with the most operating room experience. However, with combined exposure to disinfectants and surgical smoke, it is difficult to separate the risk solely to cleaning product exposure.

The sole case-control study presented evidence of risks of asthma/bronchitis symptoms in excess of a doubling for intermediate and high exposure to bleach. By contrast, there were significant inverse risks for the use of multi-use cleaners. Ultimately, there were 3 COPD cases in this study, so, in combination with a relatively small sample size (n= 40 cases), inferences from these results are limited.

5 Conclusions

Overall, the occupational epidemiological evidence for cleaning products and COPD is limited, but suggestive of increased risks. Based on this review alone, there is insufficient evidence to recommend prescription for additional occupational circumstances for COPD.

Nevertheless, given the consistent risks apparent in the available evidence, there are likely to be studies published in the near future with larger sample sizes and more rigorous exposure assessment methods. We recommend that IIAC continues to monitor this literature base as a matter of priority.

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Appendix 1 – Data Extraction Spreadsheet and List of All the References Considered


Data extraction Cleaning Products & (


Cleaning_and_COPD_ All_Papers.xlsx

Appendix 2- Current prescription for Cleaning Products and COPD

Disease Number	Name of Disease or Injury	Type of job
	Miscellaneous conditions not included elsewhere in the list	**Any job involving**
D12	Chronic obstructive pulmonary disease – COPD where, with maximum effort, where there is evidence of a forced expiratory volume in one second which is: (i) at least one litre below the appropriate mean value predicted, obtained from the following prediction formulae which give the mean values predicted in litres: 1. For a man, where the measurement is made without back-extrapolation, (3.62 x Height in metres) minus (0.031 x Age in years) minus 1.41; or, where the measurement is made with back-extrapolation, (3.71 x Height in metres) minus (0.032 x Age in years) minus 1.44 2. For a woman, where the measurement is made without backextrapolation, (3.29 x Height in metres) minus (0.029 x Age in years) minus 1.42; or, where the measurement is made with back-extrapolation, (3.37 x Height in metres) minus (0.030 x Age in years) minus 1.46 or (ii) less than one litre.	Exposure to coal dust (whether before or after 5th July 1948) by reason of working– (a) underground in a coal mine for a period or periods amounting in aggregate to at least 20 years; (b) on the surface of a coal mine as a screen worker for a period or periods amounting in aggregate to at least 40 years before 1st January 1983; or (c) both underground in a coal mine, and on the surface as a screen worker before 1st January 1983, where 2 years working as a surface screen worker is equivalent to 1 year working underground, amounting in aggregate to at least the equivalent of 20 years underground. Any such period or periods shall include a period or periods of incapacity while engaged in such an occupation.
C18	Emphysema	Inhalation of cadmium fumes for a period of, or periods which amount in aggregate to, 20 years or more.

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