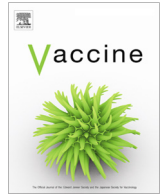




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A 16-year review of seroprevalence studies on measles and rubella

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ABSTRACT

The determination of the seroprevalence of vaccine-preventable diseases is critical in monitoring the efficacy of vaccination programmes and to assess the gaps in population immunity but requires extensive organisation and is time and resource intensive. The results of the studies are frequently reported in peer-reviewed scientific, government and non-government publications. A review of scientific literature was undertaken to advise the development of WHO guidelines for the assessment of measles and rubella seroprevalence. A search of the National Library of Medicine's PubMed online publications using key words of 'measles', 'rubella', combined with 'serosurvey', 'seroprevalence', 'immunity' and 'population immunity' was conducted. A total of 97 articles published between January 1998 and June 2014 were retrieved, 68 describing serosurveys for measles and 58 serosurveys for rubella, conducted in 37 and 36 different countries respectively. Only 13 (19%) and 8 (14%) respectively were UN classified "least developed countries". The study sample varied markedly and included combinations of male and female infants, children, adolescents and adults. The study sizes also varied with 28% and 33% of measles and rubella studies respectively, having greater than 2000 participants. Microtitre plate enzyme immunoassays were used in 52 (76%) measles studies and 40 (69%) rubella studies. A total of 39 (57%) measles and 44 (76%) rubella studies reported quantitative test results. Seroprevalence ranged from 60.8% to 95.9% for measles and 53.0% to 99.3% for rubella studies. The review highlighted that infants lost maternally-acquired immunity within 9 months of birth and were unprotected until vaccination. Two groups at higher risk of infection were identified: young adults between the ages of 15 and 30 years and immigrants.

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Abbreviations: EIA, enzyme-immunoassay; GMT, geometric mean titres; HAI, haemagglutination inhibition; IU/mL, international units per millilitre; PNT, plaque neutralisation tests; WHO, World Health Organization.

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1. Introduction

Under the Global Vaccine Action Plan 2011–2020 [1], measles and rubella are targeted for elimination in five WHO Regions by 2020. Substantial progress has been made towards achieving this goal, but the transmission of these viruses persists and outbreaks of measles and rubella continue to occur. The Global Measles and Rubella Strategic Plan 2012–2020 [2] presents strategies that country immunization managers, working with domestic and international partners, can use as a blueprint to achieve the global control and elimination goals. The plan lists serological surveys as a useful tool to assess gaps in population immunity and identify areas for potential outbreaks. A 16-year review of published seroprevalence studies was undertaken to review approaches employed.

To identify previously published measles and rubella seroprevalence surveys a Medline search was conducted using the National Library of Medicine's PubMed online search engine. Keywords included 'rubella' and 'measles' combined with 'serosurvey', 'seroprevalence', 'immunity' and 'population immunity'. The starting year selected was 1998; the end date was June 2014. No language priority was chosen. A 'related article' hyperlink was followed for each retrieved article and the list of retrieved articles was used to identify seroprevalence studies. An article was included in the review if it reported seroprevalence results and contained a description of study design, study population, age group(s) tested, and laboratory method used to determine antibody status. One article was not retrievable on-line [3] and one article was in Spanish [4]; therefore only the data from their abstracts were analysed. All other articles were reviewed and compared against principles outlined in a draft Serosurvey Guideline being prepared by the WHO, and a similar document describing best practice for conducting serosurveys for Hepatitis B [5].

2. Outcome of search

The literature search for the 16-year period identified a total of 97 articles fulfilling the criteria, of which 68 described serosurveys for measles and 58 described serosurveys for rubella (Table 1). Thirty of the articles addressed both measles and rubella. It should be noted that the table shows the year of publication, not the year of testing or the year of sample collection. In some cases, published accounts included laboratory tests conducted several years earlier, or test results on stored samples collected many years earlier. The

Table 1
Number of published serosurveys for measles and/or rubella, by year of publication.

Year	Measles publications [Reference]	Rubella publications [Reference]
1999	1 [6]	2 [6,7]
2000	1 [8]	2 [8,9]
2001	2 [10,11]	1 [11]
2002	2 [12,13]	1 [12]
2003	4 [3,14–16]	1 [14]
2004	2 [17,18]	0
2005	2 [19,20]	1 [19]
2006	6 [21–26]	6 [21,23–27]
2007	3 [28–30]	2 [28,31]
2008	7 [32–38]	3 [37,39,40]
2009	2 [41,42]	4 [42–45]
2010	2 [46,47]	1 [47]
2011	5 [48–52]	7 [4,50,51,53–56]
2012	7 [57–63]	6 [59,62–66]
2013	14 [67–80]	10 [67,69,72,74,76,81–85]
2014	8 [86–93]	11 [86–88,91,92,94–99]
Totals	68	58

Table 2
Primary purpose of published measles and rubella serosurveys.

Purpose	Measles publications	Rubella publications
Susceptibility monitoring	47 (69%)	50 (86%)
Antibody persistence	11 (16%)	4 (7%)
Vaccination coverage	3 (4%)	0 (0%)
Vaccine immunogenicity	7 (10%)	4 (7%)
Totals	68	58

observed trend over this time, however, has been for a steady increase in the number of articles on measles or rubella seroprevalence studies being published.

3. Purposes of studies

Although a range of purposes for conducting the seroprevalence studies was given in the publications, the primary aim of each study was categorised as either:

- Susceptibility studies – looking for susceptible populations and immunity gaps.
- Antibody persistence studies – looking for evidence of declining antibody levels or waning protection in known vaccine recipients, in studies usually conducted over several years.
- Vaccination coverage studies – conducted in association with immunization activities and attempting to provide biological 'validation' of vaccine coverage estimates or
- Vaccine immunogenicity studies – investigating the immunological impact of changing vaccine formulations or schedules in target populations.

Of these categories, susceptibility monitoring studies predominated with 69% of measles and 86% of rubella studies falling within this category (Table 2). The high percentage of serosurveys for rubella susceptibility is probably a reflection of the interest in assessing the need for introducing rubella vaccine into routine immunization schedules. Approximately 16% of measles serosurveys investigated waning measles immunity as either the primary or secondary purpose of the study, reflecting recent concerns linked to achieving and maintaining the measles elimination goal.

4. Countries in which studies were conducted

Measles serosurveys were conducted in 37 different countries, 12 countries having more than a single study reported. Of these 12 countries, 10 studies were conducted in China and five studies in the USA. The other 10 countries had three or fewer measles serosurveys reported. Similarly, rubella serosurveys were reported from 36 countries, with 11 countries having multiple publications. There were six rubella studies conducted in Turkey and five in Saudi Arabia. There were only three Chinese serosurveys on rubella reported over the time period studied.

Country listings from the UN Statistics Division [100] were used to classify countries in which the published studies were conducted. Of the measles and rubella studies respectively, 29 (43%) and 21 (36%) were from **developed** countries, 26 (38%) and 29 (50%) were from **developing** countries and 13 (19%) and 8 (14%) were from **least developed** countries. Developed countries included those in Europe and Northern America, together with Australia, New Zealand and Japan. Developing countries included China, India and countries in South America. Least developed countries included several in Africa, Central America, and some in Asia and Oceania. There were 48 countries categorised as least developed by the UN at the time of the review.

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