

Original Article

Vaccine-Preventable Infections in Childcare Workers

A Systematic Review and Analysis of the DEGS1 Study and of Notifiable Disease Surveillance Data

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Summary

Background: Adequate immunity to so-called childhood diseases can lower the occupational risk of vaccine-preventable infectious diseases in persons who work in day-care centers for children.

Methods: A systematic literature survey was carried out in PubMed and Embase for the period January 2000 to February 2019. Studies on immune status and vaccination status were included. In addition, data from the first wave of the German Health Interview and Examination Survey for Adults (*Studie zur Gesundheit Erwachsener in Deutschland*, DEGS1) and surveillance data on notifiable infections in Germany were evaluated.

Results: Six studies and the DEGS1 analysis of vaccination or immune status for varicella zoster, rubella, hepatitis A (HAV), pertussis, measles, and mumps in persons caring for children in day-care centers, most of whom are women, were included in this review. According to DEGS1, childcare workers are more commonly vaccinated against HAV and pertussis than the general female population (prevalence ratios [PR]: 1.46 [1.12; 1.90] and 1.57 [1.05; 2.36]), yet 57% had not been vaccinated against HAV and 77% had not been vaccinated against pertussis. Childcare workers were found to be less commonly vaccinated against rubella than the general female population, although the difference was not statistically significant (PR: 0.87 [0.71; 1.07]). In a Canadian study, positive HAV serology was found to be correlated with the duration of activity as a childcare worker. In the DEGS1 study, large proportions of the younger childcare workers in particular were seronegative against measles (16%), mumps (19%), and HAV (37%). Notifiable disease statistics show that those working in community facilities had a markedly higher risk of mumps, pertussis, and varicella (relative risk [RR]: 1.8–2.6) and a somewhat higher risk of rubella and HAV (RR: 1.47 and 1.21, respectively).

Conclusion: Childcare workers have a higher occupational risk of infection but do not always receive the appropriate vaccinations. In particular, women of child-bearing age working in day-care centers should be made more aware of the need for vaccination.

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The question of adequate immunoprotection against the so-called childhood diseases now no longer relates only to children. In Germany 73% (1) and in Europe 62% of patients with notified pertussis are older than 14 years (2), and 35% of notified cases of measles are in persons older than 20 (3). Some of these infections cause more complications in adults than in children and also last longer (4). In addition to a lack of booster vaccinations for tetanus, diphtheria, and pertussis, which are recommended by most European countries (5), decreasing effectiveness of measles vaccine with increasing age has also been observed (6).

Seronegative pregnant women are among the groups at high risk. Measles infection can cause

TABLE 1

Inclusion and exclusion criteria for systematic review

	Inclusion criteria	Exclusion criteria
Population	Working population aged between 16 and 70 years	Age below 16 years or above 70 years, people not in gainful employment
Exposure	Childcare workers in day-care centers and day carers of children aged between 0 and 6 years	Housekeeping staff with no close connection to children (caretaker, kitchen and cleaning staff), medical care staff/nursing staff, environments other than children's day-care facilities
Comparator group	Employees in occupational groups without any particular risk of infection (e.g., office staff with little customer contact) The lack of a control group is not a reason for exclusion	Occupational groups at higher risk of infection (for example, nursing staff)
Outcomes	Primary outcomes relative risk 1a: Infection rate ratio 1b: Infection risk ratio Secondary outcomes: Prevalence rates: 2: Vaccination rates of childcare workers 3: Immune status of childcare workers Communicable diseases/pathogens of interest: measles, mumps, rubella, pertussis, varicella zoster, hepatitis A, hepatitis B, diphtheria, poliomyelitis, Haemophilus influenzae type B (HIB), meningococci, pneumococci, rotavirus, TBE, influenza, rabies, tetanus	Performance testing of protective vaccinations; other pathogens
Study design	Cohort studies, case-control studies, and cross-sectional studies	Randomized controlled trials (RCTs), qualitative studies, ecological studies, case reports, studies prompted by a disease outbreak in a day-care center, experiments, editorials, conference papers/proceedings, posters, letters

Additional criteria: All studies were included regardless of their language. In order to be able to compare the identified data with regard to the study population, we included only studies from Europe, the USA, Canada, Australia, and New Zealand in our analysis. Where recruitment was based on convenience or a self-reported specimen, or where the response was < 10% or was not documented/calculable, the study was excluded from analysis.

pregnancy complications, premature birth, and miscarriage, and congenital varicella zoster or rubella can result in irreversible damage to the child (4, 7, 8). Since the spread of infection is already wide in childhood, primary infections in pregnancy and thus fetal varicella syndrome are rare (9). However, rubella is still endemic in seven EU countries (Belgium, Denmark, Germany, France, Italy, Poland, and Romania) (10), so the risk for congenital rubella infection remains high.

Childcare workers in day-care centers are in constant close contact with children, and droplet infection or smear infection can readily occur. As long as vaccination coverage is anything less than almost complete, such childcare workers have an increased risk for occupational infection with vaccine-preventable pathogens.

With the aim of estimating the infection risk, we undertook a systematic review, analyzed data from the first wave of the German Health Interview and Examination Survey for Adults (DEGS1), and documented the incidence of notifiable communicable diseases in Germany.

Methods

Systematic review

The study protocol was drawn up a priori (PROSPERO registry no. CRD42018083646). This study is part of an overarching systematic review and focuses on vaccine-preventable diseases. Two studies of non-vaccine-preventable diseases have already been published elsewhere (11, 12).

The research question was operationalized by using inclusion and exclusion criteria for population, exposure, comparator groups, and outcomes (Table 1). Our primary outcome was the relative risk of infection, which ideally is measured longitudinally by the seroconversion rate of childcare workers compared with the general population. In order to determine the secondary outcomes, we included studies that used a cross-sectional design to determine vaccination rates or antibody seroprevalence rates ("seropositivity") in childcare workers. We restricted ourselves to studies published from the year 2000 onwards, in order to obtain recent results that were not biased by any cohort effects. Earlier studies were included in the review by Elsner et al (2009) (13).

We conducted our systematic literature search in the databases PubMed and Embase (*eTable 1*) on 12 February 2019. Further information on the method, hand search, data extraction, and quality evaluation can be found in *eBox 1* and *eTable 2*.

The German Health Interview and Examination Survey for Adults and the surveillance of notifiable communicable diseases

In addition to the systematic search, we evaluated data from DEGS1 (14) and from the surveillance of notifiable communicable diseases according to Germany's Infection Protection Act (*Infektionsschutzgesetz*, IfSG). Information on study design and data analysis can be found in *eBox 2* and *eBox 3*.

Results

Study selection and characteristics of the systematic search

The flow chart in the *eFigure* shows the selection process for the 8130 publications identified during the search. Six studies met the inclusion criteria. Three of these were on varicella zoster virus (15–17), two on rubella virus (15, 18), and one each on hepatitis A virus (HAV) (19) and *Bordetella pertussis* (20). All included studies had a cross-sectional design and simultaneously collected data on immune status and/or vaccination status. We therefore did not investigate infection rates or infection risks. The study characteristics and quality evaluations are listed in *Table 2* and *eTable 3*, and the study descriptions can be found in *eBox 4*.

The German Health Interview and Examination Survey for Adults

The characteristics of the study population are summarized in *eTable 4*. One hundred twenty-six female participants (3.4%) reported that they were childcare workers. High seroprevalence rates were found for measles, mumps, rubella (MMR), with no differences between the exposure group and the reference group (*Table 3*, *eTable 5*, *eTable 6*). Of childcare workers under the age of 30 years, 15.7% were seronegative with regard to measles and 18.9% with regard to mumps, and therefore at risk of infection. More childcare workers up to the age of 29 years were seropositive with regard to HAV than in the reference group (62.9% versus 36.0), and their vaccination rates were higher (66.0% versus 38.9%). Just under 80% of childcare workers had not received the pertussis vaccine in the preceding 10 years.

The results of the systematic search and the DEGS1 data analysis are summarized in *Table 3* and *eTable 5*.

The surveillance of notifiable diseases in accordance with Germany's Infection Protection Act (IfSG)

Mumps, pertussis, and varicella were more common among workers in community facilities caring for minors, covered by § 33 of the IfSG, than in the general population between the ages of 15 and 65 years (*Table 4*).

TABLE 2

Assessing the quality of the included studies

Study ID (reference number)	Outcome: disease	Main domains					Minor domains			Overall assessment	
		1. Recruitment & follow-up (for cohort studies)	2. Exposure: definition and measurement	3. Outcome: origin and validation	4. Confounding and effect modification	5. Analysis: methods to reduce research-specific bias	6. Chronology	7. Funding	8. Conflicts of interest		
Outcome: vaccination status											
De Villemeur et al. 2011 (15)	Rubella	●	●	●	●	●	—	●	●	●	
Rebmann et al. 2018 (20)	Pertussis	●	●	●	●	●	—	●	●	●	
Outcome: immune status											
Muecke et al. 2004 (19)	Hepatitis A	●	●	●	●	●	—	●	●	●	
Reignier et al. 2005 (16)	Varicella zoster	●	●	●	●	●	—	●	●	●	
Gyorkos et al. 2005 (18)	Rubella	●	●	●	●	●	—	●	●	●	
De Villemeur et al. 2011 (15)	Rubella and varicella zoster	●	●	●	●	●	—	●	●	●	
van Rijckevorsel et al. 2012 (17)	Varicella zoster	●	●	●	●	●	—	●	●	●	

Quality assessment: Green = quality high; yellow = quality unclear; red = quality low

There are indications that HAV and rubella are also more common in such workers, but the effect did not reach significance. No effect was observed for measles (*Table 4*). In a conservative approach to the data analysis, we included persons for whom no data on a possible job in community facilities caring for minors were available. Here, except for rubella, the risk increases persisted for those employed in community facilities caring for minors (*eTable 7*). Sex-specific evaluation (*eTable 8*) showed tendentially higher risks for male employees in community facilities than for their female counterparts.

Discussion

This systematic review with linked DEGS1 data analysis showed no difference in seroprevalence for mumps, measles, and rubella between childcare workers and the general population. Of the three studies of varicella zoster, one (methodologically limited) analysis showed a significantly higher proportion of female childcare workers who tested seropositive. In a methodologically sound study, positive HAV serology was associated with the length of employment as a childcare worker (odds ratio for every 5 years 1.3; 95% confidence interval [1.0; 1.8]).

According to DEGS1, the vaccination status for HAV and pertussis was higher in female childcare workers than in the female general population (prevalence ratio 1.46 [1.12; 1.90] and 1.57 [1.05; 2.36]); however, 57% of the childcare workers had not been vaccinated against HAV and 77% had not been vaccinated against pertussis.

A substantial proportion of childcare workers were seronegative for HAV (37% of 18–29 year old) and for measles/mumps (16% and 19% of 18–29 year olds, respectively) and therefore at risk of infection.

For childcare workers in community facilities, a consistently raised risk of infection was found for HAV, mumps, rubella, pertussis, and varicella. The risks were tendentially higher for male than for female workers in community facilities. This might indicate greater awareness of the infection risk among female employees.

Regional and disease-specific features

Varicella zoster

The two French studies did not find any differences in seroprevalence, but the Dutch study reported by van Rijckevorsel et al. (17) showed a higher proportion of seropositivity for childcare workers in day-care centers than for women in the general population. Varicella vaccination was not provided for childcare workers at the time we conducted our study. The difference in the seroprevalence rates could therefore be explained by occupational exposure. For Germany, the evaluation of surveillance data for notifiable communicable diseases in childcare workers in community facilities for 2016–19 showed an increased risk of infection with varicella. Since 2009, two-dose vaccination has been generally recommended for children in this country

(21). Currently in Germany, 87.8% of children starting school have received the first and 84.3% the second varicella vaccination (22). This meant that the incidence was substantially reduced (23), but the duration of vaccine protection after two doses and the effects on the development of passive immunity in infants remain uncertain (23, 24).

Rubella

Rubella has been considered eliminated in the entire Americas region since 2005 (25), but rubella infections can still re-occur. Although Canada continues to recommend the vaccination of children and childcare workers (26), the methodologically adequate Canadian study found that 4–20% of female childcare workers of child-bearing age tested seronegative (18). In the study from France (15), almost all female childcare workers and comparator persons tested seropositive, with a tendency for fewer childcare workers to have been vaccinated against rubella. In France as in Germany, rubella remains endemic (10). In Germany, 12 cases of congenital rubella infection have been notified since 2001; since 2015 no further cases have been reported (27). But the risk remains: In the past 4 years, 14 cases of rubella infection have been reported among persons working in community facilities. This translates into a risk increase of 47% in this occupational group compared with the general population, although the difference is not statistically significant.

Hepatitis A

HAV seroconversion mostly does not occur in children of day-care age; only 0.8–3.4% of Canadian children up to age 13 years (28) and 7.2% of German children aged up to 6 years (29) tested seropositive for HAV. In outbreak situations, an increased risk of infection has been described for day-care centers (30, 31). According to the DEGS1 results, a higher proportion of 18- to 29-year-old childcare workers than of women in the general population had been vaccinated and tested seropositive for HAV. Nevertheless, an average of 50.6–64.4% of childcare workers had no HAV antibodies, and this proportion was even higher in certain subpopulations: 84.1% of childcare workers born in Canada (19) and 65.2–72.4% of German female childcare workers aged between 30 and 49 years (14). An association was found between the length of time spent in the job and HAV seropositivity (19). Furthermore, the analysis of surveillance data for notifiable disease in Germany found a 21% increase in the risk of being infected with HAV for workers in community facilities.

Pertussis

A greater proportion of the childcare workers than of persons in the general population had been vaccinated (in the USA, 45.8% [20] against 31.7% [32]; in Germany, 22.5% against 14.3% [14]); however, the data also indicated that a high proportion of childcare workers had not received a pertussis booster vaccination in the preceding 10 years. Since the protection

TABLE 3

Results of the systematic review and the German Health Interview and Examination Survey for Adults (DEGS1)

Study first author (reference number)	Outcome: vaccination status						Outcome: immune status						Results ^{a3}
	Exposed			Not exposed			Exposed			Not exposed			
	N	Posi- tive (%)	[95% CI]	N	Posi- tive (%)	[95% CI]	N	Posi- tive (%)	[95% CI]	N	Posi- tive (%)	[95% CI]	
Varicella zoster													
Reignier 2005 (16)							241	99.6	[96.0; 100]	–			
De Villemeur 2011 (15)							395	100	–	382	99.7	–	PR: 1.00 ^{a3}
Van Rijckevorsel 2012 (17)							242	100	[98.7; 100]	298	93.6	[90.2; 96.2]	PR: 1.07 [1.04; 1.10] ^{a3}
Rubella													
Gyorkos 2005 (18)							476	89.8	–				
De Villemeur 2011 ^{a1} (15)	395	30.2	–	382	34.5	–	395	98.7	–	382	98.2	–	Vaccination status: PR: 0.87 [0.71; 1.07] ^{a3} Immune status: PR: 1.01 [0.99; 1.02] ^{a3}
DEGS1 2015 ^{a2}	100	42.9	[31.8; 54.8]	2719	43.7	[41.3; 46.0]	109	97.8	[92.0; 99.4]	2987	96.4	[95.3; 97.2]	Vaccination status: PR: 0.98 [0.75; 1.29] Immune status: PR: 1.02 [0.98; 1.05]
Hepatitis A													
Muecke 2004 (19)							492	35.6					
DEGS1 2015 ^{a2}	116	42.7	[32.4; 53.7]	3292	29.2	[27.0; 31.5]	115	49.4	[37.7; 61.2]	3099	44.6	[42.1; 47.0]	Vaccination status: PR: 1.46 [1.12; 1.90] ^(*) Immune status: PR: 1.11 [0.87; 1.42]
Pertussis (vaccinated in preceding 10 years)													
DEGS1 2015 ^{a2}	118	22.5	[14.6; 33.0]	3169	14.3	[12.6; 16.2]							Vaccination status: PR: 1.57 [1.05; 2.36] ^(*)
Rebmann 2018 ^{a1} (20)	96	45.8	–										
Measles													
DEGS1 2015 ^{a2}	98	47.5	[36.8; 58.5]	2693	39.3	[36.6; 42.0]	108	91.3	[82.3; 96.0]	2988	91.7	[30.0; 93.1]	Vaccination status: PR: 1.21 [0.95; 1.54] Immune status: PR: 1.00 [0.93; 1.07]
Mumps													
DEGS1 2015 ^{a2}	97	34.2	[24.8; 45.1]	2673	30.6	[28.3; 33.1]	108	90.0	[81.4; 94.9]	2962	86.2	[84.2; 87.9]	Vaccination status: PR: 1.12 [0.82; 1.53] Immune status: PR: 1.04 [0.97; 1.13]

(*) Significant difference between groups < 0.05

^{a1}Vaccination status determined on basis of self-reported data; ^{a2}vaccination status determined on basis of vaccination passport (70.2 %) and self-reported data (29.8 %); ^{a3}authors' own calculation
CI, Confidence interval; PR, prevalence ratio

TABLE 4

Relative risk in community facilities caring for minors versus general population, 2016–2019

Infection	Cases, community facility	Cases, missing data ^{*1}	Total cases ^{*2}	Unadjusted RR ^{*3} [95% CI]	RR ^{*3+4} [95% CI]
Hepatitis A	80	611	3330	1.04 [0.83; 1.30]	1.21 [0.97; 1.52]
Measles	33	189	1448	0.92 [0.65; 1.30]	0.97 [0.69; 1.38]
Mumps	118	537	2206	2.61 [2.16; 3.14]	2.60 [2.15; 3.15]
Rubella	14	159	441	1.79 [1.05; 3.06]	1.47 [0.86; 2.52]
Pertussis	1964	13 246	47 770	2.07 [1.97; 2.16]	1.90 [1.81; 1.99]
Varicella	406	2 775	11 305	1.71 [1.55; 1.89]	1.78 [1.61; 1.96]

^{*1} Cases without any information on possible employment in a community facility.

^{*2} Total notified cases, including lacking data and workers in community facilities

^{*3} Lacking data were not included

^{*4} Mantel-Hänszel estimate, adjusted for sex

Community facility N, > 15–65 years, 2016–2019: 1 529 720; general population N, > 15–65 years, 2016–2019: 52 398 657

CI, Confidence interval; RR, relative risk

conferred by the pertussis vaccine mostly lasts no longer than 5–7 years after vaccination (33–36, e1), these childcare workers are at risk of infection. As a matter of fact, the German surveillance data indicated that the risk of pertussis for workers in community facilities is roughly double than in the general population.

Measles and mumps

The seroprevalence rates for measles and mumps in Germany were high in both the exposure group and the reference group (86–90%). However, 3–16% of female childcare workers had no measles antibodies. Almost one in five female childcare workers tested seronegative for measles and mumps. The risk of mumps infection was almost three times higher for workers in community facilities. The risk of infection was not increased for measles, however. One possible explanation for the differences in risk is the decrease in protection offered by the mumps vaccine over time (37, 38).

Lack of immunity in childcare workers

Overall, the results indicate that a substantial proportion of childcare workers are at risk of infection. Possible reasons for the lack of immunity include inadequate occupational healthcare arrangements and insufficient awareness among childcare workers of the importance of vaccine protection.

Strengths and limitations

The main strengths of this article lie in the systematic approach to the review: The study protocol was drawn up and published a priori. The literature search on the basis of a sensitive search was carried out by two scientists independently of one another, as was the quality evaluation.

Because of the low number of studies, the results of the review should be interpreted with caution. Only two studies (18, 19) showed a low risk for bias. One

of these two high-quality studies (19) found an increased risk of infection with HAV for female childcare workers. The cross-sectional design of the reviewed studies means that it is not possible to pinpoint the date of seroconversion. The individual patients' medical histories or vaccination histories, the most important factors influencing seropositivity, had not been asked about at all or only to an unsatisfactory degree. There is a risk of recall bias due to the self-reporting of vaccination history. Furthermore, there was mostly no adequate description of occupational characteristics and socioeconomic background. Relevant confounders, such as travel abroad or whether the participant had children of their own, were not considered. In some studies (15–17), all childcare workers were included, independently of their contact with children. The study populations investigated to date have consisted almost exclusively of women. Men are increasingly working in child care (39) and should be included to a greater extent in the future.

In 2013, compulsory notification was introduced for all of the communicable diseases reported in this review. One difficulty in assessing risks on the basis of surveillance data lay in finding a suitable denominator for all workers in community facilities. Appropriate employee numbers for children's residential institutions or holiday camps were not available, which means that our estimates of the infection risk may be slightly too high. The inclusion of teaching staff who had contact with children above the age of 6 years and adolescents in the surveillance of notifiable communicable diseases may have led to underestimation of the risks involved in working at day-care centers.

Implications for research

Future studies should determine childcare workers' serostatus before they start their jobs, to enable later risk

assessment according to their duration of employment and their specific activities, taking relevant confounders into account. The inclusion of appropriate comparator groups is crucial.

Occupational and infection protection in Germany

In the occupational area of children's preschool education, the increased risk of infection mandates the duty of prevention, in accordance with the German Labor Protection Act and the Ordinance on Occupational Health Care. Before starting a job, and thereafter at regular intervals, childcare workers have to be educated about their immunoprotection. The provision of vaccinations is integral not only to general healthcare but also to workplace protection measures for which the employer is responsible. Sero-negative women of childbearing age are at risk of pregnancy complications and congenital infections. This means that the provisions of the German Maternity Protection Act also apply. In the case of justified suspicion of an occupational (also congenital) infection, a duty of disclosure exists in the context of statutory occupational accident insurance.

The measures of Germany's Infection Protection Act (IfSG) for children's day-care centers to date include a temporary work ban for childcare workers with MMR, varicella, or pertussis (§ 34 IfSG), as well as a ban on entering a facility in the case of a measles outbreak unless immunity has been confirmed (§ 28 section 2 IfSG).

Since the diseases we have been discussing are highly contagious, and infection can be transmitted before symptoms develop, the existing legal provisions do not yet ensure the effective prevention of disease outbreaks in day-care centers. Strengthening prevention by means of vaccination, as was achieved for medical hospitals/clinics and facilities by the German Prevention Act, could help attain this goal. In this setting, employers are permitted to collect information on the vaccination status and serostatus of their employees in order to decide about the start date or nature of employment if the diseases are vaccine preventable (§ 23a IfSG).

Conclusions

The results of our study show that working in children's day-care centers and schools is associated with a higher risk of infection with hepatitis A, mumps, rubella, pertussis, and varicella. We also found indications that childcare workers in day-care centers are lacking immunity against HAV, pertussis, and mumps, as well as—especially for female childcare workers of childbearing age—measles and rubella. Appropriate advice from a pediatrician and a primary-care physician before starting a new job is therefore very important in prevention of risk, as are occupational healthcare services providing clear information and vaccination advice. Family physicians and gynecologists know their patients' occupations and should work towards effective vaccination protection.

Key Messages

- One of three studies showed a significantly higher proportion of female childcare workers who tested seropositive for varicella zoster (100% versus 93.6%, $P < 0.001$). In Germany, 77% of female childcare workers are not currently vaccine-protected against pertussis.
- An association exists between the length of time spent in an occupation and seropositivity for hepatitis A. About half the educational personnel in Germany do not have immunity against hepatitis A.
- In spite of their occupational exposure and the risk of rubella embryopathy as a result of congenital infection, female childcare workers tend to be vaccinated against rubella to a lesser extent than the general population.
- Surveillance data on notifiable communicable diseases in Germany show a notably increased risk of infection with mumps, pertussis, and varicella for employees of community facilities caring for minors, as well as a tendentially increased risk of infection with rubella and HAV.
- To interrupt the transmission and spread of vaccine-preventable infectious diseases, immunoprotection in childcare workers should be checked regularly in the context of occupational medical screening as well as primary-care or gynecological screening, and appropriate protective vaccination should be offered. From a public health perspective, widening the existing provisions of the German Infection Protection Act to include day-care centers should be considered. The importance of adequate vaccination protection must be pointed out.

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Conflict of interest statement

The authors declare that no conflict of interest exists

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► Supplementary material

For eReferences please refer to:
www.aerzteblatt-international.de/ref2120
eTables, eBoxes, eFigure:
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Supplementary material to:

Vaccine-Preventable Infections in Childcare Workers

A Systematic Review and Analysis of the DEGS1 Study and of Notifiable Disease Surveillance Data

by Marlen Kofahl, Karla Romero Starke, Wiebke Hellenbrand, Alice Freiberg, Melanie Schubert, Stefanie Schmauder, Mascha Luisa Groß, Janice Hegewald, Daniel Kämpf, Johanna Stranzinger, Albert Nienhaus, and Andreas Seidler

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eTABLE 1

Search algorithm of the systematic database interrogation

	Medline via PubMed	Embase via Ovid
1)	nursery nurse[tw] OR nursery teacher[tw] OR nursery-school teacher[tw] OR kindergarten[tw] OR nurser*[tw] OR schools, nursery[mh] OR nurseries[mh] OR child care[tw] OR child care[mh] OR infant care[tw] OR infant care[mh] OR child day*care center[tw] OR child day care centers[mh] OR preschool teacher[tw] OR preschool work*[tw] OR preschool educat*[tw] OR education work*[tw] OR family day care[tw] OR in-home day care[tw] OR family day homes[tw] OR private home child care[tw] OR baby minder[tw] OR child minder[tw] OR day-care mother[tw] OR day nanny[tw] OR early childhood educat*[tw] OR day*care worker[tw]	(nursery nurse\$.mp.) OR (nursery adj1 teacher\$.mp.) OR (kindergarten.mp.) OR (exp nursery school/) OR (child adj1 care.mp.) OR (exp child care/) OR (infant adj1 care.mp.) OR (child day care center\$.mp.) OR (exp day care/) OR (preschool teacher\$.mp.) OR (preschool educat\$.mp.) OR (preschool work\$.mp.) OR (education work\$.mp.) OR (family day care.mp.) OR (in-home day care.mp.) OR (family day homes.mp.) OR (private home child care.mp.) OR (baby minder.mp.) OR (child minder.mp.) OR (day-care mother.mp.) OR (day nanny.mp.) OR (early childhood educat\$.mp.) OR (day\$care worker.mp.)
2)	mumps[tiab] OR "mumps virus"[mh] OR measles[tiab] OR "measles virus"[mh] OR rubella[tiab] OR "rubella virus"[mh] OR "whooping cough"[tiab] OR "whooping cough"[mh] OR pertussis[tiab] OR "bordetella pertussis"[mh] OR chickenpox[tiab] OR varicella[tiab] OR "varicella zoster"[tiab] OR "herpesvirus 3, human"[mh] OR "hepatitis A"[tiab] OR "hepatitis B"[tiab] OR diphtheria[tiab] OR polio[tiab] OR poliomyelitis[tiab] OR "infantile paralysis"[tiab] OR Poliomyelitis[mh] OR "Haemophilus influenzae type b"[tiab] OR "Pneumococcal Infections"[mh] OR "pneumococcal"[tiab] OR "Meningococcal infection"[tiab] OR "Meningococcal disease"[tiab] OR Meningitis[tiab] OR "Meningitis, Meningococcal"[mh] OR rotavirus[tiab] OR influenza[tiab] OR "tick-borne encephalitis"[tiab] OR "Encephalitis, Tick-Borne"[mh] OR "Encephalitis Viruses, Tick-Borne"[mh] OR rabies[tiab] OR tetanus[tiab] OR cytomegaly[tiab] OR cytomegalovirus[tiab] OR "parvovirus b19"[tiab] OR "fifth disease"[tiab] OR borreliosis[tiab] OR "lyme disease"[tiab] OR "borrelia infections"[mh] OR "epstein-barr-virus"[tiab] OR "eb virus"[tiab] OR "Epstein-Barr Virus Infections"[mh] OR "human herpesvirus 4"[tiab] OR "Herpesvirus 4, Human"[mh] OR "hepatitis C"[tiab] OR "hepatitis D"[tiab] OR "hepatitis E"[tiab] OR "hepatitis G"[tiab] OR "herpes simplex virus"[tiab] OR "human herpesvirus 1"[tiab] OR "human herpesvirus 2"[tiab] OR "HSV-1"[tiab] OR "HSV-2"[tiab] OR "HHV-1"[tiab] OR "HHV-2"[tiab] OR Simplexvirus[mh] OR legionella[tiab] OR legionellosis[tiab] OR "legionnaire* disease"[tiab] OR "pontiack fever"[tiab] OR "Mycoplasma pneumoniae"[tiab] OR "Mycoplasma hominis"[tiab] OR "Ureaplasma urealyticum"[tiab] OR ((Enteritis[mh] OR enteritis[tiab]) AND ("enterohemorrhagic Escherichia coli"[mh] OR "enterohemorrhagic Escherichia coli"[tiab] OR "enterohaemorrhagic E* coli"[tiab] OR EHEC[tiab])) OR Shigella[tiab] OR Shigellosis[tiab] OR "bacillary dysentery"[tiab] OR "Dysentery, Bacillary"[mh] OR "Streptococcus pyogenes"[tiab] OR scarlet[tiab] OR "Streptococcus pneumoniae"[tiab] OR "Pneumococcal Infections"[mh] OR "Staphylococcus aureus"[tiab] OR "impetigo contagiosa"[tiab] OR impetigo[tiab] OR impetigo[mh] OR Salmonella[tiab] OR Salmonella[mh] OR Salmonellosis[tiab] OR "Salmonella Infections"[mh] OR Hantavirus[tiab] OR Hantavirus[mh] OR "Hantavirus Infections"[mh] OR HFRS[tiab] OR HPS[tiab] OR HCPS[tiab] OR "head louse"[tiab] OR "pediculus humanus capitis"[tiab] OR Pediculus[mh] OR scabies[tiab] OR Cryptosporidiosis[tiab] OR crypto[tiab] OR cryptosporidium[tiab] OR conjunctivitis[tiab] OR "pink eye"[tiab] OR Conjunctivitis[mh] OR "giardia lamblia"[tiab] OR giardiasis[tiab] OR "beaver fever"[tiab] OR tuberculosis[tiab] OR "Toxoplasmosis"[mh] OR toxoplasmosis[tiab] OR "HIV"[Mesh] OR HIV[tiab]	(mumps.ti.ab.) or (exp Mumps virus/) or (measles.ti.ab.) or (exp Measles virus/) or (rubeola.ti.ab.) or (rubella.ti.ab.) or (exp Rubella virus/) or (whooping cough.ti.ab.) or (pertussis.ti.ab.) or (exp pertussis/) or (chickenpox.ti.ab.) or (varicella.ti.ab.) or (exp chickenpox/) or (human herpesvirus 3.ti.ab.) or (hepatitis a.ti.ab.) or (hepatitis b.ti.ab.) or (diphtheria.ti.ab.) or (exp diphtheria/) or (polio\$.ti.ab.) or (exp Poliomyelitis virus/) or (exp poliomyelitis/) or (infantile paralysis.ti.ab.) or (Haemophilus influenzae type b.ti.ab.) or (exp pneumococcal infection/) or (pneumococcal.ti.ab.) or (meningococcal disease.ti.ab.) or (exp meningococcosis/) or (exp meningitis/) or (meningitis.ti.ab.) or (rotavirus.ti.ab.) or (exp Rotavirus/) or (influenza.ti.ab.) or (tick-borne encephalitis.ti.ab.) or (rabies.ti.ab.) or (tetanus.ti.ab.) or (Cytomegal\$.ti.ab.) or (parvovirus b19.ti.ab.) or (borrel\$.ti.ab.) or (lyme disease\$.ti.ab.) or (exp borrelia infection/) or (epstein-barr-virus.ti.ab.) or (eb virus.ti.ab.) or (exp Epstein Barr virus/) or (human herpesvirus 4.ti.ab.) or (hepatitis c.ti.ab.) or (hepatitis d.ti.ab.) or (hepatitis e.ti.ab.) or (hepatitis g.ti.ab.) or (Herpes Simplex Virus.ti.ab.) or (human herpesvirus 1.ti.ab.) or (human herpesvirus 2.ti.ab.) or (HSV-1.ti.ab.) or (HSV-2.ti.ab.) or (HVV-1.ti.ab.) or (HVV-2.ti.ab.) or (exp Herpes simplex virus/) or (legionella.ti.ab.) or (legionellosis.ti.ab.) or (legionnaire\$ disease.ti.ab.) or (exp legionnaire disease/) or (Mycoplasma pneumoniae.ti.ab.) or (Mycoplasma hominis.ti.ab.) or (Ureaplasma urealyticum.ti.ab.) or (((exp enteritis/) or (enteritis.ti.ab.)) and ((exp enterohemorrhagic Escherichia coli/) or (enteroh?emorhagic E\$ coli.ti.ab.) or (EHEC.ti.ab.))) or (shigella.ti.ab.) or (shigellosis.ti.ab.) or (bacillary dysentery.ti.ab.) or (exp shigellosis/) or (Streptococcus pyogenes.ti.ab.) or (scarlet.ti.ab.) or (Streptococcus pneumoniae.ti.ab.) or (pneumococcal infection.ti.ab.) or (exp pneumococcal infection/) or (impetigo.ti.ab.) or (exp impetigo/) or (Staphylococcus aureus.ti.ab.) or (exp Staphylococcus aureus/) or (salmonella.ti.ab.) or (exp Salmonella enterica serovar Enteritidis/) or (exp salmonellosis/) or (salmonellosis.ti.ab.) or (hantavirus.ti.ab.) or (exp Hantavirus infection/) or (exp Hantavirus/) or (HFRS.ti.ab.) or (HPS.ti.ab.) or (HCPS.ti.ab.) or (head louse.ti.ab.) or (head lice.ti.ab.) or (Pediculus humanus capitis.ti.ab.) or (scabies.ti.ab.) or (Cryptosporidiosis.ti.ab.) or (cryptosporidium.ti.ab.) or (crypto.ti.ab.) or (exp conjunctivitis/) or (conjunctivitis.ti.ab.) or (pink eye.ti.ab.) or (giardiasis.ti.ab.) or (giardia lamblia.ti.ab.) or (exp Giardia intestinalis/) or (tuberculosis.ti.ab.) or (exp tuberculosis/) or (toxoplasmosis/) or (toxoplasmosis.ti.ab.) or (exp Human immunodeficiency virus/) or (hiv.ti.ab.)
3)	#1 AND #2	#1 AND #2
4)	#3 AND „2000/01/01“[DP] : „3000“[DP]	#3 AND 2000:2019.(sa_year).

eBOX 1

Additional information about the systematic literature search

The review follows the recommendations of the “Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)” statement (e2) and of the “Strengthening the Reporting of Observational Studies in Epidemiology (STROBE)” statement (e3). The systematic literature search in the databases PubMed and Embase (*eTable 1*) was performed on 14 February 2018 and updated on 12 February 2019. Two authors independently reviewed the titles and abstracts (MK, MLG) and full texts (MS, SS). Where disagreements occurred, the principal investigator was consulted. A list of the excluded studies can be obtained from the authors on request.

Hand search

In addition to the electronic database interrogation we undertook a hand search of the reference lists of the included studies and review on the same topic, as well as citation tracking using the search engine Google Scholar (e4, e5). The search for gray literature was carried out using the key words of the search strings in German and English in Google Scholar, BASE, and the database Open Grey. The reasons for exclusion of full texts were documented.

Data extraction

The data from the extracted studies were entered by a member of staff into an extraction table and checked by another member of staff. Disagreements were discussed in consensus conferences. In the event of unclear or missing information, the authors of the relevant study were contacted.

Quality assessment

The studies were assessed by using a risk of bias approach adapted from Ijaz et al. (e6). This approach was adapted to the specifics of this reviews and put in concrete terms by using the criteria of the Scottish Intercollegiate Guidelines Network (SIGN) (e7) and the Critical Appraisal Skills Programme (CASP) (e8). Eight quality domains were defined.

The main domains were

- Recruitment
- Definition and measurement of exposure
- Data collection and validation of the outcomes
- Confounding and effect modification
- Methods of analysis
- The minor domains were
 - Chronology
 - Funding
 - Conflicts of interest

As it can be assumed that the serostatus does not affect whether a person is employed as a childcare worker in a day-care center, cross-sectional studies are acceptable for the derivation of prevalence estimates in this study. For this reason, the chronology was categorized as a minor domain. The studies were classified as low quality, high quality, or unclear quality. Studies were declared to be of overall high quality (“low risk of bias”) if all main domains were of high quality.

The quality was assessed by two persons independently. Disagreements were resolved in consensus meetings.

Data synthesis

The results were summarized descriptively. Quantitative evaluation of the results by means of a meta-analysis was not applicable in view of the small number of studies per outcome.

eBOX 2

Data analysis of the German Health Interview and Examination Survey for Adults (DEGS1)

Study design

The DEGS1 collects—in the context of health monitoring in Germany—representative nationwide data on the health of adults, in the form of surveys and medical examinations.

The sample was drawn using a two-stage stratified approach and consisted of persons who had repeatedly been invited to participate in the German National Health Interview and Examination Survey 1998 (GNHIES98) as well as persons invited for the first time. Additional information on the DEGS1 study is available elsewhere (e9–e11). In short, the first wave of data collection took place from 2008 to 2011. The response among reinvited persons was 62% and in those invited for the first time, 42%. In total, 8152 persons aged 18–91 years participated in DEGS1, with 88.8% undergoing the interviewing and examination program at an examination center. Vaccination rates were collected on the basis of the vaccination card and self-reported data, and blood specimens were taken. Among other parameters, antibody laboratory values for measles, mumps, rubella, and hepatitis A were measured. Earlier publications—also using data from the DEGS1 study—were on the topic of vaccination status in adults and the seroepidemiology of hepatitis A and B in the general adult population of Germany (e12, e13). To date, no publication has used the DEGS1 data to investigate the seroepidemiology or the vaccination status of childcare workers in day-care centers.

Modifications of the data set

The data set was restricted to persons aged 18–70 years, in order to adjust the population to the systematic search. As only one male childcare worker had been included, we restricted the data set to women. Their occupation was coded in the data set by using the “classification of occupations 2010” (e14). Persons whose occupations was coded 8311 (occupations in childcare and education) were categorized as exposed staff in day-care centers for the purpose of this study. All remaining persons were included in the comparator group.

The data include the vaccination and immune status for measles, mumps, rubella, and hepatitis A, as well as the vaccination status for pertussis (ever and in the preceding 10 years).

For this study we established age groups (18–29 years, 30–39 years, 40–49 years, and 50–70 years) so as to be able to present seroprevalence rates and vaccination rates stratified by age.

The antibody serology results were coded positive, negative, and borderline in DEGS1. A borderline serology result was re-coded for this analysis: If, additionally, a vaccination was reported, the person concerned was considered seropositive. Where no vaccination had taken place, the person was considered seronegative. If the serology result was borderline and no details on vaccination were given, we assumed a “missing result.”

Data analysis

We used the statistics software package IBM SPSS Statistics 25 to conduct frequency analyses for complex sampling procedures and calculate age-stratified prevalence ratios, which showed the relationship between childcare workers and the general population with regard to antibody serology and vaccination history. This was compared with the results of the systematic search.

eBOX 3

Evaluation of data from the surveillance of notifiable communicable diseases

Study design

The German Infection Protection Act (IfSG) § 6 mandates nationwide notification of hepatitis A, measles, mumps, rubella, pertussis, and varicella. Hepatitis A and measles have been notifiable since the law was introduced in 2001, whereas mumps, rubella, pertussis, and varicella were not added to the list of notifiable diseases until 2013. The notifiable data contain demographic, clinical, and laboratory diagnostic information as well as information on occupations in certain institutions, including community facilities caring for minors. Community facilities are defined in § 33 as children's day-care centers and after-school care, schools and other educational institutions, childminders, residential homes, and holiday camps. The responsible federal state authorities transmit the notifiable data to the Robert Koch Institute (RKI).

The present analysis includes the surveillance data sent to the RKI for hepatitis A, measles, mumps, rubella, pertussis, and varicella in men and women aged 15–65 years for the period 2016–2019. It can be assumed that after a period of habituation following the introduction of mandatory notification in 2013, all these diseases were duly notified from 2016 at the latest. The volume of notifications (incidence of infection) of workers in community facilities was compared with that in persons not working in community facilities.

The numbers of childcare workers in day-care centers and of teachers in schools and vocational schools in 2016–2019 (as the denominator of infection incidence in exposed persons) were obtained from the German Federal Statistical Office (e15–e17); the above-mentioned number of workers was used as an estimate for the number of persons working in community facilities according to IfSG § 33. The number of people between the ages of 15 and 65 years in gainful employment in the period 2016–2019 was also obtained from the Federal Statistical Office.

Data analysis

For each of the communicable diseases mentioned above in each of the years 2016–2019, the unadjusted relative risk and the relative risk adjusted for sex (with 95% confidence intervals) were calculated using the ratio of infection incidence between workers in community facilities and workers in the general population in Germany. Notification data that did not include the location of the infection were excluded from the core analysis. The proportion of notifications that did not include details of occupation in community facilities was relatively high, at 8–38%. For this reason, in a sensitivity analysis, the notified persons with missing details were classed as persons not working in community facilities. In another sensitivity analysis we calculated the results separately for men and women.

Instrument for evaluating the quality of studies included in the systematic review

Deutsches Ärzteblatt International | Dtsch Arztebl Int 2020; 117: 365–72 | Supplementary material

Major risk of bias domains*	Risk	Criteria	Hints/ notes
For cross-sectional studies <i>HINT: We are looking for selection bias:</i> – Was the study population representative of a defined population? # – Was everybody included who should have been included? # – If response on day care center level is slightly <50% but does not indicate selection bias, it will be listed as a demerit in extraction table. <i>Preliminary ruling:</i> – If the recruitment is based on a convenient/ self-reported sampling OR if response is <10% OR if response was not reported/ calculable, the study will be excluded from analysis.	low	☐ Recruitment of the study population was acceptable # ☐ Non-response was less than 50% OR it was >50% and <70%, but substantial differential selection of the study population could be excluded (e.g. by a non-responder analysis).*	
	high	☐ Recruitment of the study population was not acceptable.# ☐ Non-response was >70% OR it was >50% and <70%, but substantial differential selection of the study population could not be excluded.* ☐ Response not reported/ not calculable.	
2. Exposure definition and measurement	low	☐ Exposure definition included at least basic job characteristics (e.g., job tasks, length of employment). ☐ Exposure was accurately measured to minimize bias. ☐ Adequate comparison group of non-exposed workers (e.g. office workers) included.	
	high	☐ Exposure does not cover basic job characteristics. ☐ Exposure was not accurately measured.# ☐ Different methods were used to measure exposure in different groups/cases and control subjects (in case-control studies). ☐ No adequate comparison group of non-exposed workers included (only for outcome 1b)	
	unclear	☐ Not reported.	
	low	☐ Outcome was accurately/ objectively measured to minimize bias (positive serology, medical diagnosis).# ☐ Measurement methods were similar in the different groups.#	
3.1a Outcome “infection rate”. Source and validation	high	☐ Outcome was not accurately or subjectively measured (self-reported).# ☐ Measurement methods were different in the groups.#	
	unclear	☐ Not reported.	
	low	☐ Outcome was accurately/ objectively measured to minimize bias (e.g. positive serology, medical diagnosis).# ☐ Measurement methods were similar in the different groups.#	
	high	☐ Outcome was not accurately or subjectively measured (e.g. self-reported).# ☐ Measurement methods were different in the groups.#	
3.1b Outcome “risk of infection”. Source and validation	unclear	☐ Not reported.	
	low	☐ Outcome was accurately/ objectively measured to minimize bias (e.g. checked by certificates of vaccination, use of validated instruments).# ☐ Measurement methods were similar in the different groups.#	
	high	☐ Outcome was not accurately or subjectively measured (e.g. self-reported).# ☐ Measurement methods were different in the groups.#	
	unclear	☐ Not reported.	
3.2 Outcome “immunization coverage of the nursery-school teachers”. Source and validation Only applicable to vaccine-preventable diseases.	low	☐ Outcome was accurately/ objectively measured to minimize bias (e.g. checked by certificates of vaccination, use of validated instruments).# ☐ Measurement methods were similar in the different groups.#	
	high	☐ Outcome was not accurately or subjectively measured (e.g. self-reported).# ☐ Measurement methods were different in the groups.#	
	unclear	☐ Not reported.	
	low	☐ Outcome was accurately/ objectively measured to minimize bias (e.g. positive serology).# ☐ Measurement methods were similar in the different groups.#	
3.3 Outcome “immunity status of the nursery-school teachers”. Source and validation	low	☐ Outcome was accurately/ objectively measured to minimize bias (e.g. positive serology).# ☐ Measurement methods were similar in the different groups.#	

Major risk of bias domains*	Risk	Criteria	Hints/ notes
4. Confounding and effect modification <i>HINT: If the immunity status of the children in care is not being considered, it will be listed as a demerit in extraction table.</i>	high	☐ Outcome was not accurately or subjectively measured.# ☐ Measurement methods were different in the groups.#	
	unclear	☐ Not reported.	
	low	☐ If risk estimators were calculated, major confounding factors (at least age, sex, SES and for vaccine-preventable diseases, immunization status of child care workers) & effect modifiers were considered. ☐ If only prevalence or incidence was assessed, at least sex, age and immunization coverage (at least mean values for the study population) are described.	
	high	☐ Major confounding factors or effect modifiers were not considered.	
5. Analysis method: methods to reduce research specific bias <i>HINT: If the prevalence of serology is very high, we will not accept Prevalence Odds Ratios as adequate.</i>	unclear	☐ Not reported.	
	low	☐ Authors used adequate statistical models to reduce bias (e.g., standardization, matching, adjustment in multivariate model, stratification, propensity scoring). For prevalences, matching/stratification may not be required as long as a good description of the age structure and immunization status of the population is given.	
	high	☐ Authors did not use adequate statistical models to reduce bias.	
	unclear	☐	
6. Chronology	low	☐ Incident diseases were included.# ☐ Temporal relation may be established (exposure precedes the outcome).# ☐ Negative serology known at baseline (career entry, baseline of study) AND was accurately/ objectively measured. ☐ For outcomes 2 and 3, cross-sectional studies are appropriate.	
	high	☐ Prevalent diseases were included OR prevalent diseases of baseline were not excluded (in cohort studies).# ☐ Temporal relation cannot be established. ☐ Serology is unknown at baseline. ☐ Cross-sectional studies without basic information about temporal course (not applicable to outcomes 2 or 3)	
	unclear	☐ Not reported.	
	low	☐ Grant/ non-profit-organizations* ☐ Study was clearly not affected by sponsors.*	
7. Funding	high	☐ Sponsoring organization participated in data analysis. ☐ Study was probably affected by sponsors.	
	unclear	☐ Industry, combined industry+grant*, unclear if study was affected by sponsors. ☐ Not reported.	
	low	☐ Reported not having conflict of interest or clear from report/ communication that study was not affected by author(s) affiliation.*	
	high	☐ Conflict of interest exists (at least one author).*	
8. Conflict of interest	unclear	☐ Not reported.	

*according to Jaz et al. (2013), with modifications; # SIGN/CASP

eTABLE 2b

eTable 2 a continued

Overall risk of bias assessment:					
Major domains			Low Risk	High Risk	Unclear Risk
	1. Recruitment procedure & follow-up (in cohort studies)				
	2. Exposure definition and measurement				
	3.1a Outcome "infection rate". Source and validation				
	3.1b Outcome "risk of infection". Source and validation				
	3.2 Outcome "immunization coverage of the nursery-school teachers". Source and validation				
	3.3 Outcome "immunity status of the nursery-school teachers. Source and validation				
	4. Confounding and effect modification				
	5. Analysis method: methods to reduce research specific bias				
Minor domains	6. Chronology				
	7. Funding				
	8. Conflict of interest				
General rule for rating:		Low risk of bias: low risk in all major domains High risk of bias: if not low risk	Overall assessment:		

eTABLE 3

Characteristics of the included studies

Study (reference number)	Pathogen	Population		Recruitment	Measurement of exposure	Measurement of outcome
		Study population	Sample			
Muecke et al. 2004, Canada (19)	Hepatitis A	Exposed: Childcare workers in 81 day-care centers Comparator group: None	N = 492, including women = 482 Age: 35.7 (± 9.8) years Response: Day-care center level: 53.3% Employee level: 55.2%	October–December 2001	Data collection: Questionnaires completed by management and childcare workers (participants themselves) Active in age group: < 3 y: n = 218 (46%); ≥ 3 y: n = 200 (42%); no definite age group: n = 54 (11%) Length of time in job: 8.2 (± 6.3) years	Immune status determined by drawing blood sample (AxSYM HAV AB 2.0, Abbott Laboratories, Ill.) No information given about how unclear results were handled.
Reignier et al. 2005, France (16)	Varicella zoster	Exposed: All employed women in 41 day-care centers Comparator group: None	N = 250 (all female) for questionnaire N = 241 (all female) for serology specimens Age: 40-year range: 23–62 years Response: Day-care center level: n.d. Employee level: 89.3%	March–May 2001	Data collection: Two questionnaires (interviewer assisted and completed by participants themselves) Active in age group: n.d. Length of time in job: 15 (range: 1–38) years	Immune status determined by drawing blood sample (Enzygnost anti-VZV/IgG, Dade-Behring) Sera with unclear results were re-tested. If their classification remained uncertain they were considered dubious and were not analyzed.
Gyorkos et al. 2005, Canada (18)	Rubella	Exposed: Female childcare workers in 81 day-care centers; over 18 years old, working more than 15 h/week with children younger than 60 months Comparator group: None	N = 481 (all female) Age: < 20 y: n = 5 (1.1%) 20–29 y: n = 150 (31.5%) 30–39 y: n = 168 (35.3%) > 40 y: n = 153 (32.1%) Response: Day-care center level: 53.3% Employee level: 55.2%	October–December 2001	Data collection: Questionnaires (completed by participants themselves) Active in age group: < 3 y: n = 224 (47.3%) > 3 y: n = 2496 (52.7%) Length of time in job: < 5 y: n = 164 (34.1%) 5–9 y: n = 132 (27.4%) > 10 y: n = 185 (38.5%)	Immune status determined by drawing blood sample (Rubella IgG ELISA) An index value of 1.10 was assessed as positive and 0.90 as negative. Values in between were assessed as unclear; however, none of the results fell into this category.
De Villemeur et al. 2011, France (15)	Rubella and varicella zoster	Population: Women aged 20–50 years, not pregnant Exposed: Women employed in 83 day-care centers Comparator group: Women employed at two French technology companies	N = 777 (all female), of whom exposed: n = 395, comparator group n = 382 Age: Exposed: 39.0 (± 0.7) years Comparator group: 33.9 (± 0.8) years Response: Day-care center level: n.d. Employee level: 63.3% Comparator group: n.d.	2005–2007	Data collection: Questionnaires (completed by participants themselves) Active in age group: n.d. Length of time in job: n.d.	Rubella: Vaccination status determined by questionnaire; immune status determined by drawing blood sample (Enzygnost antirubellavirus/IgG [Dade-Behring]) Varicella zoster: Immune status determined by drawing blood sample (Enzygnost anti-VZV/IgG); unclear results were re-tested with the same test and other commercially available assays. They were classified according to the results of the control tests. If the control results were also unclear, they were not included in the statistical analysis.

Study (reference number)	Pathogen	Population			Measurement of exposure	Measurement of outcome
		Study population	Sample	Recruitment		
Van Rijkevorsel et al. 2012, Netherlands (17)	Varicella zoster	Population: Women aged 18–44 years Exposed: All women employed in 38 day-care centers Comparator group: Women from the Amsterdam Health Monitor Survey, not working in day-care center/care activities	N = 540 (all female), of whom exposed n = 242, not exposed n = 298 Age: Exposed: 29 (IQR = 24–39) years Comparator group: 35 (IQR = 28–40) years Response: Day-care center level: 60.3% Employee level: n.d. ("nearly all")	Exposed: 2007 Comparator group: 2004	Data collection: Interviews Active in age group: n.d. Length of time in job: n.d.	Immune status determined by drawing blood sample: Exposed: SERION ELISA classic VZV IgG Comparator group: EUROIMMUN Anti-VZV IgG-ELISA Only women whose specimens tested positive (cut-off ≥ 110 mIU/mL), were categorized as seropositive.
Rebmann et al. 2018, USA (20)	Pertussis	Exposed: Childcare workers in 23 day-care centers aged between ≤ 30 and ≥ 61 years Comparator group: No suitable group	N = 96, of whom women = 93 Age: ≤ 30 y: 25.0% (n = 24) 31–40 y: 13.5% (n = 13) 41–50 y: 27.1% (n = 26) 51–60 y: 20.8% (n = 20) ≥ 61 y: 13.5% (n = 13) Response: Day-care center level: 76.7% Employee level: 30.4%	September–December 2014	Data collection: Online questionnaires (completed by participants themselves) Active in age group: n.d. Length of time in job: n.d.	Vaccination status determined by questionnaire

n.d.: No data; y, years; IgG, immunoglobulin G; VZV, varicella zoster virus; HAV, hepatitis A virus; ELISA, enzyme-linked immunosorbent assay

eTABLE 4

Characteristics of the DEGS1 population

	Childcare workers in day-care centers (women)	General population (women)
	N (%)	N (%)
Total	126 (3.4)	3541 (96.6)
Age		
Median (SD)	48 (14.8) years	49 (14.4) years
18–29 years	24 (19.0)	523 (14.8)
30–39 years	15 (11.9)	526 (14.9)
40–49 years	30 (23.8)	793 (22.4)
50–70 years	57 (45.2)	1699 (48.0)
Survey type		
Examination and questionnaire	115 (91.3)	3127 (88.3)
Questionnaire only	11 (8.7)	414 (11.7)
Determination of vaccination status		
With vaccination card	99 (78.6)	2474 (69.9)
Without vaccination card	27 (21.4)	1067 (30.1)
Complete information on vaccination status (with or without vaccination passport) and immune status known		
Measles, mumps, rubella	88 (69.5)	2324 (65.6)
Hepatitis A	107 (84.9)	2905 (82.0)
Pertussis (vaccination only in the preceding 10 years)	118 (93.7)	3169 (89.5)

DEGS1, German Health Interview and Examination Survey for Adults; SD, standard deviation

eBOX 4

Description of the studies in the systematic review

Varicella zoster (VZV)

In the study conducted in France by Villemeur et al. (15), almost all participants were seropositive (varicella seroprevalence in childcare workers 100%, in the comparator group 99.7%) (eTable 5). An occupational infection risk could not be calculated because of the seropositivity of almost all comparator subjects. In the study by Reignier et al., which was also conducted in France (16), almost all childcare workers in day nurseries tested seropositive (99.6%; 95% CI [96; 100]). In the Dutch study reported by van Rijckevorsel et al. (17), all female childcare workers in day-care centers tested seropositive for varicella zoster virus (95% CI [98.7; 100]), whereas 93.6% (95% CI [90.2; 96.2]) of women in the comparator group tested seropositive.

Rubella

De Villemeur et al. (15) found seropositivity for rubella in 98.7% of childcare workers in day-care centers and 98.2% of the reference group. In both groups, rubella seroprevalence increased with age (92.9% in 20- to 24-year-olds and 100% from age 35, in each case; fewer childcare workers in day-care centers than members of the comparator group reported that they had been vaccinated against rubella (30.2% versus 34.5%). The Canadian study by Gyorkos et al. (18) showed rubella seroprevalence of 89.8%. Prevalences differed by birth region (89.5% in high-income regions, 94.6% in lower-income regions) and by age (between 80.0% in those under 20 and 95.4% in those over 40). Three factors had a significant effect on seronegativity: young age, no children of one's own, and no rubella vaccination.

HAV

The study by Muecke et al. (19) investigated the seroprevalence of HAV in 482 female childcare workers and 10 male childcare workers in day-care centers in Canada. The overall seroprevalence was 35.6%; the seroprevalence in childcare workers born in highly endemic or lower-income regions was five times as high as in others. Among the childcare workers born in Canada, only 15.9% tested seropositive. In this subgroup, the HAV seroprevalence was associated with the length of time they had worked in a day-care center (5-year odds ratio 1.3; 95% CI [1.0; 1.80]).

Pertussis

The study by Rebmann et al. (20) in the USA found that 45.8% of childcare workers had been vaccinated against pertussis in the preceding 10 years. Only 10.5% of childcare workers reported that their employer had asked them to get vaccinated. Unvaccinated childcare workers reported willingness to have the vaccine as long as this was provided free of charge (74.5%) or on site (70.0%).

Table 3 and eTable 5 summarize the results of the included studies.

eTABLE 5

Results of the included studies and DEGS1

Study	Outcome: vaccination status						Outcome: immune status				Results ³			
First author (reference number)	Vaccination rate	Exposed			Not exposed			Sero-prevalence	Exposed		Not exposed			
		N	positive (%)	[95% CI]	N	positive (%)	[95% CI]		N	Positive (%)	[95% CI]	N		Posi- tive (%)
Varicella zoster														
Reignier 2005, France (16)	–						Total:	241	99.6	[96.0; 100]	–		–	
De Villemeur 2011, France (15)	–						Total:	395	100	–	382	99.7	–	PR = 1.00 ⁴
Van Rieckeversel 2012, Netherlands (17)	–						Total:	242	100	[98.7; 100]	298	93.6	[90.2; 96.2]	PR = 1.07 95% CI [1.04; 1.10] ⁴
Rubella														
Gyorkos 2005, Canada (18)	–						Total:	476	89.8	–			–	
							< 20 y:	5	80.0					
							20–29 y:	150	82.0					
							30–39 y:	168	91.7					
							≥ 40 y:	153	95.4					
De Villemeur 2011, France (15)	Total: ^{*1}	395	30.2	–	382	34.5	–	395	98.7	–	382	98.2	–	Vaccination status (total): PR = 0.87; 95% CI [0.71; 1.07] ⁴
	20–24 y:	14	37.5		57	43.9		14	92.9		57	92.9		Immune status (total): PR = 1.01; 95% CI [0.99; 1.02] ⁴
	25–29 y:	45	46.7		81	49.4		45	95.5		81	97.5		
	30–34 y:	47	36.2		82	32.9		47	97.9		82	98.8		
	35–39 y:	69	34.8		49	26.5		69	100		49	100		
	40–44 y:	112	21.4		55	18.2		112	100		55	100		
	45–50 y:	108	22.2		58	20.7		108	100		58	100		
DEGS1 2015, Germany	Total: ^{*2}	100	42.9	[31.8; 54.8]	2719	43.7	[41.3; 46.0]	109	97.8	[92.0; 99.4]	2 987	96.4	[95.3; 97.2]	Vaccination status (total): PR = 0.98; 95% CI [0.75; 1.29]
	18–29 y:	24	75.4	[53.1; 89.2]	487	80.6	[75.9; 94.5]	22	100	[100; 100]	497	96.2	[93.8; 97.6]	
	30–39 y:	12	40.9	[14.4; 74.1]	477	54.9	[48.7; 60.9]	13	100	[100; 100]	404	96.2	[92.9; 98.0]	Immune status (total): PR = 1.02; 95% CI [0.98; 1.05]
	40–49 y:	29	33.1	[16.2; 55.9]	722	38.8	[34.1; 42.7]	25	100	[100; 100]	645	96.9	[94.6; 98.2]	
	50–70 y:	35	14.7	[6.0; 31.9]	1033	13.8	[11.5; 16.4]	49	92.7	[76.4; 98.1]	1441	96.2	[95.0; 97.1]	
Hepatitis A														
Muecke 2004, Canada (19)	–						Total:	492	35.6					
							Born in Canada:							
							Yes:	339	15.9					
							No:	153	79.1					

Vaccination status (total):
PR = 0.87; 95% CI [0.71; 1.07]⁴

Immune status (total):
PR = 1.01; 95% CI [0.99; 1.02]⁴

Vaccination status (total):
PR = 0.98; 95% CI [0.75; 1.29]

Immune status (total):
PR = 1.02; 95% CI [0.98; 1.05]

Study	Outcome: vaccination status				Outcome: immune status				Results ^{a3}						
	Vaccination rate	Exposed		Not exposed	Sero-prevalence	Exposed		Not exposed							
	N	positive (%)	[95% CI]	N	positive (%)	[95% CI]	N	Positive (%)	[95% CI]						
DEGS1 2015, Germany	Total: ^{a2}	116	42.7	[32.4; 53.7]	3292	29.2	[27.0; 31.5]	Total:	115	49.4	[37.7; 61.2]	3 099	44.6	[42.1; 47.0]	Vaccination status (total): PR = 1.46 95%-K; [1.12; 1.90](*) Relevant difference in age group 18–29 years: PR = 1.70; 95% CI [1.24; 2.32](*) Immune status (total): PR = 1.11; 95% CI [0.87; 1.42] Relevant difference in age group 18–29 years: PR = 1.75; 95% CI [1.26; 2.43](*)
	18–29 y:	23	66.0	[44.4; 82.4]	484	38.9	[34.5; 43.4]	18–29 y:	24	62.9	[42.0; 79.9]	515	36.0	[31.5; 40.8]	
	30–39 y:	12	52.2	[19.3; 83.3]	470	34.3	[29.6; 39.4]	30–39 y:	13	34.8	[12.7; 66.1]	415	42.1	[36.3; 48.2]	
	40–49 y:	28	27.1	[12.8; 48.3]	727	29.6	[25.4; 34.2]	40–49 y:	27	27.6	[13.2; 48.9]	664	33.8	[29.0; 38.9]	
	50–70 y:	53	32.1	[18.6; 49.4]	1611	22.2	[19.4; 25.3]	50–70 y:	51	63.7	[46.6; 77.9]	1505	56.3	[53.0; 59.6]	
Pertussis (vaccinated in preceding 10 years)															
DEGS1 2015, Germany	Total: ^{a2}	118	22.5	[14.6; 33.0]	3169	14.3	[12.6; 16.2]	–							Vaccination status (total): PR = 1.57; 95% CI [1.05; 2.36](*) Relevant difference in age group 40–49 years: PR = 3.31; 95% CI [1.76; 6.22](*)
	18–29 y:	21	26.4	[11.2; 50.4]	468	30.8	[26.0; 36.1]								
	30–39 y:	13	7.8	[1.6; 31.2]	448	12.2	[9.3; 15.7]								
	40–49 y:	28	37.3	[18.4; 61.0]	707	11.3	[8.7; 14.5]								
	50–70 y:	56	13.3	[6.4; 25.7]	1546	8.7	[7.0; 10.7]								
Rebmann 2018, USA (20)	Total: ^{a1}	96	45.8	–				–							
Measles															
DEGS1 2015, Germany	Total: ^{a2}	98	47.5	[36.8; 58.5]	2 693	39.3	[36.6; 42.0]	Total:	108	91.3	[82.3; 96.0]	2 988	91.7	[30.0; 93.1]	Vaccination status (total): PR = 1.21; 95% CI [0.95; 1.54] Immune status (total): PR = 1.00; 95% CI [0.93; 1.07]
	18–29 y:	24	86.4	[65.4; 95.5]	484	82.0	[77.4; 85.9]	18–29 y:	22	84.3	[64.5; 94.1]	490	82.5	[77.7; 86.5]	
	30–39 y:	13	47.1	[18.6; 77.6]	465	47.2	[41.3; 53.1]	30–39 y:	13	95.1	[70.1; 99.4]	405	81.5	[76.0; 86.0]	
	40–49 y:	27	33.3	[15.1; 58.4]	707	27.1	[23.1; 31.6]	40–49 y:	25	88.9	[56.8; 98.0]	643	94.7	[92.1; 96.5]	
	50–70 y:	34	14.9	[6.1; 32.2]	1037	13.3	[11.0; 16.1]	50–70 y:	48	97.4	[86.8; 99.5]	1450	98.8	[98.0; 99.3]	
Mumps															
DEGS1 2015, Germany	Total: ^{a2}	97	34.2	[24.8; 45.1]	2 673	30.6	[28.3; 33.1]	Total:	108	90.0	[81.4; 94.9]	2962	86.2	[84.2; 87.9]	Vaccination status (total): PR = 1.12; 95% CI [0.82; 1.53] Immune status (total): PR = 1.04; 95% CI [0.97; 1.13]
	18–29 y:	24	82.3	[61.3; 93.2]	482	77.6	[72.7; 81.8]	8–29 y:	22	81.1	[59.3; 92.7]	493	82.8	[78.0; 86.7]	
	30–39 y:	12	32.6	[10.3; 67.2]	462	31.2	[25.8; 37.1]	30–39 y:	13	93.7	[64.2; 99.2]	401	78.8	[72.3; 84.1]	
	40–49 y:	26	–	–	698	14.8	[11.8; 18.3]	40–49 y:	25	92.1	[65.1; 98.6]	642	85.5	[81.5; 88.7]	
	50–70 y:	35	14.0	[5.5; 31.1]	1031	8.9	[7.1; 11.0]	50–70 y:	48	94.0	[80.2; 98.4]	1426	91.4	[89.5; 92.9]	

DEGS, German Health Interview and Examination Survey for Adults; y, years; CI, confidence interval; PR, prevalence ratio; (*), significant difference between groups, $p < 0.05$

^{a1} Vaccination status determined on the basis of self-reported data

^{a2} Vaccination status determined on the basis of vaccination card (70.2%) and self-reported data (29.8%)

^{a3} The expanded DEGS 1 results table with all age-stratified prevalence ratios can be found in *eTable 6*

^{a4} Authors' own calculation

eTABLE 6

Expanded table of DEGS1 results

DEGS1 2015	Age	Exposed (women)			Not exposed (women)			Prevalence ratio (PR)		
		N	Positive (%)	[95% CI]	N	Positive (%)	[95% CI]	PR	[95% CI]	P value *
Rubella vaccination, ever	18–70 y	100	42.9	[31.8; 54.8]	2 719	43.7	[41.3; 46.0]	0.98	[0.75; 1.29]	0.90
	18–29 y	24	75.4	[53.1; 89.2]	487	80.6	[75.9; 94.5]	0.94	[0.73; 1.21]	0.57
	30–39 y	12	40.9	[14.4; 74.1]	477	54.9	[48.7; 60.9]	0.75	[0.32; 1.73]	0.43
	40–49 y	29	33.1	[16.2; 55.9]	722	38.8	[34.1; 42.7]	0.87	[0.46; 1.63]	0.64
	50–70 y	35	14.7	[6.0; 31.9]	1 033	13.8	[11.5; 16.4]	1.07	[0.45; 2.57]	0.88
Rubella antibody result	18–70 y	109	97.8	[92.0; 99.4]	2 987	96.4	[95.3; 97.2]	1.02	[0.98; 1.05]	0.46
	18–29 y	22	100.0	[100; 100]	497	96.2	[93.8; 97.6]	1.04	[1.02; 1.06]	0.41
	30–39 y	13	100.0	[100; 100]	404	96.2	[92.9; 98.0]	1.04	[1.01; 1.07]	0.56
	40–49 y	25	100.0	[100; 100]	645	96.9	[94.6; 98.2]	1.03	[1.01; 1.05]	0.45
	50–70 y	49	92.7	[76.4; 98.1]	1 441	96.2	[95.0; 97.1]	0.96	[0.87; 1.07]	0.33
Hepatitis A vaccination, ever	18–70 y	116	42.7	[32.4; 53.7]	3 292	29.2	[27.0; 31.5]	1.46	[1.12; 1.90]	0.01(*)
	18–29 y	23	66.0	[44.4; 82.4]	484	38.9	[34.5; 43.4]	1.70	[1.24; 2.32]	0.01(*)
	30–39 y	12	52.2	[19.3; 83.3]	470	34.3	[29.6; 39.4]	1.52	[0.73; 3.19]	0.34
	40–49 y	28	27.1	[12.8; 48.3]	727	29.6	[25.4; 34.2]	0.91	[0.46; 1.82]	0.79
	50–70 y	53	32.1	[18.6; 49.4]	1 611	22.2	[19.4; 25.3]	1.45	[0.87; 2.40]	0.18
Hepatitis A antibody result	18–70 y	115	49.4	[37.7; 61.2]	3 099	44.6	[42.1; 47.0]	1.11	[0.87; 1.42]	0.43
	18–29 y	24	62.9	[42.0; 79.9]	515	36.0	[31.5; 40.8]	1.75	[1.26; 2.43]	0.01(*)
	30–39 y	13	34.8	[12.7; 66.1]	415	42.1	[36.3; 48.2]	0.83	[0.35; 1.97]	0.65
	40–49 y	27	27.6	[13.2; 48.9]	664	33.8	[29.0; 38.9]	0.82	[0.41; 1.65]	0.56
	50–70 y	51	63.7	[46.6; 77.9]	1 505	56.3	[53.0; 59.6]	1.13	[0.87; 1.46]	0.39
Pertussis vaccination in preceding 10 years	18–70 y	118	22.5	[14.6; 33.0]	3 169	14.3	[12.6; 16.2]	1.57	[1.05; 2.36]	0.04(*)
	18–29 y	21	26.4	[11.2; 50.4]	468	30.8	[26.0; 36.1]	0.86	[0.39; 1.88]	0.69
	30–39 y	13	7.8	[1.6; 31.2]	448	12.2	[9.3; 15.7]	0.64	[0.14; 2.99]	0.56
	40–49 y	28	37.3	[18.4; 61.0]	707	11.3	[8.7; 14.5]	3.31	[1.76; 6.22]	0.00(*)
	50–70 y	56	13.3	[6.4; 25.7]	1 546	8.7	[7.0; 10.7]	1.54	[0.75; 3.14]	0.25
Measles vaccination, ever	18–70 y	98	47.5	[36.8; 58.5]	2 693	39.3	[36.6; 42.0]	1.21	[0.95; 1.54]	0.15
	18–29 y	24	86.4	[65.4; 95.5]	484	82.0	[77.4; 85.9]	1.05	[0.89; 1.25]	0.60
	30–39 y	13	47.1	[18.6; 77.6]	465	47.2	[41.3; 53.1]	1.00	[0.48; 2.06]	1.00
	40–49 y	27	33.3	[15.1; 58.4]	707	27.1	[23.1; 31.6]	1.23	[0.62; 2.45]	0.57
	50–70 y	34	14.9	[6.1; 32.2]	1 037	13.3	[11.0; 16.1]	1.12	[0.47; 2.66]	0.80
Measles antibody result	18–70 y	108	91.3	[82.3; 96.0]	2 988	91.7	[90.0; 93.1]	1.00	[0.93; 1.07]	0.92
	18–29 y	22	84.3	[64.5; 94.1]	490	82.5	[77.7; 86.5]	1.02	[0.86; 1.22]	0.82
	30–39 y	13	95.1	[70.1; 99.4]	405	81.5	[76.0; 86.0]	1.17	[1.04; 1.31]	0.14
	40–49 y	25	88.9	[56.8; 98.0]	643	94.7	[92.1; 96.5]	0.94	[0.77; 1.14]	0.37
	50–70 y	48	97.4	[86.8; 99.5]	1 450	98.8	[98.0; 99.3]	0.99	[0.94; 1.03]	0.36
Mumps vaccination, ever	18–70 y	97	34.2	[24.8; 45.1]	2 673	30.6	[28.3; 33.1]	1.12	[0.82; 1.53]	0.49
	18–29 y	24	82.3	[61.3; 93.2]	482	77.6	[72.7; 81.8]	1.06	[0.87; 1.29]	0.60
	30–39 y	12	32.6	[10.3; 67.2]	462	31.2	[25.8; 37.1]	1.05	[0.39; 2.81]	0.93
	40–49 y	26	–	–	698	14.8	[11.8; 18.3]	–	–	0.06
	50–70 y	35	14.0	[5.5; 31.1]	1 031	8.9	[7.1; 11.0]	1.57	[0.64; 3.90]	0.33
Mumps antibody result	18–70 y	108	90.0	[81.4; 94.9]	2 962	86.2	[84.2; 87.9]	1.04	[0.97; 1.13]	0.33
	18–29 y	22	81.1	[59.3; 92.7]	493	82.8	[78.0; 86.7]	0.98	[0.80; 1.21]	0.84
	30–39 y	13	93.7	[64.2; 99.2]	401	78.8	[72.3; 84.1]	1.19	[1.02; 1.39]	0.17
	40–49 y	25	92.1	[65.1; 98.6]	642	85.5	[81.5; 88.7]	1.08	[0.92; 1.26]	0.47
	50–70 y	48	94.0	[80.2; 98.4]	1 426	91.4	[89.5; 92.9]	1.03	[0.95; 1.12]	0.57

, P value of chi square tests; (), significant differences between groups ($p < 0.05$); DEGS, German Health Interview and Examination Survey for Adults; y, years; PR, prevalence ratio; CI, confidence interval

eTABLE 7

Risk for workers in German community facilities caring for minors (2016–2019)

Infection	RR ^{*1,2} [95% CI]
Hepatitis A	2.05 [0.84; 1.31]
Measles	0.83 [0.59; 1.18]
Mumps	1.94 [1.61; 2.34]
Rubella	0.93 [0.54; 1.58]
Pertussis	1.90 [1.81; 1.99]
Varicella	1.32 [1.20; 1.46]

*¹ Missing data are included in the calculation

*² Adjusted by sex

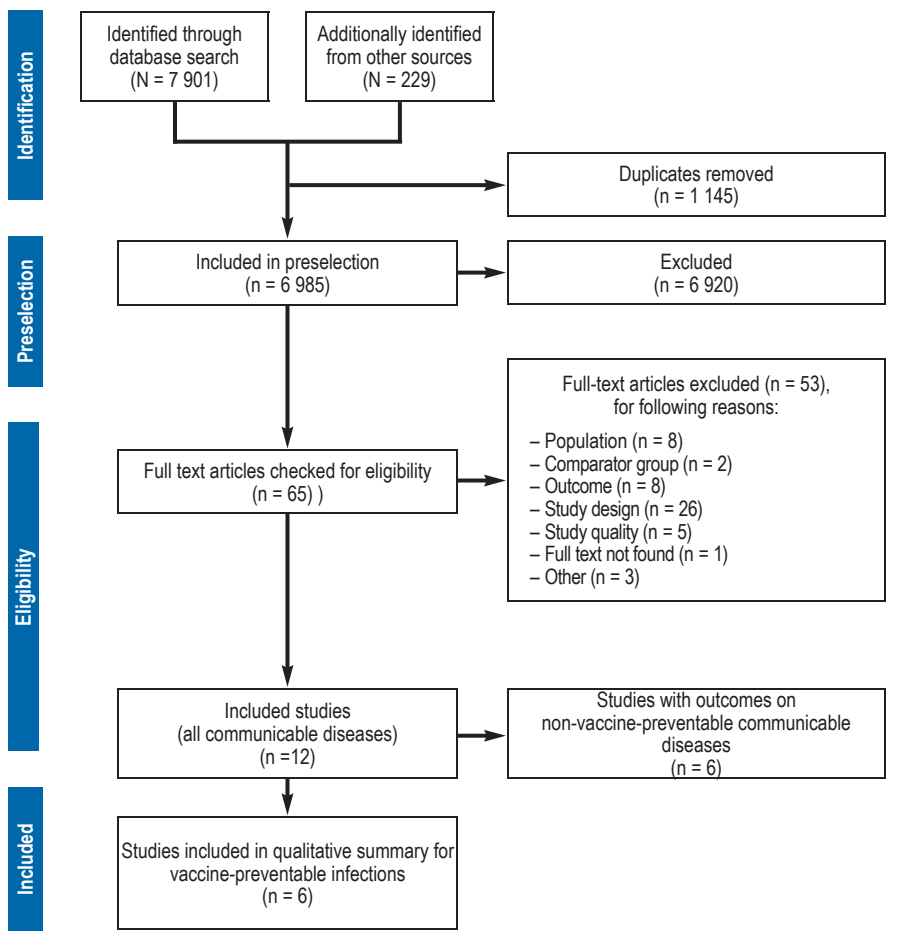
eTABLE 8

Relative risk for certain infectious diseases in workers of community facilities caring for minors versus the general population in Germany (men and women, 2016–2019)

Infection	Sex	Cases in community facilities caring for minors	Cases, total	RR* [95% CI]
Hepatitis A	Men	25	2049	1.33 [0.90; 1.98]
	Women	55	1270	1.16 [0.89; 1.53]
Measles	Men	8	770	1.03 [0.52; 2.08]
	Women	25	677	0.95 [0.64; 1.42]
Mumps	Men	30	1093	3.32 [2.31; 4.78]
	Women	87	1103	2.42 [1.94; 3.02]
Rubella	Men	3	144	2.97 [0.94; 9.39]
	Women	11	296	1.29 [0.70; 2.36]
Pertussis	Men	362	14 124	2.23 [2.01; 2.48]
	Women	1600	18 374	1.83 [1.74; 1.93]
Varicella	Men	117	5902	2.36 [1.96; 2.83]
	Women	287	5329	1.61 [1.43; 1.82]

* Missing data excluded from calculations

eFIGURE



Selection process for publications