STATENS BEREDNING FÖR MEDICINSK OCH SOCIAL UTVÄRDERING

Bilaga till rapport

Exponering för sensibiliserande och irriterande ämnen i arbetsmiljön och koppling till allergisk astma / Exposure to sensitizing and irritating substances in the work environment and its association with allergic asthma
rapport [10] (2024)

Bilaga 2 Sammanfattning inkluderade översikter

Appendix 2 Included reviews

Exposure to sensitizing and irritating substances in the work environment and its association with allergic asthma

Author year, ref	Population studies exposure	Conclusions (quotes from systematic reviews)	RoB SR[1]	Comments
Romero Starke et al 2021, [1]	Health care workers 14 studies, 101 361 individuals **Occupational cleaning or disinfection agents**	”In this systematic review, evidence of an increased risk of asthma in nurses exposed to cleaning or disinfection agents was found. Although the overall evidence was rated as low, the limitations found in this review hint at a potential underestimation of the real risk. These findings highlight the obligation for prevention practices. There is a need to sensitize healthcare workers (as patients), as well as primary care physicians and employers.” Alternative cleaning products that are safer for the respiratory system should be made available to nurses.”	Low[2]	**Systematic review (SR) from updated search at SBU** Risk of bias (RoB) of included studies assessed. Partly comprehensive literature search 12 of 14 studies with asthma as outcome.
Archangelidi et al 2020, [2]	Occupational cleaners 39 studies, number of individuals not given. **Occupational cleaning products**	”In our systematic review and meta-analysis, we found that working as a cleaner is associated with an increased risk of reversible and even irreversible obstructive airway diseases. All studies lacked quantitative exposure assessment to cleaning products; this would help elucidate underlying causal agents and mechanisms. Exposure control and respiratory surveillance among cleaners is warranted to prevent the associated respiratory health burden.”	Moderate[2]	**SR from updated search at SBU** RoB of included studies assessed. Partly comprehensive literature search 21 studies with asthma as outcome.
Vincent et al 2017, [3]	Adults, children 69 studies, number of individuals not given. **Occupational and non-occupational indoor cleaning products**	”Although research indicates an association between asthma and the use of cleaning products, no study robustly investigates exposure to cleaning products or ingredients along with asthma risk. This limits determination of causal relationships between asthma and specific products or ingredients in chemical safety assessment. These limitations, and a lack of robust animal models for toxicological assessment of asthma, create the need for a weight-of-evidence (WoE) approach to examine an ingredient or product's asthmatic potential. This proposed WoE method organizes diverse lines of data (i.e., asthma, sensitization, and irritation information) through a systematic, hierarchical framework that provides qualitatively categorized conclusions using hazard bands to predict a specific	High[3]	RoB of included studies partly assessed. Partly comprehensive literature search

Author year, ref	Population studies exposure	Conclusions (quotes from systematic reviews)	RoB SR[1]	Comments
		product or ingredient's potential for asthma induction. This work provides a method for prioritizing chemicals as a first step for quantitative and scenario-specific safety assessments based on their potential for inducing asthmatic effects. Acetic acid is used as a case study to test this framework."		
Folletti et al 2014, [4]	Cleaners in public buildings 24 studies, 71 163 individuals **Occupational and nonoccupational cleaning products**	"Increased risk of asthma or rhinitis has been shown in 79% of included epidemiological studies. In four studies the increased risk of asthma in cleaning workers was confirmed by objective tests, such as bronchial hyper-reactivity or airflow obstruction. Level of exposure to cleaning products, cleaning sprays, bleach, ammonia, mixing products and specific job tasks has been identified as specific causes of asthma and rhinitis. Possible preventive measures encompass the substitution of cleaning sprays, bleach and ammonia, avoidance of mixing products, the use of respiratory protective devices, worker education and medical surveillance."	Moderate[3]	RoB of included studies partly assessed. No comprehensive literature search
Siracusa et al 2013, [5]	Indoor cleaning workers and cleaners in industrial settings, public or private buildings 24 studies, 320 455 individuals **Occupational cleaning products**	"A large number of studies have demonstrated that domestic and professional cleaning work, especially when associated with the use of household cleaning sprays, bleach, ammonia, disinfectants, and mixing products, may have relevant implications for public health. This is particularly important for common exposure such as the use of cleaning and airrefreshing sprays that are often associated with adult asthma. However, the conclusions of research on cleaners and consequent policy implications have not been heeded by commercial cleaning stakeholder organizations, such as manufactures, vendors, and commercial cleaning companies."	High[3]	RoB of included articles not assessed. No comprehensive literature search
Zock et al 2010, [6]	Cleaners adults 18 studies, 792 061 individuals **Occupational cleaning products**	"Recent studies have strengthened the evidence of asthma and other adverse respiratory effects in cleaning workers. Similar effects were seen in other settings where cleaning products are used such as healthcare professionals and homemakers. Both new-onset asthma and work-exacerbated asthma due to cleaning exposures may play a role. Exposure to cleaning sprays, chlorine bleach and other disinfectants may be particularly relevant. The predominant effect mechanisms remain largely unclear and may include both specific sensitisation and irritant-related features."	High[3]	RoB of included articles not assessed. No comprehensive literature search

Author year, ref	Population studies exposure	Conclusions (quotes from systematic reviews)	RoB SR[1]	Comments
Jaakkola and Jaakkola 2006, [7]	Domestic and industrial cleaners 12 studies, number of individuals not given. **Occupational and nonoccupational cleaning products**	"Recent studies strengthen the evidence of an increased asthma risk among cleaners and individuals in other jobs in which they are involved in cleaning. Further research should be directed to elaborate how much of asthma is related to specific sensitization to certain chemicals and how much to airway inflammation induced by exposure to a mixture of irritants."	High[3]	RoB of included articles not assessed. No comprehensive literature search
Baatjies et al 2023, [8]	Wood industry workers 9 studies, 4 084 individuals **Wood dust**	"This review has highlighted that occupational exposure to wood dust in various wood industries, remains a concern for both high and low and middle income countries due to its association with respiratory symptoms, asthma and decline in lungfunction. This risk may be enhanced due to traditional processing techniques as well as the development of new wood products that produce complex exposures of bioaerosols, which may also include chemicals. Whilst there have been recent advances in characterizing these exposures, significant gaps still remain in preventive strategies, including health protective exposure standards to reduce risk. Future studies should focus on better characterization of wood allergens and other bioaerosol components, characterization of specific IgE responses to different wood species, improved understanding of the pathophysiological mechanisms underlying asthma, modelling of the dose-response relationships using refined exposure metrics that go beyond wood dust particulate levels, and harmonization of various international exposure standards for wood dust particulate (bard and soft woods), endotoxins and 13-glucans, to reduce the risks of asthma in wood workers."	High[2]	**SR from updated search at SBU** RoB of included studies not assessed. No comprehensive literature search
Wiggans et al 2016, [9]	Woodworkers in wood processing and furniture manufacturing 55 studies, number of individuals not given.	"In summary, this review found an increased risk of respiratory symptoms and asthma in people working in the wood processing and furniture manufacturing industries. Accelerated lung function decline due to ongoing exposure was evident for specific study groups. It is important to note that although much of the more robust research included was conducted in lower exposure environments, ill health occurred across all exposure groups. Further study is required considering other ways of assessing airway inflammation in the	Moderate[3]	RoB of included studies assessed. Partly comprehensive literature search

Author year, ref	Population studies exposure	Conclusions (quotes from systematic reviews)	RoB SR[1]	Comments
	Occupational wood dust	workplace, to explore the mechanisms through which wood dust causes respiratory disease and asthma and most importantly how to define interventions to reduce wood related respiratory ill health."		
Jacobsen et al 2010, [10]	Wood industry workers e.g., sawmill workers 25 studies, number of individuals not given. **Occupational fresh wood and mixed wood dust**	"In conclusion, this review supports, despite the limitations in study design and exposure assessments, that wood dust exposure is a risk factor for development of asthma, chronic bronchitis, rhino-conjunctivitis and chronic impairment in lung function. The mechanisms are mostly unknown. Concurrent exposures, such as moulds, endotoxin and terpenes, contribute to the health effects in the wet wood industry."	High[3]	RoB of included studies partly assessed. No comprehensive literature search 17 of 25 studies with asthma as outcome.
Jacobsen et al 2010, [10]	Wood industry workers e.g., furniture workers 37 studies, number of individuals not given. **Occupational dry wood dust**	"In conclusion, this review, despite the limitations in study design and exposure assessment, supports that wood dust exposure is a risk factor for development of asthma, chronic bronchitis, rhino-conjunctivitis and chronic impairment in lung function. The mechanisms are mostly unknown. Concurrent exposures like moulds, endotoxin and terpenes might contribute to the health effect, though these exposures are most likely to be present in the fresh wood industry. Formaldehyde may contribute to the health effects, especially in the plywood and MDF processing industry."	High[3]	RoB of included articles not assessed. No comprehensive literature search 16 of 37 studies with asthma as outcome.
Perez-Rios et al 2010, [11]	General populations, woodworkers 19 studies, 18 040 individuals **Occupational and non-occupational wooddust**	"In summary, the relatively large number of studies included, the magnitude of the associations found, the consistency of the results through settings and the existence of mechanisms that give strong biological plausibility to the relation provide evidence that occupational exposure to wood dust may increase the risk of asthma. Future research should include careful evaluation of ethnicity and nativity as risk modifiers and assess duration and intensity of exposure to wood dust."	Low[3]	RoB of included studies assessed. Partly comprehensive literature search
Schlunssen and Schaumburg 1998, [12]	Industrial woodworkers	"The conclusion is that despite possible methodological problems there seems to be a relationship between occupational exposure to the types of wood dust used in Denmark and the development of	High[3]	RoB of included studies not assessed.

Author year, ref	Population studies exposure	Conclusions (quotes from systematic reviews)	RoB SR[1]	Comments
	15 studies, number of individuals not given. **Occupational wood dust**	asthma, KOL and bronchitis. The results would indicate that further studies are clearly needed in order to study the incidence of these diseases and the relation to the specific types and amount of wood dust."		No comprehensive literature search Article in danish. 8 of 15 studies with asthma as outcome.
Caillaud et al 2018, [13]	General and working population adults and children. 61 studies, number of individuals not given. **Occupational and nonoccupational indoor mold**.	"In children, visible mould and mould odour were associated with the development and exacerbations of asthma, providing sufficient evidence of a causal relationship. Results from population-based studies in adults were too few and divergent to conclude at more than a limited level of evidence. Exposure to mould in a work building was associated with the incidence and exacerbations of occupational asthma, and we concluded at sufficient evidence for an association. "	High[3]	RoB of included studies not assessed Partly comprehensive literature search
Sharpe et al 2015, [14]	Adults, children 17 studies, 7 269 individuals **Nonoccupational indoor environment fungi (home)**	"Longitudinal studies assessing increased exposure to indoor fungi before the development of asthma symptoms suggests that Penicillium, Aspergillus, and Cladosporium species pose a respiratory health risk in susceptible populations. Increased exacerbation of current asthma symptoms in children and adults were associated with increased levels of Penicillium, Aspergillus, Cladosporium, and Alternaria species, although further work should consider the role of fungal diversity and increased exposure to other fungal species."	Low[3]	RoB of included articles assessed. Partly comprehensive literature search
Kolstad et al 2002, [15]	Nonindustrial workers e.g day care and office workers 59 studies, 25 560 individuals **Occupational molds in non-industrial**	"Overall, we conclude that the weight of evidence indicates that exposure to exceptionally high mold levels may cause allergic alveolitis and inhalation fever, and this finding may also pertain to buildings severely damaged by extensive and prolonged mold growth. However, the studies we reviewed provide no evidence that increasing levels of viable mold exposure in nonindustrial work environments or dwellings are related to an increasing occurrence of asthma or to nose, eye, and skin symptoms; fatigue; or headache in the adult population, which may be due to inappropriate or insufficient measures of mold	Moderate[3]	RoB of included studies assessed. No comprehensive literature search 14 of 59 studies with asthma as outcome.

Author year, ref	Population studies exposure	Conclusions (quotes from systematic reviews)	RoB SR[1]	Comments
	indoor environments or dwellings	exposure. No consistent indications were presented that related total fungal biomass to health effects; however, the studies were few."		
Antoniou and Zeegers 2022, [16]	Production and manufacturing workers 14 studies, 5 742 individuals **Toluene diisocyanate**	"In conclusion, based on the results of this systematic review and meta-analysis, there seems to be no meaningful association between toluene diisocyanate exposure, occupational asthma, and lung function when comparing exposed to non-exposed individuals. Considering all methodological limitations, the results of the existing human epidemiological studies should be interpreted and used with caution."	High[2]	**SR from updated search at SBU** RoB of included studies partly assessed. Partly comprehensive literature search
Macan et al 2022, [18]	Hairdressers 42 studies, **Persulphate salts**	"To conclude, hairdressers are occupationally more exposed to persulphate salts (PS) than the general population using hair bleach, with a calculated 20 times higher risk of developing respiratory symptoms from PS exposure than people with no occupational exposure. PS are the main cause of occupational rhinitis and asthma in hairdressers and one of the leading causes of occupational asthma in some European countries. Preventive safety at work measures for reducing inhalatory exposure to PS in hair salons should be re evaluated and implemented, including adopting a harmonized occupational exposure levels (OEL) at EU level. Use of safer bleach formulations and further research in this field should be encouraged. For the last 20 years, epidemiological data regarding adverse respiratory effects of PS in hairdressers are generally scarce, and the lack of well conducted cohort studies at EU level is particularly evident."	High[2]	**SR from updated search at SBU** RoB of included studies not assessed. Partly comprehensive literature search
Coureau et al 2021, [19]	Workers in automotive, chemical and wood industry 39 studies, number of individuals not given.	"Occupational asthma caused by isocyanates is still a current occupational health problem, and its reduction over time has stagnated for several years despite the implementation of individual and collective preventive measures. Several animal studies included in the literature reviews that we analyzed have shown that sensitization to isocyanates in animals is possible by the cutaneous route. In	High[2]	**SR from updated search at SBU** RoB of included studies not assessed.

Author year, ref	Population studies exposure	Conclusions (quotes from systematic reviews)	RoB SR[1]	Comments
	Isocyanates	humans, we currently have only indirect evidence of pulmonary sensitization by this route, i.e., urinary biomarkers and HDI-conjugated keratin found in employees whose workplace was subject to analytical measurements of respiratory exposure below the detection threshold. It would be very useful to study this exposure route more closely, as it could explain why the incidence of isocyanate-related occupational asthma seems to have plateaued. This could then help to define which skin protection equipment would be most effective against these agents. We also need to develop precise, rigorous and reproducible methods that should be used in future cohort studies. This common methodology would enable us to perform meta-analyses with acceptable power to compare the relative risk for isocyanate used between different occupations and different types of industry."		Partly comprehensive literature search
Mohammadian and Nasirzadeh 2021, [20]	Workers in 3D printing workplaces. 28 studies, number of individuals not given. **Occupational exposure to synthetic polymers in the 3D printing and bioprinting industries**	"In 3D printing industries, respiratory symptoms such as irritation, asthma, allergic rhinitis oxidative stress, COPD, DNA damage, and central nervous system effects have been reported. Also, several monomers emitted from the thermal deposition of synthetic polymers were known as carcinogenic materials. There was no study on occupational exposure to pollutants or toxicity and bioprinting processes. However, some studies reported that most resins including acrylates and epoxy resins that are used in bioprinting have toxic effects. So, this systematic review emphasizes the need for more studies about toxicity of 3D printing- and bioprinting-induced air pollutants. Also, consideration of safety and health principles is necessary in 3D printing and bioprinting workplaces.	High[2]	**SR from updated search at SBU** RoB of included studies not assessed. Partly comprehensive literature search
Daniels 2018, [17]	Working population 11 studies, number of individuals not given. **Occupational toulene diisocyanate**	"This study synthesized epidemiologic data to characterize the toulene diisocyanate -occupational asthma dose-risk relationship. This approach yielded prospective occupational exposure limits estimates below recent recommendations by the American Conference of Governmental Industrial Hygienists, but given significant study limitations, this should be interpreted with caution. Confirmatory research is needed."	Moderate[3]	RoB of included studies not assessed. Partly comprehensive literature search
Nett et al 2017, [21]	Industry workers e.g automobile, plastic, fabric, tire	"In summary, a review of available case reports, cross-sectional studies, and mortality studies suggested occupational exposure to styrene is a potential risk factor for non-malignant respiratory disease (NMRD), and related morbidity and mortality. This review highlighted	High[3]	RoB of included studies not assessed.

Author year, ref	Population studies exposure	Conclusions (quotes from systematic reviews)	RoB SR[1]	Comments
	manufacturing workers 57 studies, number of individuals not given. **Occupational styrene**	the need for higher quality data. Additional animal exposure studies using novel humanized rodent models that better mimic human physiology would help address remaining questions regarding the development of lung disease following inhalational exposure to styrene. Additional studies should also include prospective and longitudinal investigations to further describe the risk for respiratory morbidity and mortality among short- and long-tenured workers in industries using styrene, both during and after employment, particularly for those with high styrene exposures. Finally, assessing for styrene and other chemical exposures in future epidemiologic studies could allow for added clarification of the influence styrene has on respiratory toxicity in workers with mixed chemical exposures."		No comprehensive literature search
Canova et al 2013, [22]	General population 20 studies, 51 239 individuals **Occupational and nonoccupational domestic paint**	"The variable quality of the exposure assignment and heterogeneous study design makes it difficult to draw firm conclusions on whether domestic paint exposures cause or exacerbate asthma in children and/or adults."	High[3]	RoB of included studies not assessed. No comprehensive literature search
Jaakkola and Knight 2008, [23]	Workers e.g., industry workers, children, animals 41 studies, number of individuals not given. **Occupational phthalate from PVC**	"High levels of phthalates from PVC products can modulate the murine immune response to a co-allergen. Heated PVC fumes possibly contribute to development of asthma in adults. Epidemiologic studies in children show associations between indicators of phthalate exposure in the home and risk of asthma and allergies. The lack of objective exposure information limits the epidemiologic data."	High[3]	RoB of included studies not assessed. No comprehensive literature search
Arcangeli et al 2020, [24]	Farming and agriculture workers 36 studies, number of individuals not given.	"Agriculture is widely acknowledged as being one of the most hazardous of all employment sectors throughout the world, causing many occupational accidents and diseases in farm workers every year. Elicitors and triggering factors attributable to the agricultural environment and activity may lead to anaphylactic reactions. This	High[2]	**SR from updated search at SBU** RoB of included studies assessed.

Author year, ref	Population studies exposure	Conclusions (quotes from systematic reviews)	RoB SR[1]	Comments
	Occupational organic dust	study purposes to improve awareness of such a risk within the articulated sector with wide-ranging profiles both in terms of employment and of enterprise. Within the multiple agriculture sub-sectors, including the variability of production processes (ranging from the highly mechanized and large scale operations (intensive agriculture), to the less mechanized and more labor-intensive farming (extensive agriculture), and to the biological ones, their seasonal trend and the complexity of multiple tasks involved, all determine different exposure conditions that are associated to precise risk profiles. Furthermore, awareness of anaphylaxis risk in particular groups of workers, such as women and migrant workers, should be of particular concern. Hence, the need to assess the potential risk of allergic anaphylaxis linked to individual activities, so as to be able to suggest accurate prevention and protection measures, as well as management strategies, specifically addressed to all specialists who deal with occupational health and safety."		Partly comprehensive literature search 3 studies focus on asthma.
Zhang et al 2019, [25]	Working population 17 studies, 10 204 individuals **Occupational organic dust**	"Our results showed that organic dust exposure was positively associated with asthma, whether among population-based case-control studies or hospital-based case-control studies. Subgroup analysis indicated that paper/wood, flour/grain, and textile dust exposure, namely, most varieties of organic dust are related with asthma significantly. In conclusion, our meta-analysis revealed an overall asthma susceptibility rate in excess of 48% among individuals exposed to organic dust compared with controls, especially for those exposed to paper/wood, flour/grain and textile dust."	Moderate[3]	RoB of included studies assessed. Partly comprehensive literature search
Wunschel and Poole 2016, [26]	Farming, agriculture workers 14 studies, number of individuals not given. **Occupational organic dust, pesticides**	"The occupation of agriculture represents a complex exposure environment for farm workers, and the resultant airway disease outcomes depend on the interplay of genetic factors, gender, atopic predisposition, type of livestock, pesticide exposure, and magnitude and duration of exposure in the adult subject. Retrospective and cross-sectional studies have supported that farming exposure can decrease the risk of asthma in the adult subject with longer exposure duration to occupational farming further decreasing asthma risk. However, the healthy worker effect might be missed in the retrospective study designs as evident by a longitudinal study demonstrated that	High[3]	RoB of included studies not assessed. No comprehensive literature search

Author year, ref	Population studies exposure	Conclusions (quotes from systematic reviews)	RoB SR[1]	Comments
		agricultural work is an independent risk factor for developing asthma. Multiple types of livestock exposure appear to increase asthma risk, particularly for the development of nonatopic asthma. Prospective and longitudinal studies of adult populations focused on genetic polymorphisms and objective lung function assessments coupled with environmental sampling are suggested to further define risk factors for occupational exposed adult farmers to ultimately reduce asthma disease burden."		
Reynolds et al 2013, [27]	Dairy workers, farmers 30 studies, 18 784 individuals **Occupational organic dust**	"Recent studies focusing on larger modern dairies are consistent with historical studies providing evidence of an association between lung disease and both the extent and duration of exposure to endotoxin-containing aerosols in dairies. Generally mild obstructive changes are reported, but decreases in FVC have been noted in some studies rather than or in addition to decreases in both baseline, cross-shift, and longitudinal FEV1. Although a few studies have shown a reduction in respiratory effects among workers in modern dairies, both exposures and health effects remain significant. There is new evidence concerning the important role of inhalation exposures in addition to endotoxin and indicating that intrinsic factors such as genetic factors are likely powerful modifiers of exposure-response relationships. Future efforts should focus on the development and evaluation of cost-effective interventions that reduce the burden of lung disease among dairy workers."	High[3]	RoB of included studies not assessed. No comprehensive literature search 7 of 30 studies with asthma as outcome.
Lai and Christiani 2013, [28]	Textile/clothing industry workers 8 studies, number of individuals not given. **Occupational textile dust**	"Organic dust exposure in the textile industry leads to obstructive lung disease that has features of both asthma and COPD. Cessation of workplace exposure may lead to improved lung function. An inversion of the pulmonary macrophage:dendritic cell ratio may be a mechanistic explanation for persistent inflammation and obstructive lung disease seen in endotoxin-related textile exposures. Further research on the anatomic lesion (reversible or irreversible airways disease vs. emphysema) and the mechanism underlying textile dust related obstructive lung disease needs to be done."	High[3]	RoB of included studies not assessed. No comprehensive literature search
Jurewicz et al 2007, [29]	Greenhouse workers	"The review has revealed that working in greenhouses may increase the risk of respiratory disorders, sensitization to allergens and skin effects. Exposure to dust, bacteria, allergens, fungi and gases may	High[3]	RoB of included studies not assessed.

Author year, ref	Population studies exposure	Conclusions (quotes from systematic reviews)	RoB SR[1]	Comments
	16 studies, 32 822 individuals **Occupational bacterial and fungal biopesticides, endotoxin, fungi and mites**	cause or exacerbate asthma, asthma-like syndrome, mucous membrane irritation, chronic bronchitis, and dermatitis. Also, some studies present evidence for the carcinogenicity of many pesticides used in greenhouses."		Partly comprehensive literature search
Mamane et al 2015, [30]	Agricultural and industry workers 41 studies, number of individuals not given. **Occupational pesticides**	"In conclusion, this review clearly demonstrates that occupational exposure to pesticides presents a risk to the respiratory tract. Only a few studies measured lung function parameters, but results always showed a decrease in some parameters in association with exposure to certain pesticides, suggestive of an obstructive or restrictive syndrome. It is also worth noting that in some studies, symptoms or diseases were self-reported by subjects, although it would be preferable to use validated questionnaires from lung specialists and respiratory societies, with questions referring to diseases diagnosed by a doctor or to measures of respiratory function. When possible, respiratory function measures and medical check-ups would be useful. Regarding the sample size, larger groups of subjects are required in order to better highlight the risks associated with specific contexts and specific chemical classes of pesticides. Further studies should particularly focus on pesticide exposure assessment (cumulative lifetime exposure) and specific pesticide identification, in order to determine possible dose–effect relationships, and finally assess the causal relationship."	High[3]	RoB of included studies not assessed. No comprehensive literature search
Doust et al 2014, [31]	Primary agricultural workers and children 23 studies, number of individuals not given. **Occupational and nonoccupational pesticides**	"Results suggest that exposure to pesticides may be associated with prevalent asthma, but methodological issues, such as cross-sectional/case–control design, measurements of exposure and limited adjustment for confounders, limit the strength of the evidence base in this area. The association between pesticide exposure and asthma appears to be more evident and consistent in children than in adults."	Low[3]	RoB of included studies partly assessed. No comprehensive literature search 17 of 23 studies with asthma as outcome.

Author year, ref	Population studies exposure	Conclusions (quotes from systematic reviews)	RoB SR[1]	Comments
Cartier 2015, [32]	Working population with asthma 10 studies, 18 individuals **Occupational exposures**	”The list of agents causing immunologic occupational asthma is continuously growing in our industrialized countries and clinicians should always suspect the diagnosis in new-onset adult asthma or in subjects with newly uncontrolled asthma. In 2012–2014, 10 new agents (seven high molecular weight and three low molecular weight agents) were reported as airway sensitizers whereas new occupational environmental exposures were reported for eight known airway sensitizers. A good medical history is critical for the diagnosis but it should always be combined with objective evidence of work-related asthma. The documentation of any new case of occupational asthma should be considered as a sentinel health event leading to proper assessment of the workers' environment and reduction of exposure in other workers.”	High[3]	RoB of included studies not assessed. No comprehensive literature search The objective of the study was to review all new cases of well documented immunologic occupational asthma between January 2012 and mid- 2014
Baur and Bakehe 2014, [33]	Working population 865 studies, number of individuals not given. **Occupational exposures**	”This work comprises the largest list of occupational agents and worksites causing allergic asthma. For the first time, these agents are assessed in an evidence based manner. The identified respiratory allergic agents or worksites with at least moderate evidence for causing work-related asthma may help primary care physicians and occupational physicians in diagnostics and management of cases suffering from work-related asthma. Furthermore, this work may possibly provide a major contribution to prevention and may also initiate more detailed investigations for broadening and updating these evidence-based evaluations.”	Moderate[3]	RoB of included studies partly assessed. No comprehensive literature search Two systematic reviews (SR) by Baur reported in Dalboege et al [33, 34], since both were overlapping the SR restricted to sensitizing exposures was selected by review authors This SR contains approx 70 percent of the studies included in Dalboege et al.

[1]RoB SR: Risk of bias of systematic reviews assessed using AMSTAR 2 tool [35], [2]Risk of bias assessed at SBU, [3]Risk of bias assessed by review authors

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