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A Global Perspective of Vaccination of Healthcare Personnel against Measles: Systematic Review

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Abstract

Measles transmission has been well documented in healthcare facilities. Healthcare personnel who are unvaccinated and who lack other evidence of measles immunity put themselves and their patients at risk for measles. We conducted a systematic literature review of measles vaccination policies and their implementation in healthcare personnel, measles seroprevalence among healthcare personnel, measles transmission and disease burden in healthcare settings, and impact/costs incurred by healthcare facilities for healthcare-associated measles transmission. Five database searches yielded 135 relevant articles; 47 additional articles were found through cross-referencing. The risk of acquiring measles is estimated to be 2 to 19 times higher for susceptible healthcare personnel than for the general population. Fifty-three articles published worldwide during 1989–2013 reported measles transmission from patients to healthcare personnel; many of the healthcare personnel were unvaccinated or had unknown vaccination status. Eighteen articles published worldwide during 1982–2013 described examples of transmission from healthcare personnel to patients or to other healthcare personnel. Half of European countries have no measles vaccine policies for healthcare personnel. There is no global policy recommendation for the vaccination of healthcare personnel against measles. Even in countries such as the United States or Finland that have national policies, the recommendations are not uniformly implemented in healthcare facilities. Measles serosusceptibility in healthcare personnel varied widely across studies (median 6.5%, range 0%-46%) but was consistently higher among younger healthcare personnel. Deficiencies in documentation of two doses of measles vaccination or other evidence of immunity among healthcare personnel presents challenges in responding to measles exposures in healthcare settings. Evaluating and containing exposures and outbreaks in healthcare settings can be disruptive and costly. Establishing policies for measles vaccination for healthcare personnel is an important strategy towards achieving measles elimination and should be a high priority for global policy setting groups, governments, and hospitals.

Keywords

measles vaccine policy; healthcare personnel; MMR vaccine; measles transmission

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Introduction

Measles, a highly infectious viral disease characterized by a febrile respiratory prodrome and a generalized maculopapular rash, can lead to severe complications and death [1]. In 1980, before widespread measles vaccine use globally, an estimated 2.6 million measles-associated deaths occurred worldwide [2]. With implementation of routine measles immunization policies globally, there have been dramatic reductions in measles morbidity and mortality [1].

The World Health Organization (WHO) has established global measles goals focusing on reduction of measles mortality (≥95% compared with 2000 levels) and achievement of regional measles elimination[1] [3]. Achieving these goals will pave the way for a variety of achievements including reducing childhood mortality by two-thirds between 1990 and 2015 (i.e., the Millennium Development Goal #4) [4], establishing a target date for global measles eradication [4, 5], and ultimately, accomplishing the vision of "achieving and maintaining a world without measles" [3]. Measles was eliminated from WHO's Region of the Americas in 2003 [6, 7] and the Pan American Health Organization is currently certifying measles and rubella elimination for every country in the Region [8]. Elimination goals for 2015 have been established for four other WHO regions in the world [9, 10]. Nonetheless, measles remains endemic in Europe, Asia, Africa, and the Middle East [11] leading to measles importations and outbreaks in many countries that have achieved elimination [12–16].

The majority of measles cases occur in the community but due to the severity of measles, ill persons are likely to seek medical care in primary healthcare facilities, emergency departments, or hospitals resulting in nosocomial/healthcare-associated transmission. The high potential for transmission of measles poses considerable challenges in healthcare facilities, particularly because the illness may not be recognized immediately resulting in a failure to implement appropriate isolation precautions [17–19]. Patients can be highly contagious in the prodromal phase prior to rash onset [1]. Healthcare personnel, including students in healthcare fields who have clinical rotations and volunteers in medical facilities, should be protected against measles either through vaccination or other acceptable evidence of measles immunity [20, 21]. However, measles outbreaks occurring over the last decade have continued to document the problem of healthcare personnel acquiring and transmitting measles, suggesting deficiencies in establishing or implementing measles vaccine policies for this occupational group [18, 22–24].

We conducted a systematic review of literature regarding measles vaccine policies for healthcare personnel, measles seroprevalance, disease burden and transmission in healthcare personnel and impact/costs incurred by healthcare facilities for healthcare-associated measles transmission. This information is intended to help policy makers make, implement, and evaluate policies to prevent measles transmission to and from healthcare personnel.

[1] absence of circulation of measles virus >12 months.

Methods

We reviewed the following databases from the dates indicated through January 2013: PubMed (June 1973), CINAHL (June 1990), Web of Science (1982), Embase (1988), and Ovid Medline/Ovid OLDMedline (1946). We used the following search terms: ("measles" or "MMR vaccine" or "measles transmission" or "measles vaccine policy") and ("healthcare workers" or "health-care workers" or "health care workers" or "healthcare personnel" or "health-care personnel" or "health care personnel"). We included articles written in English. We also cross-referenced articles referenced in the above searches that were not captured in the online database searches. Additionally, we conducted a Google search of governmental health agencies (e.g., Public Health Agency of Canada, Public Health England), as well as international health agencies (e.g., WHO), to search for measles vaccine policies and measles evidence of immunity requirements. For calculating summary statistics (mean, median, interquartile range) for percent of healthcare personnel who were measles seronegative by region, we excluded studies that reported on a non-representative sample (i.e., those reporting only on persons without evidence of measles immunity).

Results

Literature search findings

The database searches yielded 135 relevant articles out of 931 potential articles retrieved and an additional 47 articles were found through cross-referencing for a total of 182 relevant articles. Of these, we included 125 articles in the results section of the review. The remaining 57 articles had outdated findings on vaccine coverage, were previous versions of articles that had subsequently been updated, did not have results broken down by antigen, had serosurvey results based on vaccination rather than titers, were review articles that included references we had already cited, or were commentaries that provided no new information.

Vaccination policies and their implementation in healthcare personnel

Globally, the WHO recommends measles vaccination for susceptible adults but there is no specific WHO policy recommending measles vaccination or evidence of measles immunity for healthcare personnel [25]. The United States was the first country to establish a measles vaccine policy for healthcare personnel in 1987 [26] though measles vaccine had been recommended for eligible persons of all ages who were considered "susceptible" since 1977 [27]. A number of other countries have policies for measles vaccination of healthcare personnel including Canada, Australia, countries of the Caribbean and some countries in Europe [28–31]. As of 2011, Maltezou et al. reviewed vaccination policies for healthcare personnel in acute healthcare facilities in Europe through surveying infection control or occupational health providers in all 27 European Union member states, as well as Norway, Russia and Switzerland. Of the 30 countries, 15 had no measles vaccination recommendations for healthcare personnel, 12 countries (i.e., Belgium, Cyprus, Germany, Ireland, Italy, Lithuania, Luxemburg, Malta, Russia, Spain, Switzerland and the United Kingdom [UK]) recommend measles vaccination for all healthcare personnel, France recommends vaccination for healthcare personnel in direct patient care, Austria recommends

vaccination for pediatricians only, and Finland has a policy for mandatory measles vaccination of healthcare personnel [32]. In France, measles is one of 4 vaccines that is recommended for healthcare personnel (as well as influenza, pertussis, and varicella), in contrast to 5 other vaccines (diphtheria, tetanus, poliomyelitis, hepatitis B virus, and tuberculosis) which are mandated for healthcare personnel [33]. A study in Japan in 2008 reported that vaccination of medical students in Japan was not mandatory [34].

To support implementation of vaccine policy, the United States defined criteria for "evidence of measles immunity" in 1978 [35]. Since a number of children and the majority of adults in the population had experienced measles disease when the measles vaccine program was implemented, these definitions were established to guide healthcare personnel in decision making regarding who needed measles vaccine. Persons were considered immune to measles if they had documentation of: 1) adequate (age-appropriate) immunization with a single dose of live measles vaccine on or after the first birthday, 2) physician-diagnosed measles, 3) laboratory evidence of measles immunity (measles Immunoglobulin G [IgG] antibodies, or 4) birth before 1957, since most persons born before 1957 were considered to have been naturally infected and, therefore, were not considered to be susceptible. These definitions were further refined in 1998 [36] and for healthcare personnel in 2011 to require written documentation of 2 doses of live measles or MMR vaccine administered at least 28 days apart (both on or after the first birthday), laboratory evidence of immunity, laboratory confirmation of disease, or birth before 1957 except during outbreaks [37]. Physician diagnosis of prior measles disease is no longer considered acceptable evidence of immunity in the United States [38]. Measles evidence of immunity requirements for healthcare personnel in Canada and the UK are similar to the United States, except there are no exclusions based on birth year [28, 39] and Australia has accepted birth year before 1966, 2 doses of MMR vaccine or serologic evidence as evidence of immunity [29]. France requires 2 doses of vaccine for healthcare personnel born after 1980 and one dose for those born before 1980, unless they have a documented history of disease or vaccination [31].

The presence of a national measles vaccine policy for healthcare personnel does not guarantee implementation. In the United States in 2004–2005, although over half of states (n=32) had laws for vaccination (for any vaccine) of healthcare personnel in traditional healthcare settings (e.g., hospitals, ambulatory care), few laws regulating vaccine administration for healthcare personnel included penalties for non-compliance [40]. Approximately 80% of states do not have laws requiring the vaccination of healthcare personnel with measles-containing vaccine [41]. Even among states that do have policies, in many cases, there is room for interpretation on whether those policies are mandatory or optional [41]. Studies of healthcare professional schools in the United States between 2001 and 2011 found rates of compliance regarding a measles vaccine requirement ranging from 90% to 98% [42, 43]; however, Miller et al. found that 67 (12.3%) of 547 schools that responded to their survey accepted at least one form of immunity evidence that is not recommended (i.e., disease history which was not verified by a physician, acceptable evidence in the United States at the time, although no longer acceptable) and 156 (28.4%) allowed any non-medical exemption to vaccination, including exemptions based on personal beliefs against the vaccination [44].

In a 2008 study in England of 104 (64.2%) hospital trusts, all respondents offered MMR vaccine to healthcare personnel. However, only 48 (46.2%) hospital trusts had information recorded in a central database on MMR vaccinations [45]. In a survey in France in 2011, 17% of occupational physicians from 30 healthcare institutions reported that measles vaccinations were never suggested to healthcare personnel at their annual occupational health visit [46].

Global measles control and measles seroprevalence among healthcare personnel

Before use of measles vaccines, almost all adults had natural infection in childhood and were immune to measles [1]. Regions of the world where measles is still endemic may currently have a low proportion of healthcare personnel with seronegative measles titers due to natural infection (e.g., in a study in Uganda, all 311 [100%] sera tested of randomly selected healthcare personnel in a nationwide study were positive for measles IgG) [47]. However, this is likely to change, especially among young healthcare personnel, as WHO regions implement regional measles elimination goals.

Studies from most regions of the world have described proportions of healthcare personnel without measles IgG antibodies ranging from 0–46% (median 6.5%) [17, 18, 22, 47–98] (Table 1). The proportion of healthcare personnel without measles IgG antibodies was lowest in Africa (median 1.8%, interquartile range 0.9%– 2.6%) and highest in Asia and the Western Pacific (median 10.3%, interquartile range 7.2%- 12.2%) and the Middle East (median 9.2%, interquartile range 4.6%- 13.4%). (Table 2). Thirteen studies among students in healthcare professions found a median measles seronegativity rate of 14.0% (range 1.2% - 46.0%) [49, 50, 57, 58, 60, 63, 64, 73, 81–83, 86, 98] (Table 1).

In the measles pre-elimination era in the United States (i.e., before 2000), studies during 1981 and 1999 reported a range of 2.1%- 14% of healthcare personnel who lacked measles antibodies [17, 84–95] (Table 1). The percentage of seronegative personnel was dependent on age, with older healthcare personnel more likely to have had natural infection and, therefore, higher measles seroprevalence [17, 84, 87–89, 92, 93, 95]. Two studies from the post-elimination era conducted in 2008 and 2009 reported that among the subset of healthcare personnel without documentation of measles immunity who had serologic testing done, 9% and 11.6% lacked measles antibodies [18, 97]. However, if we assume persons with documented receipt of two doses of vaccine and persons born prior to 1957 are immune, then the overall susceptibility of all healthcare personnel in the study institutions would have been 1.9% and 4.8% [18, 97]. In a study published in 2010, Weber et al. reported that 1.3% of healthcare personnel born before 1957 lacked antibodies to measles [96].

Studies from Europe on measles seroprevalence of healthcare personnel published between 1994 and 2013 reported that a median of 6.0% (interquartile range 3.3%-14%) of healthcare personnel were seronegative to measles, including those who thought they had a history of measles disease and/or history of measles vaccination [22, 48–65]. These articles also found differences in seroprevalence based on age, with older personnel less likely to be seronegative [49, 51–55]. For instance, in France, although overall 4% of healthcare personnel in one healthcare facility were measles seronegative, this proportion was almost 4-

fold higher in younger personnel (11% for those aged ≤ 30 years versus 3% for those >30 years) [53].

Only one study from Central or South America on seroprevalence of healthcare personnel was retrieved; the authors reported that during 1998, 1.2% of medical residents in a pediatric hospital in Mexico were seronegative to measles [98]. In Asia and the Western Pacific, studies published between 1994–2012 found 1.7%- 18.9% (median 10.3%) of healthcare personnel had negative measles titers [66–73] with younger age groups at higher risk for being measles seronegative [67, 68, 70–72]. Studies from the Middle East published between 2005–2012 found a median proportion of healthcare personnel who were seronegative of 9.2%, with seronegativity ranging from 1.4% in a study of healthcare staff in Turkey to 46% in medical students in United Arab Emirates [74–82]. In South Africa, a study published in 1990 found 3.5% of 433 medical, nursing, dentistry, and speech/hearing students tested seronegative for measles [83].

Measles in healthcare settings

The problem of nosocomial measles transmission, including the associated high mortality and morbidity, has been documented in two reviews [20, 21]. Deaths from measles acquired in hospital settings highlight that patients exposed to measles in hospitals may be at increased risk for severe outcomes from measles due to age, underlying medical conditions and/or medications that result in an immunocompromised state [99]. Transmission of measles in hospitals and emergency rooms was described during the 1989–1991 U.S. measles resurgence [100] and these settings continue to be documented as sites of measles transmission in recent years in countries around the world [18, 22–24]. In rural communities in developing countries, nosocomial transmission is less well documented as a problem possibly because access to health facilities or their use by community members for diseases such as measles is more limited [21].

Healthcare personnel are at higher risk of acquiring measles than other adults with three studies estimating the risk to be 2, 13 and 19 times higher for susceptible healthcare personnel than for the general population [100–102]. Due to their higher susceptibility, young healthcare personnel (<30 years of age) are at higher risk of becoming infected with measles in work settings than older healthcare personnel [52, 103].

Measles transmission from patients to healthcare personnel has been well documented from studies in the U.S. prior to, during and after the 1989–1991 measles resurgence [17, 18, 84, 85, 89, 90, 97, 99–102, 104–112]. During 1980–1984, surveillance data from 30 states in the U.S. showed that 57 (23.7%) of 241 healthcare–associated measles infections occurred in healthcare personnel [104] and from 1985–1989, 300 healthcare personnel were reported to have acquired measles from patients [101]. During the 1989–1991 U.S. measles resurgence, there were many reports of healthcare personnel who developed measles due to occupational-related exposures [89, 90, 99, 108–110, 112], including personnel who were born before 1957 [112] and some who had preexisting positive measles antibody titers (i.e., not all measles serologic assays are 100% specific for measles immunity and false positives may occur, albeit rarely and some studies were conducted before the establishment of what was considered to be the protective level of measles antibody titers) [90]. Post-resurgence

and in the elimination era in the United States, measles cases have continued to be reported occasionally among healthcare personnel, including a one-dose vaccinated healthcare provider who required 6 days of mechanical ventilation in a hospital [111] and a healthcare provider with unknown vaccination status who acquired measles from a patient and subsequently transmitted it to another patient [18].

In Europe, Asia and the Western Pacific, articles published mainly over the last decade including as recently as 2013 have documented measles cases in healthcare personnel because of exposures from patients; many of the healthcare personnel were unvaccinated, had unknown vaccination status or thought they were up-to-date with their vaccinations but actually were not [14, 22–24, 52, 53, 65, 103, 113–137].

Transmission of measles from healthcare personnel to patients or to other healthcare personnel has also been documented from the United States, Australia, Korea, France, Italy, Spain, and Bulgaria [18, 22, 24, 52, 84, 100, 101, 103–107, 110, 127, 130, 131, 138, 139]. In the United States during 1985–1989, of 295 measles cases among patients and visitors to healthcare facilities who had a known source of infection, 31 (10.5%) acquired measles from healthcare personnel; additionally, 31 (9.4%) healthcare personnel acquired measles from another healthcare personnel [101]. In the post-elimination era, during a measles outbreak that was focused in healthcare facilities, a healthcare provider transmitted measles to a patient who developed complications requiring admission to the intensive care unit [18].

Impact/ costs of responding to measles in healthcare facilities

Costs of measles outbreaks in healthcare facilities have been assessed in the United States only. In the pre-elimination era, two studies documented absence of documentation of vaccination or immunity status that resulted in the need for vaccination of healthcare personnel, loss of employee work days or both [17, 99]. In the post-elimination era in the United States, 3 studies reported costs of responding to a measles outbreak in healthcare facilities. In 2005 in Indiana, one hospital spent more than $113,000 responding to a measles outbreak with 3 hospitalizations including a one-dose vaccinated healthcare provider (phlebotomist) who required six days of ventilator support in an intensive care unit for pneumonia complicated by acute respiratory distress syndrome [111]. In 2008 in Arizona, two hospitals spent a combined $799,136 responding to and containing seven measles cases in their facilities. Additional costs were incurred due to vaccination of healthcare personnel. The Arizona outbreak response required rapid review of measles documentation of 14,844 healthcare personnel at seven hospitals and emergency vaccination of approximately 4,500 (30%) healthcare personnel who lacked documentation of measles immunity [18]. In 2008 in Chicago, one measles case-patient who spent 63 minutes in the emergency department without proper isolation led to 201 potential exposures and resulted in over 600 hours spent by staff in 12 departments on response activities for a financial impact of $18,900 [140].

Discussion

Due to the infectiousness of measles and the status of measles control globally, the risk of measles transmission in healthcare settings remains a serious concern. Measles has the highest reproduction rate (Ro) of any of the vaccine-preventable diseases and transmission

frequently takes place before the onset of rash, impeding the potential effectiveness of isolation measures in preventing transmission [141]. Nosocomial measles puts healthcare personnel and patients at risk of severe morbidity and mortality. This health burden and the public health impact of measles in healthcare facilities underscores the importance of ensuring protection of healthcare personnel through vaccination. Nevertheless, many countries lack policies to protect healthcare personnel against measles. Maltezou et al, following a systematic review of national vaccination policies for healthcare personnel in Europe, noted that policies related to two vaccines, hepatitis B and influenza, were implemented in almost every (29 of 30) country in Europe, whereas only half the countries had any recommendations for measles vaccination [32]. The authors surmised that long-standing recommendations issued by the WHO for hepatitis B vaccination of healthcare personnel and the 2000 European Union directive and 2005 WHO recommendations to increase seasonal influenza vaccine were instrumental in promoting national vaccine policy setting for these 2 vaccines. Despite the risk of measles exposures and the effectiveness of vaccination in preventing measles transmission, there is currently no global WHO policy for the vaccination of healthcare personnel against measles [25].

The potential for healthcare personnel to acquire and/or transmit measles depends on the stage of the country's measles vaccine program. Globally, young healthcare personnel are much more likely to be susceptible; however, in countries where measles has been eliminated and vaccine coverage is high, the highest measles susceptibility may be in older cohorts [18, 142]. With improved measles control, changes in measles epidemiology and implementation of case-based measles surveillance in countries throughout the world, data on sources of exposure and occurrence of measles cases in healthcare personnel and patients are available to provide key scientific evidence for vaccine policy decision making. In Australia, a measles outbreak in the late 1990s that was sparked by a young adult returning from overseas highlighted the changing measles epidemiology in Australia [134]. The median age of case-patients was 22 years and the fact that 5 cases occurred in healthcare personnel spotlighted that there was no systematic, uniform approach to preventing nosocomial transmission of vaccine-preventable diseases in Australia. This prompted the state of Victoria to publish immunization guidelines for healthcare personnel in 1998 and Australia to publish national guidelines [29].

There are also unique challenges in elimination or near-elimination environments. Since measles is not a common disease in many countries, it may not be considered as a potential diagnosis when an infected person presents in a healthcare setting resulting in a delay in instituting the appropriate airborne precautions and increasing the risk of transmission [18]. Additionally, the severity and contagiousness of measles before rash onset results in measles exposures in healthcare settings before it is recognized that the patient has measles [18]. The only strategy to protect healthcare personnel from these exposures is to ensure that all healthcare personnel are protected from measles on an ongoing basis.

An essential component of implementation and evaluation of MMR vaccine policies for healthcare personnel is defining and documenting criteria for evidence of measles immunity. Not all healthcare personnel require measles vaccine; many may have naturally acquired immunity, especially older healthcare personnel and those from countries where measles

remains endemic [17, 47, 84, 87–89, 92, 93, 95]. Evidence of measles immunity is also essential for interpreting data on measles vaccine coverage among healthcare personnel. With rare exception [143, 144], most of the articles we reviewed which reported on vaccination coverage did not describe whether healthcare personnel had other evidence of measles immunity, making it impossible to assess true vaccination coverage and the potential numbers of susceptible healthcare personnel. These issues also complicated interpreting studies on measles susceptibility in healthcare personnel; while some studies were comprehensive and representative in testing all or almost all healthcare personnel irrespective of evidence of measles immunity, many studies did not provide details regarding the subset of healthcare personnel tested. Additionally, test methods for measles IgG vary in sensitivity and specificity complicating comparisons across studies.

Although it is recognized that criteria for evidence of immunity do not provide 100% guarantee that the person is “immune” (e.g. 2 doses of measles vaccine are not 100% effective, laboratory tests may have false positive and negative results, and IgGs measured using commercially available tests provide less assurance regarding “protection” than the level of antibodies measured by the plaque reduction neutralization assay) [90, 97, 145], for practical program implementation, these criteria have been very useful. Documenting evidence of measles immunity, particularly in a computerized system, facilitates retrieval of vaccination records to enable rapid identification of potentially susceptible healthcare personnel following measles exposures in healthcare facilities which reduce the disruptions and the costs associated with measles in such facilities [18, 20, 37].

Monitoring vaccine coverage on a country or hospital-specific level is an important component of a vaccine program for ensuring measles immunity in healthcare personnel. Only one published article from France documented national tracking of measles vaccine coverage among healthcare personnel from occupational health records, though interpreting these data was limited because the authors did not report whether unvaccinated staff had other evidence of measles immunity [146]. There was wide variability in reported vaccine coverage in specific healthcare facilities or healthcare training institutions that could be due to several factors: age group (e.g., healthcare personnel aged <30 years had significantly higher coverage rates than older personnel though this may also reflect not taking into account other evidence of measles immunity in the older age group), lack of implementation or enforcement of national vaccination recommendations at specific institutions [18, 140], or status of measles elimination at the country-level (e.g., only 47% of healthcare personnel in Uganda reported having received measles vaccine, but 100% had positive measles IgG tests) [47].

An association between vaccine policy recommendations and vaccine coverage levels achieved in healthcare personnel has been demonstrated for influenza vaccine. Mandatory vaccination policies, if enforced with consequences for non-compliance, are associated with the highest vaccine coverage rates for influenza vaccines, though vaccine coverage levels close to 90% have been reached through implementing strategies to encourage vaccination at the work site [147, 148]. However, healthcare personnel or related organizations may object to mandatory policies on the grounds that such policies are a breach of individual rights. Therefore, the individual and public health benefit of the intervention must be clear

and a mandate should require an active opt-out or allow for exemptions for medical, religious or other beliefs and there should be some penalty for refusing to abide by it [149]. In a recent study, only 582 (47.9%) healthcare personnel surveyed in Germany supported mandatory vaccination of healthcare personnel against MMR and varicella [150]. Consideration should also be given to whether a mandate is the only way to obtain individual medical and/or public health benefits [149]. On the other hand, healthcare facilities need to consider the medical and legal consequences should one of their employees who refused immunization become ill and transmit measles to patients, such as those with immunocompromising conditions who cannot be vaccinated and are only protected from measles through herd immunity and lack of exposure. Measles vaccine programs pose fewer challenges for implementation than annual influenza vaccination. Implementation strategies may include checking evidence of immunity for all incoming healthcare personnel and vaccination as needed. In addition, efforts should be made to check the status of immunity of currently employed healthcare personnel and provide vaccination to those in need.

Measles transmission in healthcare settings remains a serious public health concern that may result in severe and fatal consequences in high risk patients. Measles cases and outbreaks in these settings result in significant disruption and response costs. Occupational health departments play a critical role in ensuring that healthcare personnel have evidence of measles immunity with appropriate documentation. Electronic records are the preferable mechanism for maintaining this information and are critical to providing a rapid, efficient public health response to measles exposures. Establishing policies for measles vaccination for healthcare personnel is an important strategy towards achievement of measles elimination and should be a high priority for global policy setting groups, governments, and hospitals.

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Table 1

Percent of Healthcare Personnel Seronegative for Measles[1]

Authors	Year published	Country	Methods	Setting (outbreak vs. non-outbreak context)	Total healthcare personnel (HCP) tested	Percent of HCP who were measles seronegative	Percent seronegative by age group (N= total tested in age group)	Type of personnel tested (e.g., staff vs trainees, age range)
Europe								
Fedeli	2002	Italy	Hospital staff who visited Occupational Health during 1998–2001 were asked to submit blood samples	non-outbreak	333	1.8%[2]	N/A[3]	Staff (23- 60 years)
Trevisan	2006	Italy	The 1024 students of the triennial degree courses of health professions at the university medical school participated	non-outbreak	1024	13.7%[2]	≤25 years: 15.7%[2] (N=781) >25 years: 7.0% (N=243)	Paramedical students
Trevisan	2007	Italy	From 2003- 2005, all 616 paramedical students who matriculated into the medical school participated	non-outbreak	616	16.9%[2]	N/A	Paramedical students
Barbadoro	2013	Italy	In response to a cluster of measles cases during January- March 2011, immunity status of 72 exposed HCP was assessed; of whom, 22 underwent serologic screening.	outbreak	22	4.5% [4]	N/A	Staff
Germanaud	1994	France	In 1993, 14% of employees were tested but no data given on whether this was a convenience sample, a random sample, if these were the only HCP who agreed to participate, or if they only tested what was available from preexisting samples	non-outbreak	465	0.9%	Born during or after 1957: 2% Born before 1957: 0%	Staff
Botelho-Nevers	2011	France	From April to November 2010, all staff in selected departments were invited to participate, but only 42.4% participated.	outbreak	154	6.5%	19–29 years: 11.6% (N=86) > 30 years: 0% (N=68)	Staff, medical students, and residents
Huoi	2012	France	The HCP who were tested represented a selected group of all the hospital employees. They were tested either because they: were clinically diagnosed with measles, were exposed to a measles	outbreak outbreak	1365 1365	4.0% 4.0%	16- 30 years: 11% (N=311) 16- 30 years: 3% (N=1054)	Staff Staff

Authors	Year published	Country	Methods	Setting (outbreak vs. non-outbreak context)	Total healthcare personnel (HCP) tested	Percent of HCP who were measles seronegative	Percent seronegative by age group (N= total tested in age group)	Type of personnel tested (e.g., staff vs trainees, age range)
			case, they were high risk for frequent exposure to measles (ER case, they were high risk for frequent exposure to measles (ER staff), or they were potentially susceptible. Testing was done between January 1, 2010 and July 8, 2011.					
Freund	2012	France	Between April 27 and June 30, 2011, 353 HCP from three university hospitals in Paris participated; did not state tota number of HCP at the hospitals	outbreak occurring in France, but authors did not state whether there was an active outbreak in any of the three participating hospitals	35	8.2%	≥ 35 years: 6% (N=105) HCP aged 18–24 years had an odds ratio of 11.8 for being seronegative HCP aged 25–34 years had an odds ratio of 8.4 for being seronegative	Staff (18–67 years, mean: 36 years)
Ziegler	2003	UK	Between April and July 1998, all 528 staff were invited to participate, but only 41% of the staff returned the survey and provided an oral fluid sample. Those with a negative saliva were asked to provide a serum sample.	non-outbreak (the study was done after an infected patient transmitted measles to a non-immune HCP, but not at the time of the transmission)	218	3.3%	20–39 years: 3.9% (N=155) ≥ 40 years: 1.6% (N=62)	Staff (19–60 years)
Gerike	1994	Germany	In 1992, serum samples were taken from 452 HCP, with students at the medical vocational schools comprising the largest group	non-outbreak	452	6%[2]	16–18 years: 10.3% (N=78)	Staff and students (72% were ≤20 years)
Wicker	2007	Germany	Presumably all 270 enrolled medical students were asked to participate, but the mansucript does not state this[5] Enrollment occurred in October 2005.	non-outbreak	223	16.1%[2]	N/A	Medical students (20- 45 years, median: 23.4 years)
Wicker	2008	Germany	150 (55.6%) of 270 medical students who were enrolled in their first clinical semester participated[5] Enrollment occurred in October 2005.	non-outbreak	150	14.0%[2]	N/A	Medical students (20- 45 years, median: 23.4 years)
Wicker	2012	Germany	Studied 424 pregnant HCP at the University Hospital between	non-outbreak	424	15.1%[2]	N/A	Staff (pregnant women)

Authors	Year published	Country	Methods	Setting (outbreak vs. non-outbreak context)	Total healthcare personnel (HCP) tested	Percent of HCP who were measles seronegative	Percent seronegative by age group (N= total tested in age group)	Type of personnel tested (e.g., staff vs trainees, age range)
			2007–2011; did not state whether this represented all pregnant					
			2007–2011; did not state whether this represented all pregnant HCP at the hospital during this timeframe					
Baer	2005	Switzerland	Fourth year medical students with a rotation at the University Children's Hospital from 1999–2003 were eligible; 170 students were enrolled in the study but only 149 provided a serum sample	non-outbreak	149	15%	N/A	Medical students (22- 48 years, median: 25.3 years)
Uckay	2007	Switzerland	In February 2005, mass screening and vaccination of HCP was initiated. Of all 3233 HCP with direct patient contact, 1/3 preferred to directly receive MMR vaccine and 2/3 were tested for IgG antibodies.	outbreak	~2,300	5.1%[6]	N/A[7]	Staff
Markou	2009	Greece	Serum samples were taken from 144 HCP who work in different hospital departments; total number of HCP at the hospital not provided	outbreak occurring in Greece, but authors did not state whether there was an active outbreak in the participating hospital	144	2.1%	N/A	Staff (28–50 years)
Pavlopoulou	2009	Greece	Medical and nursing students were eligible for participation during their clerkship in pediatrics at the Children's Hospital from April through November 2007. 187 (90%) eligible students volunteered to participate, of whom 182 were tested for measles antibodies.	non-outbreak	182	1.6%	N/A	Medical and nursing students (20–45 years, median: 23 years)
Socan	2008	Slovenia	In November 2006, 256 serum specimens were collected from all first-grade medical students. Of the 256 specimens, 138 were tested for measles antibodies.	non-outbreak	138	3.6%	N/A	Medical students (range: 18–32 years, mean: 19 years)
Mrvic	2012	Slovenia	From June to October 2011, data were collected form 3424 HCP, of whom 1747 (51%) could not provide a written	non-outbreak (the study was done after measles	1747	19%[2, 4]	N/A[7]	Staff

Authors	Year published	Country	Methods	Setting (outbreak vs. non-outbreak context)	Total healthcare personnel (HCP) tested	Percent of HCP who were measles seronegative	Percent seronegative by age group (N= total tested in age group)	Type of personnel tested (e.g., staff vs trainees, age range)
			vaccination record and had measles IgG testing done.	occurred in HCP, but not at the time of the reported cases)				
			vaccination record and had measles IgG testing done.					
Asia and Western Pacific								
Lee	2008	Taiwan	In 2007, serological tests were performed on 32 HCP who cared for the measles-infected patient.	outbreak	32	12.5%	N/A	Staff
Ho	2012	Taiwan	A cross-sectional, hospital-based study of measles seroprevalence was conducted at the University Hospital from 2004–2009 on 1584 newly hired employees.	non-outbreak	1584	18.9%[2]	20–29 years: 21.9%[2] (N=1286) ≥ 30 years: 6.0%[2] (N=298)	Staff (20–57 years, median: 25 years)
Williamson	2010	New Zealand	2029 HCP in high-risk areas were identified, of whom 1862 had their immune status evaluated (no response was obtained from 167 HCP). Of these, 424 were serologically tested to determine their measles immune status.	non-outbreak	424	14%[2, 4]	Born after 1969: 14%[2, 4] (N= 424)	Staff
			3439 pre-employment screening tests were done between January 2006- August 2009.		3439	10.3%[2]	Born after 1969: 13.3%[2] (N= 2527) Born before 1969: 2.1%[2] (N= 912)	
Ferson	1994	Australia	235 staff at the Children's Hospital between April 1989 and September 1991 provided a serum sample (total number of staff not reported).	non-outbreak	235	1.7%	N/A	Staff 20.5- 63.5 years (mean: 28.1 years)
Vagholkar	2008	Australia	From September 2003 to August 2005, 743 staff at one healthcare facility (67% of employees) and 577 staff at another facility (72% of employees) participated in the occupational screening and vaccination program.	non-outbreak	1297	6.9%[8]	Born >1980: 12.9% (N= 85) Born between 1966-1980: 12% (N= 450) Born before 1966: 3.2% (N=754)	Staff (range at one center was: 16–84 years, mean age: 42.3 years; range at other center was: 19–75 years, mean age: 41.9 years)
Asari	2003	Japan	Blood samples were taken from all 271 newly hired HCP in the	non-outbreak	271	7.4%	21–30 years: 9% of men and 5% of women	Staff 21–50 years (93.7% were ≤30 years)

Authors	Year published	Country	Methods	Setting (outbreak vs. non-outbreak context)	Total healthcare personnel (HCP) tested	Percent of HCP who were measles seronegative	Percent seronegative by age group (N= total tested in age group)	Type of personnel tested (e.g., staff vs trainees, age range)
			2001 cohort at the Univesity Hospital. 2001 cohort at the Univesity Hospital.				31–40 years: 11.1% of men and 14.3% of women 41–50 years: 0% of men and 0% of women	
Hatakeyama	2004	Japan	Between September and October 2002, serologic testing was recommended for 860 HCP without documentation of measles vaccination, history of measles disease, or serologic evidence of immunity, regardless of age (out of 2100 total employees).	non-outbreak	860	1.5%[4]	≤35 years: 2.3% (N=570) > 35 years: 0% (N=290)	Staff 20- 65 years (mean 34.4 years)
Srichomkwun	2009	Thailand	250 third year medical students during 2006–2007 were recruited in a cross-sectional study at the University Hospital, of whom 237 (94.8%) consented and were enrolled.	non-outbreak	237	11.8%	N/A	Medical students 20–38 years (median: 22 years)
Middle East								
Almuneef	2006	Saudi Arabia	From September 2001 through March 2005, 3918 (98%) of 4006 newly hired HCP had measles serologic testing done.	non-outbreak	3918	13%	20–29 years: 15% 30–39 years: 12% 40–49 years: 10% ≥50 years: 17%	Staff (newly hired) of whom 45% were aged <30 years
Abbas	2007	Saudi Arabia	From January to March 2006, 380 hospital staff representing a comprehensive sample of workers at the national hospital, were included in the study.	non-outbreak	380	5.3%[2]	20–39 years: 5.1%[9] 40–59 years: 4%[9] ≥60 years: 0%[9]	Hospital staff; 56.6% were aged 20–39 years
Yavuz	2005	Turkey	From January to March 2005, 73 (22.1%) female HCP from the University Hospital and State Hospital were enrolled in a cross-sectional study.	non-outbreak	73	12.3%	N/A	Female staff with a mean age of 32.7 years
Celikbas	2006	Turkey	363 HCP from 2 hospitals with a combined staff of 3060 HCP volunteered to participate in the study from March-May 2005.	non-outbreak	363	1.4%	N/A[10]	Staff aged 17–52 years, mean: 29 years

Authors	Year published	Country	Methods	Setting (outbreak vs. non-outbreak context)	Total healthcare personnel (HCP) tested	Percent of HCP who were measles seronegative	Percent seronegative by age group (N= total tested in age group)	Type of personnel tested (e.g., staff vs trainees, age range)
Hatipoglu	2010	Turkey	81 HCP were included in the study (total number of HCP not provided).	non-outbreak	81	2.5%	N/A	Staff aged 20–57 years (mean: 34.4 years)
Alp	2012	Turkey	Between December 2010 and April 2011, 1255 (81.9%) of 1532 HCP at the University Hospital participated in the study.	non-outbreak	1255	6%	N/A[11]	Staff aged 19–60 years; median: 30 years
Aypak	2012	Turkey	From September- October 2010, 284 HCP without documentation of vaccination, history of disease, or serologic evidence of immunity, regardless of age, were serologically tested for measles IgG antibodies (out of a total of 550 HCP at the hospital).	non-outbreak	284	9.2%[4]	≤25 years: 20.8% (N= 72) 26–35 years: 3.3% (N= 122) 36–45 years: 7.5% (N= 53) 46–55 years: 6.2% (N= 16) ≥56 years: 9.5% (N= 21)	Staff aged 18–65 years, mean: 33.5 years
Chamat	2011	Lebanon	Between November 2007 and April 2008, 502 (77%) of 648 medical and paramedical university students solicited were enrolled in the cross-sectional study.	non-outbreak	502	14.4%	N/A	Medical and paramedical students aged 17 26 years; median: 20 years
Sheek-Hussein	2012	United Arab of Emirates	Among 397 matriculated medical students, 319 (80%) enrolled in the prospective study. Between July 1, 2011 and May 30, 2012, blood was collected from 261 (82%) students. Measles serology was available in 180 (69%) of 261 medical students.	non-outbreak	180	46%[2]	N/A	Medical students
Africa								
Schoub	1990	South Africa	Students enrolled in 1988 for first and final year medicine, dentistry, nursing, and speech and hearing courses at the university were approached; 433 students enrolled (total number of students not provided).	non-outbreak	433	3.5%	6% of first year students were seronegative (age range not provided) 1% of final year students were seronegative (age range not provided)	Students in various heatlhcare professions

Authors	Year published	Country	Methods	Setting (outbreak vs. non-outbreak context)	Total healthcare personnel (HCP) tested	Percent of HCP who were measles seronegative	Percent seronegative by age group (N= total tested in age group)	Type of personnel tested (e.g., staff vs trainees, age range)
Lewis	2006	Uganda	In 2003, a sample of 289 HCP from 98 health units in 48 of 56 districts throughout the country participated in the cross-sectional study.	non-outbreak	311	0%	N/A	Staff aged 20–62 years (mean: 36.9 years)
North, Central, and South America								
Seavy	1982	USA	In March of 1981, 4316 HCP responded to a questionnaire; 1736 were "susceptible" of whom 1565 received measles vaccine. Of the 1565 vaccinated, 1031 consented to serologic testing	outbreak	1031	10.9%[4]	N/A[7]	Staff
Watkins	1987	USA	In May of 1984, antibody titers were drawn on 307 staff who were reluctant to be immunized (out of 2200 HCP total at the facility).	outbreak	307 existing staff	3.9%	Existing staff: Born 1956 or later: 5% (N= 114); born between 1950–1955: 5% (N= 101); and born before 1950: 3% (N= 38)	Staff and new hires
			Between July 1984 and June 1985, a prospective screening program was initiated for all new hires; 149 new hires were tested.	non-outbreak	149 new hires	7%	New hires: Born 1956 or later: 11% (N= 82); born between 1950–1955: 6% (N= 34); and born before 1950: 0% (N= 33)	
Murray	1988	USA	From 1982 through 1985, 878 students entering medical school participated (95% of all students entering medical school), of whom 816 had measles serologic testing.	non-outbreak	816	14%	N/A	Medical students aged 20-46 years (mean: 25 years)
Raad	1989	USA	In 1985, 401 HCP at the University Hospital were tested for measles immunity (total number of HCP at this facility not provided).	outbreak	401	2.2%	22–26 years: 8.7% (born 1959–1963) ≥27 years: < 1.0% (born before 1957)	Staff
Subbarao	1991	USA	Employees were prospectively screened upon hire or during their annual tuberculin skin testing visit. Sera were obtained from 222 HCP without evidence of immunity (total number of HCP not provided).	non-outbreak	222	14%[2, 4]	HCP born in 1957 or later: 14.9% (N= 181) HCP born before 1957: 7.3% (N= 41)	Staff and new hires

Authors	Year published	Country	Methods	Setting (outbreak vs. non-outbreak context)	Total healthcare personnel (HCP) tested	Percent of HCP who were measles seronegative	Percent seronegative by age group (N= total tested in age group)	Type of personnel tested (e.g., staff vs trainees, age range)
Kim	1992	USA	From June through October 1990, all of the facility's HCP were tested for measles antibodies. Additionally, from June through October 1990, all new hires were tested. A total of 2075 HCP were serologically tested.	non-outbreak	2075	5.8%[2]	15–19 years: 9.1% (N= 22) 20–29 years: 14.1% (N= 451) 30–39 years: 3.6% (N= 749) 40–49 years: 1% (N= 506) 50–59 years: 0.8% (N= 260) 60–69 years: 1.3% (N= 75) >69 years: 0% (N= 12)	Staff and new hires (all ages)
Schwarcz	1992	USA	Between March and June 1990, 1694 (approximately 80%) of hospital employees who were unable to document proof of measles immunity were serologically screened for measles antibody (the remaining 427 HCP were vaccinated instead of serologically tested).	outbreak	1694	5.3%[2, 4]	Born ≥ 1957: 10.3%[2] (N= 478) Born < 1957: 3.9%[2] (N= 1023)	Staff
Ammari	1993	USA	From July through November 1990, 900 (68.6%) HCP had their sera tested for antibody to measles virus.	non-outbreak (screening started after a patient infected with measles was admitted to the Children's Hospital, but before the large Philadelphia outbreak occurred)	900	2.1%[2]	N/A	Staff
Huang	1994	USA	117 HCP volunteered to be screened (total number of HCP not provided).	non-outbreak	117	7.7%	N/A	Staff aged 21–60 years
Willy	1994	USA	From July 1990 to June 1992, 2473 newly hired HCP who could not provide documentation of measles immunity at their	non-outbreak	2473	6%[2, 4]	Born after 1956: 8%[2] (N= 1718)	Newly hired HCP

Authors	Year published	Country	Methods	Setting (outbreak vs. non-outbreak context)	Total healthcare personnel (HCP) tested	Percent of HCP who were measles seronegative	Percent seronegative by age group (N= total tested in age group)	Type of personnel tested (e.g., staff vs trainees, age range)
			preplacement medical examination were tested for measles immunity.				Born between 1951 to 1956: 1.9%[2] (N= 427) Born ≤ 1950: 1.2%[2] (N= 328)	
Wright	1994	USA	In 1991, 5825 (47.8%) of 12,192 HCP from 6 urban and 10 rural hospitals were screened over a four month period.	non-outbreak	5825	10.3%[2]	Born 1970s: 33.7%[2] (N= 288) Born 1960s: 16.3%[2] (N= 1801) Born 1957–59: 8.1%[2] (N= 628) Born < 1957: 4.7%[2] (N= 3094)	Staff
L'Ecuyer	1998	USA	From January 1991 through November 1995, the employee health database was retrospectively reviewed on 5007 medical school employees; 4864 HCP had history of measles disease or documentation of vaccination and the remaining 143 HCP were tested for measles antibodies.	non-outbreak	143	2.1%[4]	N/A[12]	Staff aged 17–93 years, mean: 35.3 years
Seo	2002	USA	Seroprevalance of measles antibody was assessed on 400 randomly selected HCP hired between 1983–1988 (total number of HCP during this timeframe not provided)	non-outbreak	400	4%	Born 1970s: 0% (N= 3) Born 1960s: 4.8% (N= 147) Born 1950s: 3.6% (N= 140) Born 1940s: 3.6% (N= 110)	Staff
			Seroprevalance of measles antibody was assessed on 1349 randomly selected HCP hired between 1998–1999 (total number of HCP during this timeframe not provided)	non-outbreak	1349	9%	Born 1980s: 0% (N= 9) Born 1970s: 11.6% (N= 663) Born 1960s: 8.0% (N= 437) Born 1950s: 1.1% (N= 182)	

Authors	Year published	Country	Methods	Setting (outbreak vs. non-outbreak context)	Total healthcare personnel (HCP) tested	Percent of HCP who were measles seronegative	Percent seronegative by age group (N= total tested in age group)	Type of personnel tested (e.g., staff vs trainees, age range)
							Born 1940s: 1.9% (N= 53)	
Weber	2010	USA	From 2006–2008, 6597 newly hired HCP who were born before 1957 were evaluated, of whom 469 were serologically tested for measles antibodies because they could not provide written evidence of immunity other than birth before 1957.	non-outbreak	469	1.3%[4]	N/A	Newly hired HCP born before 1957
Chen	2011	USA	Serological testing was done on 1583 (89%) of 1776 HCP who lacked measles evidence of immunity (there were a total of 7195 HCP at 2 hospitals who were screened).	outbreak	1583	9%[4]	Born ≥ 1957: 11%[4] (N= 1077) Born before 1957: 4%[4] (N= 506)	Staff
CDC (MMWR)	2012	USA	Serological testing was done on 69 of 72 HCP who lacked measles evidence of immunity (out of a total of 168 hospital employees).	outbreak	69	11.6%[4]	N/A	Staff
Villasis-Keever	2001	Mexico	During March and May 1998, 89 (94.6%) of 94 medical residents had serological testing done.	non-outbreak	89	1.2%	N/A	Medical residents (74% were <30 years)

[1] Abbreviations used throughout table are: HCP = healthcare personnel. N/A = not applicable

[2] Includes equivocal results

[3] Authors did age breakdown, but did not separate age results by antigen.

[4] The percentage of HCP who were measles seronegative among those who did not have evidence of measles immunity. The percentage would have been lower had the denominator included all HCP.

[5] The Wicker 2007 and Wicker 2008 papers use the same group of medical students with different subsets.

[6] Only 2300 of the 2600 tested were HCP, however the authors did not breakdown how many of the 117 seronegative were staff versus patients/family. The percentage in the table does not match the cited manuscript, because we used 2300 as the denominator (HCP only) rather than 2600 (HCP and patients)

[7] Although seronegativity status by age group was mentioned in the article, we did not include it because the percentage was calculated by taking the number in an age group who were seronegative out of the total number who were seronegative (rather than the number in a certain age group who were seronegative out of the total number in that age group).

[8] Our percentages do not match text in the cited manuscript, because the authors included the missing data in the total. We excluded the missing data from the number who were tested, because the authors stated “for clinical reasons, serology not indicated”.

[9]Percentages in this cell do not include equivical serological test results (age breakdown by negative and equivical status was not available).

[10]Data not provided, but the mean age of the susceptibles was 26 years compared with 29 years among the immune.

[11]Age was significantly associated with immunity in multivariate analysis, but age breakdown was not provided.

[12]The manuscript reported the relative risk by age group, but the sample size was such a small proportion of the total number of HCP, that we did not include the results in the table.

Table 2

Percent of Healthcare Personnel Seronegative for Measles by Region

Region	Studies (N)	Median[1] (range)	25% IQR[2]	75% IQR	Mean[3]
Europe	17	6.0 (0.9 – 16.9)	3.3	14.0	7.9
Asia and Western Pacific	7	10.3 (1.7 – 18.9)	7.2	12.2	9.9
Middle East	8	9.2 (1.4 – 46.0)	4.6	13.4	12.6
Africa	2	1.8 (0–3.5)	0.9	2.6	1.8
Americas	9	5.8 (1.2 – 14.0)	3.1	8.4	6.1

[1] For calculation of median, Interquartile Range (IQR) and mean values, studies that reported testing a non representative subset of healthcare personnel (i.e. those without other evidence of measles immunity) were excluded. One study (Williamson et al. 2010), tested 2 different groups, one of which was a subset and the other was all new hires. We included the study but only reported the summary statistics on the group for which everyone was tested.

[2] IQR= Interquartile range

[3] Mean = arithmetic mean (sum of study values/N of studies)