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REVIEW



A review of measles supplementary immunization activities and the implications for Pacific Island countries and territories

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ABSTRACT

Introduction: Standard measles control strategies include achieving high levels of measles vaccine coverage using routine delivery systems, supplemented by mass immunization campaigns as needed to close population immunity gaps.

Areas covered: This review looks at how supplementary immunization activities (SIAs) have contributed to measles control globally, and asks whether such a strategy has a place in Pacific Islands today. **Expert commentary:** Very high coverage with two doses of measles vaccine seems to be the optimal strategy for controlling measles. By 2015, all but two Pacific Islands had introduced a second dose in the routine schedule; however, a number of countries have not yet reached high coverage with their second dose. The literature and the country reviews reported here suggest that a high coverage SIA combined with one dose of measles vaccine given in the routine system will also do the job. The arguments for and against the use of SIAs are complex, but it is clear that to be effective, SIAs need to be well designed to meet specific needs, must be carried out effectively and safely with very high coverage, and should, when possible, carry with them other public health interventions to make them even more cost-effective.

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1. Introduction

Historically, measles outbreaks have had a devastating effect on Pacific Island countries. In 1875, between 27,000 and 50,000 Fijians died during a catastrophic outbreak of measles introduced into a nonimmune population. Other Pacific islands have suffered similarly. One-twentieth of the Tongan population died from measles in the outbreak of 1893 [1]. Even today, measles continues to take its toll in the Pacific, generating, for instance, recent measles outbreaks in Micronesia, Solomon Islands, and Vanuatu in 2014 and 2015 [2].

Two main methods have evolved for delivering measles vaccine. The first is through routine health-care/immunization services according to an age-specific schedule. The second is through supplementary immunization activities (SIAs) – 'supplementary' because they have supplemented routine immunization activities. But how effective have SIAs been, and is it appropriate to continue using them? Or are there better ways of controlling measles in this environment? This review attempts to answer these questions by drawing lessons from global measles control activities and their presumed impact when applied in the unique environment of the Pacific.

2. A second dose is essential

As measles vaccine was widely introduced into countries' immunization programs during the 1980s, WHO recommended that one dose of the vaccine should be given at 9 months of age in developing countries. It gradually became

clear that one dose was insufficient to achieve the measles control goals. Accordingly, WHO introduced the concept of 'a second opportunity' to receive the vaccine, either through routine services or during SIAs (Box 1). Although generally administered at school entry (age 4-6 years) in settings with low measles incidence, and during the second year of life in countries with higher measles incidence, WHO advised that the second dose might be offered as early as 1 month following the first dose, depending on the local programmatic or epidemiological situation [3]. Countries have clearly accepted the policy for measles SIAs, as testified by the fact that during the period 2000-2015, 966 SIAs were reported to WHO [4]. Measles elimination efforts in the Region of the Americas alone led to the implementation of 157 national immunization campaigns, immunizing a total of 440 million persons [5]. Between 2000 and 2003, SIAs in just 12 African countries covered 82 million children [6].

A number of studies have demonstrated the positive impact of a second dose of MCV. Analysis of a large measles outbreak at a school in Germany showed that receipt of more than one doses of vaccine before exposure to infection prevented infection in up to 99% of persons [7,8]. Based on such science, the global strategy to reduce measles mortality has included maintaining high coverage of the first dose of an MCV-1 administered routinely and ensuring all children receive a second dose (MCV-2). A dose given as the second opportunity may have several consequences in relation to immunity against measles virus. It may

Box 1. Basic principles of elimination.

Measles elimination is defined as the interruption of endemic measles virus transmission for a period of at least 12 months. To sustain elimination status, imported measles virus transmission should be interrupted within 12 months of importation. For the elimination of measles, population immunity must be reached and sustained at more than 95%. In the absence of endemically circulating measles infection, the number of children susceptible to measles can increase rapidly if coverage lags even slightly. It seems that when the number of susceptible children in a country reaches the equivalent of about one annual birth cohort, conditions are conducive for a measles outbreak if the virus is imported. Thus, for measles control, not only coverage but also immunity levels in each birth cohort must be calculated and monitored over the years to determine whether additional corrective actions are needed.

As only 80–85% of infants develop immunity when immunized with measles containing vaccine (MCV-1) at 9 months of age, a second dose (MCV-2) is recommended by WHO to achieve the required level of population immunity.

- immunize a child previously unimmunized,
- result in seroconversion of a child who was previously immunized but who had failed to seroconvert,
- fail to seroconvert a child who had been given the vaccine already but had failed to seroconvert after the first dose (this is the least likely of the five options),
- further boost the immune response of a child who had previously been immunized and had already seroconverted, and
- boost the immune response of a child who had already been exposed to measles infection.

(The last two consequences are probably not relevant to measles control, but are included for completeness.)

Once seroconversion has occurred in an individual (whether it is following MCV-1 or MCV-2), there is very little chance of that individual becoming infected, if exposed to the disease (so-called secondary vaccine failure). One study estimated this possibility to be less than 0.2% [9].

An SIA (either national or subnational) is an excellent opportunity to deliver the second dose of MCV, especially in countries where the routine health system is struggling to reach high coverage [10]. It is generally assumed (rightly or wrongly) that SIAs will reach children missed by routine immunization services. SIAs are also used for catch-up programs, targeting broader (older) age ranges to 'catch up' those missed previously by the routine immunization services. This strategy has been particularly useful at the point of introducing a routine second dose (MCV-2) or measles-rubella (MR) vaccine where rapid catch-up is important. SIAs are also, importantly, used in response to outbreaks (Table 1). In many countries, large-scale SIAs have been used to rapidly increase population immunity and bring measles transmission under control. Periodic SIAs have also provided children with a second opportunity for MCV where children cannot be reliably reached through routine services. The duration of impact of SIAs will be enhanced through a strong routine immunization program that prevents the subsequent rapid accumulation of susceptible children. An example of a field guide on conducting SIAs has been produced by the WHO European Region [11].

A sensitive surveillance system is also required for measles elimination to detect any suspected case of measles that may arise. Although most acute fever and rash (AFR) cases detected will likely be due to causes other than measles, it is very important that any importation of measles be picked up early so that necessary control measures can be implemented rapidly (Box 2).

3. Global situation

In 2008, all WHO Member States endorsed a target of 90% reduction in measles mortality by 2010 over 2000 levels. Using a mathematical model, it was estimated that global measles mortality decreased by 74% from 535,300 deaths in 2000 to 139,300 in 2010. All WHO regions with the exception of the Southeast Asia Region achieved a reduction by three quarters. Sadly, this rapid progress was stalled somewhat by delayed implementation in India and continued outbreaks in Africa [13].

While coverage with the second dose of MCV2 in the European region has been maintained above 90% for several years, and over 70 SIAs have been conducted, large numbers of cases continue to occur each year, mostly in older individuals. In the first half of 2015, approximately 15,000 cases of measles were reported in the region [14].

Box 2. WHO/UNICEF policy on measles mortality reduction strategies [12].

The WHO–UNICEF-recommended strategies for reducing measles mortality include the following:

- Achieve and maintain high levels of population immunity by providing high vaccination coverage with two doses of measles- and rubellacontaining vaccines through routine immunization and campaigns.
- Monitor disease using effective surveillance and evaluate programmatic efforts to ensure progress.
- (3) Develop and maintain outbreak preparedness, respond rapidly to outbreaks, and manage cases.
- (4) Communicate and engage to build public confidence and demand for immunization.
- (5) Perform the research and development needed to support costeffective operations and improve vaccination and diagnostic tools.

Table 1. Types of SIA and their indications for use*.

SIA activity	Indications for use	Typical target age group(s)
Catch-up	To immunize older children who were too old for the introductory dose	9 months–14 years
Keep-up	To maintain coverage at above 95% routine	At 9 months
Mop-up	When a rapid assessment after a campaign shows high-risk areas have been missed	As for the campaign
Follow-up	When the number of susceptible individuals approaches the size of an average birth cohort	Preschool children
National campaign/outbreak	Anticipation of an outbreak e.g. after flood, earthquake, cyclone, civil unrest, Ebola	Variable age range e.g. 9 months-
response	outbreak	5 years

*These terms are not used consistently in the global literature.

Measles mortality reduction has been among the major public health success stories in the African Region. SIAs have contributed to this success by immunizing nearly half a billion children in Africa, resulting in a decline in the number of measles cases to 199,174 in 2010, from 520,102 in 2000, an impressive 62% decline. Coverage-based modeling showed an 89% reduction in measles mortality by the end of 2009 as compared to the estimates for 2000. However, MCV-1 coverage stagnated over the period 2012-2013, leaving important immunity gaps in many countries. In some parts of the African Region, this resulted in a resurgence of the disease that was previously under control [15]. In 2015, a large epidemic occurred in DR Congo with significant loss of life less than a year after mass immunization campaigns were carried out throughout the country. One reason for the outbreak was described as a failure to reach at least 95% of the population. Routine coverage at the time was 84% [16].

Even though measles vaccination prevented an estimated 17.1 million deaths between 2000 and 2014 [17], the disease remains a significant cause of death and disease. Outbreaks have continued to occur up to the present, most often involving children too young to be immunized, and older adolescents and adults who were not immunized earlier. Such occurrences are especially concerning because of the higher measles mortality rates among very young children. But reaching and maintaining high measles vaccine coverage has not been easy. Populations that are hard to reach, and those experiencing natural disasters or civil conflicts have proved most difficult.

Any gap in the immunity profile of a community is particularly damaging for rubella control programs. Counterintuitively, the introduction of rubella vaccine with low vaccine coverage raises the possibility of an increase in congenital rubella syndrome, as happened in Greece (Box 3) [18]. Cutts et al. stressed that countries and regions aiming to eliminate measles and rubella must improve the implementation and monitoring of both mass immunization campaigns and routine strategies [19]. If we are to eliminate measles in the near future, Simons et al. propose much more effort and financial commitment to measles control as a basis for the ultimate eradication of the disease [20].

4. Mathematical models

Using a mathematical model, Verguet et al. concluded that where there was a high burden of measles, one SIA alone would not be enough [21]. But the authors suggested that regular follow-up SIAs with high-coverage levels are a viable strategy to prevent measles outbreaks. How often SIAs should be conducted to achieve this would vary very much from

Box 3. Measles-containing vaccines.

Measles vaccine may be given as the following ways:

Monovalent measles vaccine (M)

- Measles-rubella vaccine (MR)
- Measles-mumps-rubella vaccine (MMR)
- Measles-mumps-rubella-varicella vaccine (MMRV)

country to country, taking into account such factors as population density and MCV routine coverage levels.

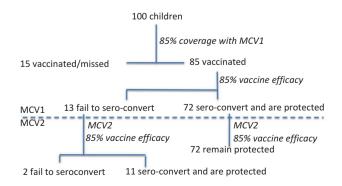
A measles immunity model was created drawing from data collected during a 2006 survey of measles immunization in Lusaka, Zambia. The authors predicted the outcome of three scenarios: measles incidence following current routine immunization coverage levels, following SIAs, and absent natural infection [22]. Routine immunization plus frequent SIAs were predicted to offer the best protection in children aged less than 5 years, even if each SIA had low coverage. Even better was a second dose at 12 months of age. The authors suggested that countries should consider frequent SIAs when resources for a two-dose routine strategy are unavailable.

In another study, the authors assessed global trends in MCV coverage and estimated the number of measles cases against how well countries had implemented the WHO strategy for measles control and the opportunity for a second dose of MCV [23]. The authors estimated that between 1999 and 2005, mortality attributable to measles was reduced by 60%. The Western Pacific Region (WPR) experienced the largest percentage reduction in estimated measles mortality (81% reduction). Globally, nearly 7.5 million deaths from measles were prevented through immunization between 1999 and 2005, with SIAs and improved routine immunization accounting for around one-third (2.3 million) of those prevented deaths.

5. Anticipated benefits of MCV-2

The figure of 80–85% vaccine efficacy (VE) is generally assumed under field conditions [24]. Ninety-five percent coverage with a VE of 85% results in only 81% of the target group protected, leaving a pool of 19% unprotected, while 85% coverage with a VE of 85% results in protection of only 72% of the population, leaving a pool of 28% unprotected. Even high coverage with one dose of vaccine, therefore, leaves many children unprotected. As countries introduce MCV-2 into their routine schedule, and as coverage for this dose rises, the pool of unvaccinated individuals will diminish.

Figure 1 and Table 2 demonstrate the anticipated improvement in protection afforded by MCV-2 coverage for a cohort of 100 children, whether given during routine immunization or during an SIA. We have assumed that the same 100 children are vaccinated with MCV1 and MCV2. We used a conservative value for VE of 85% for measles vaccine, but some authors



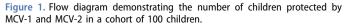


Table 2. Table demonstrating the number of children protected by MCV-1 and MCV-2 in a cohort of 100 children.

Coverage with MCV-1	А	95%	90%	85%
Number immunized with MCV1 (A \times 100)	В	95	90	85
Number protected with MCV if 85% vaccine efficacy $(B \times 85\%)$	C	81	76	72
Number failed to convert with MCV1 (B–C)	D	14	14	13
Number in row E protected with MCV2 if 85% vaccine efficacy (D \times 85%)	E	12	12	11
Total number of children protected by MCV1 and MCV2 combined (C + E)	F	93	88	83

For this table, we assume the same 100 children receive MCV1 and MCV2.

estimate it to be 95% for one dose and 99% for two doses [25,26]. After 1 dose (MCV1), 72 children will be protected, and after 2 doses (MCV2), 83 will be protected. The number of children protected by two doses of vaccine would be expected to increase further if the VE was greater than 85%, or children previously missed with MCV1 were reached and vaccinated with MCV2 (such as might occur if an SIA used a strategy to reach such children). In practice, however, there is always likely to be some correlation between the two doses: children who do not receive MCV-1 are likely to be relatively underserved compared to children who do, which makes the children who miss MCV-1 more likely to miss MCV-2 as well. Similarly, it is possible that children who get neither MCV-1 nor MCV-2 (routine doses) are less likely to receive a dose during an SIA, although this would depend a lot on the strategy employed by any given SIA.

6. Less effective SIAs

Compared to the number of SIAs reported to WHO, there are not so many reported in the published literature. Those that have been reported tend to be those that have been less successful, thereby giving a biased view of the overall impact of SIAs. It is clear from the literature that when SIAs fail to interrupt measles transmission, it is due to two principal causes: low routine coverage or low coverage by the SIA or both. Low coverage besets early SIAs. Only 51% of the target group received vaccine in a mass campaign in Yaoundé, Cameroun, in 1975 [27]. Difficulties that probably contributed to the low seroconversion rate included suboptimal vaccine titer (presumably reflecting inadequate cold chain and improper administration technique) and the exposure of the vaccine to heat and light under tropical conditions. The study estimated that a disappointing 83% of vaccine that was administered might have been wasted.

One early mass measles immunization campaign in Cape Town in 1978 failed to reach the target coverage rate of 85–90%. Rates were 55% in the first survey, 76% in the second, and 72% in the third. Failure to reach the targeted rate was attributed to in-migration, campaign design and implementation, and factors related to child and carer mobility [28,29].

An SIA in South Africa in 1990 resulted in a marked reduction in measles incidence in Natal/KwaZulu [30]. For the first 12 months after the campaign, measles hospital admissions were consistently low. Thereafter, the numbers increased steadily, rising sharply to above pre-campaign levels 21 months after the campaign. The age distribution of measles cases indicated that the initial fall in measles cases in the 10–12month age group had been reversed in the second year after the campaign, suggesting that the high immunization coverage achieved for this age group during the campaign had not been maintained through routine immunization.

An SIA implemented between 1997 and 1999 in Mozambique was evaluated to determine its impact. Epidemics subsequently occurred in the capital and in 4 of 9 provincial capitals and in 39 of 126 districts. Again, the authors attributed the principal reason for SIA failure to low routine and campaign coverage [31].

Migration has been shown to affect the outcome of SIAs. A study in Burkina Faso in 2002 showed that unimmunized children arriving from Cote d'Ivoire allowed continued circulation of measles virus and a failure of the SIA [32]. It was felt that synchronized activities for measles control in neighboring countries would be needed in such situations.

Despite a national SIA and follow-up campaigns during 2005–2006, Nigeria experienced ongoing measles outbreaks [33]. But routine immunization coverage of measles vaccine at the time varied between only 35% and 70%. Low routine coverage and the wide time interval between the catch-up and follow-up campaigns were deemed accountable for the accumulation of children susceptible to measles.

Soon after an SIA catch-up campaign in Viet Nam in 2007, the northwest of the country experienced a measles outbreak. The authors attributed this to inadequate coverage by the campaign, and also to low routine coverage in the hard-to-reach mountainous areas of the northwest [34].

A decline in measles incidence in Iranian children in 2008 was assessed one year after an SIA and was attributed to the strong routine immunization program and the recent campaign. However, cases of measles still occurred [35]. The authors suggested a number of reasons for failure to control future outbreaks such as primary vaccine failure, as well as immigration from neighboring countries with low vaccine coverage. A possible reason for vaccine failure was postulated to be a failure of the cold chain to ensure high vaccine titers. The authors suggested a second dose of measles vaccine would be needed to interrupt the endemic transmission of the measles virus.

Following a national SIA in China in 2010, there was a prolonged measles epidemic in Wenzhou City [36]. The attack rate was highest in children aged 8–11 months. The immunization rate outside the target ages (i.e. children who should already have been protected by routine immunization) was only 52%. Low coverage by routine immunization after the SIA was blamed for the outbreak as well as exposure in the emergency room at hospitals. The authors concluded that improving routine immunization coverage was the key to reaching the goal of measles elimination. They did not speculate whether the SIA had reduced the urgency of achieving high routine coverage in the minds of the service providers.

A mass campaign in Guinea achieved a coverage rate of around 75% [37]. This was not enough to control measles effectively, but it did provide cover for children not protected by previously low (42%) routine immunization coverage. Like the Chinese study (above), the authors felt it important to focus on improving routine immunization coverage, especially for hard-to-reach individuals. An outbreak of over 700 cases in the troubled Central African Republic in 2011 was the largest measles epidemic since 2003 in that country [38]. This occurred only 3 years after the last national measles campaign, reflecting the services' inability to reach some areas of the country.

7. Successful SIAs

Where the routine system in countries is not reaching a significant number of children with measles vaccine, SIAs can make a difference. Experience in 46 of 47 measles priority countries has shown that immunization using mass campaigns can reduce measles-related deaths. As countries have gradually adopted the use of SIAs, there has been a 74% reduction in measles related deaths between 2000 and 2007. The authors suggested that if measles mortality reduction strategies in all high-burden countries had been fully implemented, this would have made an important contribution to achieving Millennium Development Goal 4 (i.e. to reduce child mortality by two-thirds in 2015 as compared to 1990) [39,40].

There are many reports in the literature of effective SIAs. An SIA in 1998 in Zimbabwe targeting 9 months–14 years had a dramatic impact on measles cases, reducing them to around 1% of previous levels [41]. The authors concluded that high routine immunization coverage would, in addition, need periodic follow-up SIAs to ensure low measles virus transmission levels.

Of particular interest is the ability of an SIA to counter inequity by reaching those children who might otherwise have been missed. An SIA conducted in 2002 in Kenya reached a large percentage of children who had not been reached with even one dose of measles vaccine until then. Those children were often among the poorest households [42]. The SIA therefore reduced the coverage gap between rich and poor households.

Bangladesh implemented two massive catch-up SIAs; one immunized 35 million children, the other targeted an additional 20 million children. A positive impact was noted on health and immunization systems as a result of the SIAs. In addition, this provided a platform on which other interventions against bacterial and viral diseases could be mounted [43].

SIAs have been used successfully for many years as part of polio eradication efforts. Against a background of low routine immunization coverage, a recent impact study in Nigeria achieved high polio vaccine coverage through an SIA [44]. In evaluating the success, the authors concluded that high coverage for the SIA was particularly helped by political and financial support from the government, and appropriate planning and supervision.

8. Hard-to-reach target groups

It has been suggested that SIAs help in reaching groups or individuals not reached with routine immunization services. This was put to the test in Afghanistan when in 2002 the Ministry of Health of the Interim Government of Afghanistan conducted a countrywide SIA. It targeted children aged 6 months–12 years [45]. Two provinces reported coverage of more than 90% in two provinces, and more than 80% in two others. A subsequent cluster survey in the capital city found 91% coverage among children 6–59 months and 88% among those 5–12 years old [46]. If this complex situation can result in

impressively high SIA coverage, it is encouraging for other countries in similar situations to try the same strategy.

Children who were difficult to reach through routine services in Burkina Faso were reached by an SIA, with a resulting increase in measles vaccine coverage, closing an important immunity gap [47].

9. As part of an outbreak response

An outbreak response in Cameroon took the form of an SIA initiated 15 weeks after the start of the outbreak. A sharp drop in cases occurred from 555 cases during the period before the outbreak response to 162 cases afterward. The authors considered that these findings highlighted the potential benefits of rapid implementation of an SIA during a measles outbreak [48]. However, the authors do not comment on the impact of an SIA conducted when the peak of the outbreak has already passed. In fact, a review of outbreak responses supported the strategy that preventing outbreaks is more effective than campaigns to interrupt transmission once an outbreak has commenced [49].

10. Additional simultaneous interventions

In countries with less effective delivery systems, SIAs may offer children a second opportunity to receive a dose of measles vaccine that routine services do not. And there may also be an opportunity to receive other primary health-care interventions. Program officers in India felt that basic interventions should be included in SIAs to address such problems as nutritional deficiencies, diarrhea, and parasites [50].

A recent SIA in Papua New Guinea (PNG) included multiple interventions that all achieved relatively high coverage. It showed that it was at least feasible to deliver multiple interventions in resource-constrained settings [51]. Other developing countries have also managed to integrated health interventions with SIA. The authors suggested that in settings such as PNG there is a strong case for integrating SIAs with other health interventions.

From an evaluation in South Africa, the authors concluded that cost-effectiveness of an SIA was not uniform throughout the country. But it was substantially more cost-effective when other interventions such as vitamin A supplementation were added to the SIA [52]. Cost-effectiveness increased with multiple interventions, and better results were achieved when social mobilization was used [53].

11. Impact on other public health interventions during SIA

SIAs are intended to complement and strengthen routine immunization rather than replace it. The literature is conflicted about this. This strategy is typically used in countries with weak immunization delivery systems and where there is evidence or concern as to the ability of routine immunization programs to reach all at-risk children [54]. The aim of mass campaigns is to interrupt circulation of childhood diseases by immunizing every child regardless of immunization history, the idea being to catch children who are either not immunized or only partially immunized. Recently, there has been an increasing reliance on SIAs to boost rates particularly in relation to polio. SIAs have become one of the main strategies for the eradication of polio as promoted by the Global Polio Eradication Initiative [55]. From a cost-effectiveness perspective, SIAs are justifiable and incur marginal costs and can lead to raised overall immunization coverage [56]. However, there is evidence that during implementation, SIAs may also divert resources away from the primary health-care services [57,58].

A review of an SIA in South Africa found a significant negative impact for eight criteria that were assessed. The total number of fully immunized children under the age of one decreased by nearly a third while the SIA was being conducted; contraceptive use and antenatal visits also decreased over the same period. The review concluded that SIAs might interfere with elements of the health systems during the period of the SIA. Regular services may be disrupted and resources diverted from other activities. When conducting cost-benefit analyses of SIAs, the authors felt it important to take into consideration those other elements that may be disrupted [20,59].

One review looked at the impact on health services when conducting measles SIAs, evaluating six countries. On balance, the impact on services was largely positive in Bangladesh, Brazil, Tajikistan, and Viet Nam, while in Cameroon and Ethiopia, the impact had more negative effects. The authors concluded that weaker health systems might not be able to benefit as much from SIAs as more developed health systems where disruptions to health service delivery are much less likely to occur. They suggested that SIAs offered an opportunity to strengthen the routine immunization service and other elements of the health-care system [60].

A study from PNG revealed that 'Overall, the SIA did not damage routine services, and a number of beneficial effects were noted.' [61] For instance, it was found that the SIA was more closely combined with routine services by including vitamin A and other interventions in the strategy. As well, elements of routine services were improved through the SIA, especially better logistics and community awareness.

12. Cost-effectiveness

A recent study in Benin measured the cost and effectiveness of delivering a measles SIA compared with routine immunization [62]. Personnel and vaccines were the most important cost components for the two strategies (Table 3). Vaccine wastage rates were considerably lower for the SIA. They found that the SIA was costlier than routine immunization, but the cost per immunized child was lower for the SIA (USD 0.92 compared with USD 2.59 for routine immunization). Coverage for routine immunization was 89% of the target population, compared with 104% for the SIA. The SIA was able to immunize 35,564 under-five children in just 7 days. The estimated benefit was 5601 additional measles cases averted, equivalent to 6955 additional disability-adjusted life years averted. The authors estimated that the SIA saved the lives of 185 children who might otherwise have died from measles despite routine immunization. The SIA was found to be more cost-effective in South Africa when vitamin A was included [63].

Table 3. Cost by component for measles RI and SIA in a health district in Benin.

	RI		SIA			
Cost components	Amount (FCFA)	%	Amount (FCFA)	%		
Recurrent costs						
Vaccines	1118,400	11.35	4728,000	29.93		
Consumables	391,161	3.97	3606,188	22.83		
Personnel	3599,536	36.54	4750,000	30.07		
Transport	95,258	0.97	625,436	3.96		
Communication	0	0.00	371,000	2.35		
Trainings	0	0.00	454,000	2.87		
Supervision	220,579	2.24	830,550	5.26		
Maintenance	98,010	0.99	0	0.00		
Wastage management	58,501	0.59	137,500	0.87		
Surveillance	143,150	1.45	216,000	1.37		
Fuel for cold chain	396,900	4.03	7541	0.05		
Electricity	36,464	0.37	693	0.00		
Capital costs						
Buildings	1188,000	12.06	22,572	0.14		
Cars and motorcycles	1120,320	11.37	21,286	0.13		
Cold chain materials	1385,658	14.06	25,793	0.16		
Total	9851,938	100	15,796,560	100		

RI: routine immunization; SIA: supplementary immunization activities. 1USD is approximately 605 Francs Communauté Financière Africaine (FCFA) Reproduced with permission from [62] under the Creative Commons Attribution 4.0 International License https://creativecommons.org/licenses/by/4.0/.

13. Safety

The importance of delivering vaccine safely in SIAs was stressed by authors in China. They reported 2.14 serious adverse events per million doses of measles vaccine administered during SIAs [64]. WHO reinforced this message and stressed that SIAs offer a special opportunity for countries to develop their adverse event surveillance system (Box 4) [65].

14. The WPR

Pacific Islands are part of the WHO WPR. In 2005, the region set a goal for the elimination of measles that was defined as ending the circulation of domestic strains in the region by 2012 (Box 5) [67].

Since 2003, over 300 million persons have been immunized against measles through campaigns in the WPR; measles incidence in 2011 was at an all-time low of 12 cases per million population.

Box 4. Handling measles vaccine during routine and supplementary immunization activities.

- (1) Heat damage. Remote communities must be reached during SIAs, resulting in measles vaccine being transported over long distances in vaccine carriers. Sometimes the vaccine will suffer heat damage in transit or during reconstitution. If exposed to the ultraviolet rays of sunlight for long, the number of replicating vaccine virus particles will be diminished significantly, resulting in lowered potency.
- (2) Contamination. If the vaccine vial is used for longer than 6 h after reconstitution, the vaccine can become contaminated and result in an overgrowth of bacteria, possibly causing toxic shock to the individual receiving the vaccine. Such contamination may happen any time the vaccine is not reconstituted properly or if it is kept in its reconstituted form for more than 6 h. During campaigns, vaccine tends to be used up faster, potentially lessening this risk.

Box 5. The four main challenges for measles elimination in the WPR [66].

In September 2012, at its 63rd session, the World Health Organization Regional Committee for the Western Pacific adopted a resolution urging Member States to effectively address the four main challenges for measles elimination in the Western Pacific Region (WPR/RC63.R5, Annex 2). Strategies required to implement the Regional Committee resolution include the following:

- Interrupting and preventing measles virus transmission: To interrupt all
 endemic measles virus transmission and prevent future transmission,
 by closing immunity gaps with measles vaccine, especially among all
 underserved and marginalized communities.
- Outbreak preparedness and response: To enhance capacity for preparedness, rapid detection, and response to measles outbreaks, whether caused by an endemic or imported virus, to prevent the spread and reestablishment of measles virus transmission.
- Ensuring highly sensitive surveillance: To improve the sensitivity and performance of epidemiological surveillance and laboratory capacity to track changes in measles epidemiology, identify sources of infection, and provide evidence consistent with the absence of endemic transmission.
- Preparing for verification of measles elimination: To establish national verification committees that will develop regular progress reports for submission to the Regional Verification Commission.

15. Pacific Island countries

The 22 countries and territories known as the Pacific Island countries and territories (PICTs) are part of the WHO/WPR (Box 6) [65]. PNG has around 7 million population, and the remaining 21 PICTs jointly having only around 3 million. In contrast, the rest of the WPR has a population of around 1850,000,000. It is clear that although the PICTs are included in the WPR, their population numbers and geographical environment are profoundly different from most of the other countries. As would be expected, this influences the epidemiology of communicable diseases and vaccine preventable diseases in particular.

The PICTs are considered as one epidemiological block for the purposes of measles surveillance and verification/certification. Populations at highest risk for exposure to measles virus may be among persons from countries or territories that have historical associations with other countries that are currently experiencing measles outbreaks. Examples of countries or territories at high risk for measles virus importation may include Solomon Islands because of their low coverage and proximity and frequent cross-border exchange of goods and services with PNG; and the US-affiliated countries and territories (American Samoa, Guam, Mariana Islands, Marshall Islands, Micronesia, and Palau) and their relationship with the Philippines. The low immunization coverage in Vanuatu has also made it vulnerable to outbreaks.

The MCV schedules of PICTs vary considerably – the first dose is given at 12–15 months with a second dose between 13 months and 6 years. All but two of the PICTs provide a second dose of MCV. Table 4 shows countries in gray that are achieving less than 80% coverage for MCV-1 or MCV-2.

Despite attempts to reach and maintain high coverage with routine immunization coverage and SIAs, these efforts have not been enough to eliminate measles, with outbreaks occurring in several PICT countries in the last decade (Figure 2).

16. Case study – Solomon Islands, 2014

The Solomon Islands experienced a measles outbreak in June 2014 after a traveler returned from PNG [69]. A total of 4654 suspected measles cases were reported subsequently, with 38 cases having been confirmed by serology. The genotype B3 was the same one that was circulating in Port Moresby where the index case came from. There were nine measles-related deaths reported between 1 July and 17 November (case fatality ratio 0.2%). Most cases were from the densely populated islands of Honiara, Guadalcanal, and Malaita. Following this outbreak, a Measles–Rubella (MR) SIA was launched in a phased manner on 1 September to target all age groups from 6 months to 30 years. The campaign commenced in Honiara, the epicenter of the outbreak, and was rolled out in the provinces as resources permitted.

The target population was 376,286 persons. National administrative coverage indicated that 398,622 people were immunized (106% of the target). Disaggregated administrative data indicate that 9 provinces of 10 (90%) and 33 zones out of 47 (70%) achieved coverage above the 95% target during the SIA. The logistics were formidable – a total of 170 vaccination teams with 514 health workers, 92 supervisors, and 120 volunteers participated in the campaign, working 1176 operational posts (254 fixed, 662 outreach, and 304 mobile). A total of 395 hard-to-reach villages with 28,818 hard-to-reach people were identified and reached.

Prior to the SIA, micro-planning, training, and social mobilization were conducted in each province. Some of the major challenges, which prevented the SIA from being conducted simultaneously in all provinces included the delayed arrival of the MR vaccine and funds to the provinces; competition for priority from other activities; weak social mobilization; and difficulties in data transmission. These all resulted in the prolongation of the SIA to early December 2014. A Rapid Coverage Assessment (RCA) was conducted in three provinces after the SIA.

Annual MCV-1 routine coverage in Solomon Islands had ranged from 60% to 96% during the period 1990–2013, rising to 93% in 2014 [63]. Although no measles cases had been reported to WHO since 1990 (when there were 343 cases) such mediocre coverage made Solomon Islands vulnerable to an outbreak. MCV-2 had not been introduced at this point. There had been a national SIA in 2012 targeting 12–59 month-olds, with a reported coverage of 101% (and 90.6% for vitamin A). Not surprisingly, it did not prevent a large outbreak from occurring in 2014 – only 2 years later, as most of the cases were in adolescents and young adults who would have been missed in earlier efforts to immunize.

Box 6. 22 Pacific Island countries and territories.

The Secretariat for the Pacific Community (SPC) [68] membership includes 22 Pacific Island countries and Territories: American Samoa, Cook Islands, Federated States of Micronesia (FSM), Fiji, French Polynesia, Guam, Kiribati, Marshall Islands, Nauru, New Caledonia, Niue, Northern Mariana Islands, Palau, Papua New Guinea, Pitcairn Islands, Samoa, Solomon Islands, Tokelau, Tonga, Tuvalu, Vanuatu, and Wallis and Futuna.

Table 4. MCV coverage in selected PICTs 2010-2014.

					Covera	age (%)				
Year	2010		2011		2012		2013		2014	
	MCV1	MCV2	MCV1	MCV2	MCV1	MCV2	MCV1	MCV2	MCV1	MCV2
Am Samoa				No	data				85	N
Cook Islands	99	98	89	96	97	98	97	95	98	98
Fiji	94	94	94	94	94	94	94	94	94	94
French Polynesia				No	data				~99	Ν
Guam				No	data				82	Ν
Kiribati	89	21	91	61	91	9	91	84	91	84
Marshall Islands	97	90	88	74	78	58	79	56	79	53
Federated States of Micronesia	80	75	92	75	91	70	91	75	91	75
Nauru	99	99	99	99	96	81	97	88	98	94
New Caledonia				No	data				~99	Ν
Niue	99	99	99	98	99	98	99	99	99	99
Palau	39	39	86	83	91	86	99	98	83	81
PNG	55	-	60	-	67	-	70	-	65	-
Samoa	61	45	67	65	85	67	99	87	91	78
Solomon Islands	85	_	90	_	99	-	93	-	93	-
Tonga	68	67	66	66	62	62	67	67	67	67
Tuvalu	85	87	98	90	98	93	96	84	96	84
Vanuatu	53	-	53	_	5	-	53	-	53	_

MCV: measles containing vaccine; PICTs: Pacific island countries and territories; PNG: Papua New Guinea.

Source: Data from WHO country profiles. Data are estimates made by WHO and UNICEF.

-, MCV-2 dose not part of routine schedule.

Percentages in gray shaded boxes are less than 80%.

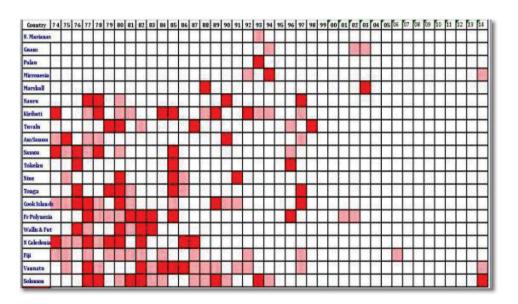


Figure 2. Measles outbreaks in selected PICTs, 1974–2014. Outbreaks with incidence of 5 or less reported cases per 1000 population. Outbreaks with incidence of more than 5 cases per 1000 population. Source: WHO Western Pacific Regional Office, Fiji.

National coverage for the 2014 post-outbreak SIA was 106% for MR and 46% for vitamin A. Provincial reported coverage ranged from 91% to 130% (Figure 3). Those locations with coverage rates in excess of 100% probably represent a mix of cross-border population movements and vaccination outside the official age range (i.e. vaccination of older children who showed up during the SIA). During the RCAs in 2014 in Honiara, Guadalcanal, Western and Central Provinces, a total of 193 villages were assessed, out of which 119 (62%) villages had coverage of less than 95%. This would seem a much more realistic coverage rate than the reported administrative coverage of over 100%. Based on RCA results, a mop-up campaign was conducted in all the villages with coverage less than 95%. In addition, a mop-up campaign was conducted in all provinces with administrative coverage of less than 95%.

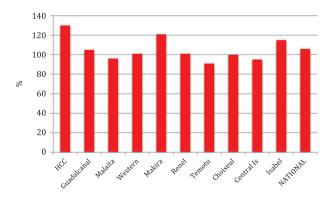


Figure 3. Measles vaccine coverage (%) for SIA by province, Solomon Islands 2014. Source: Data supplied to WHO Western Pacific Regional Office/UNICEF by the Government of Solomon Islands. HCC: Honiara City Council.

Certain problems were identified in retrospect. In the remote and hard-to-reach areas with scattered islands, there were inadequate numbers of outreach and mobile teams and inadequate appropriate transport. Funds were delayed reaching provinces. The Gavi funds arrived in the second week of October, while the funds through WHO that had been requested later for additional support to cover older adolescents and adults, came late in the second week of November. The lengthy financial process at the national and provincial levels aggravated the delay. To solve this problem, the campaign was conducted in phases, and provinces used money from provincial sources while waiting for the arrival of SIA funds. Vaccines and supplies were delayed, resulting in the need for the campaign to be rolled out in separate phases instead of being conducted simultaneously in all provinces. There were data inconsistencies and dual population denominators, with high reported coverage. Nonetheless, the outbreak stopped.

The SIA in 2014 was costed at USD 830,000 (Table 5). This included contributions from government (USD 30,000) and donors (the remainder). A crude estimate of the cost per individual immunized was approximately \$2. This cost did not include training – which would have been substantial given the numbers involved. No attempt was made to cost deaths or complications averted.

17. Case study - Republic of Marshall Islands, 2003

Until the outbreak of measles in Republic of Marshall Islands (RMI) in 2003, there had been no measles cases reported since

Expenditure category	Budgeted	Government contribution	GAVI contribution	WHO contribution	Total
Vaccine supplies	-	-	186,000	147,298	333,298
Operational costs	-	30,000	145,000	272,157	447,157
Coverage survey	-	-	-	50,000	50,000
Total	-	30,000	331,000	469,455	830,455

Source: EPI Unit, MHMS, Solomon Islands.

1989. SIAs had been administered during this period. Reported routine MCV-1 coverage among children aged 12–23 months varied widely (52–94%) between 1990 and 2000. Cluster surveys among children aged 2 years in 1998 and 2001 showed 93% and 80% MCV-1 coverage rates, respectively [70].

There were 826 measles cases reported, of which 766 (92%) were in the capital Majuro. Of those, 186 (23%) were in infants aged less than 1 year, and 309 (37%) were in persons aged less than 15 years. More than half (59%) of the cases aged less than 15 years had not been immunized prior to the SIA. One hundred cases were hospitalized, of which three died. Coverage for the SIA consequential on the outbreak was 93%, targeting persons aged 6 months–40 years.

Measles epidemics had occurred previously in RMI in 1968 [71], 1978 and 1988 (CDC unpublished data) (Figure 4). The introduction of MMR vaccine was in 1982 at 9 months of age. This was augmented to a 2-dose schedule in 1998. From 1994 to 2002, three SIAs were conducted: a campaign in response to a measles outbreak in the nearby state of Chuuk in 1994, a catch-up campaign targeting children aged 1–14 years in 1998, and a follow-up campaign targeting children aged 1–4 years in 2002.

For 10 days after the start of the outbreak, domestic air and sea travel was interrupted, and the start of the school year was postponed for a week. Immunization teams focused on schoolaged children, even visiting the outlying islands. Evidence of vaccination was required for school entry. Rapid implementation of control and prevention efforts in the Outer Islands and Ebeye confined the outbreak primarily to Majuro, the atoll most populated. Spread to other countries was probably limited by the unprecedented requirement that departing international passengers had to show evidence of measles immunization. It would have helped that localities where importation might have occurred generally had high population immunity.

The population of RMI at the time of the outbreak was around 51,800. The island of Majuro had around 6700 persons per square mile, and Ebeye had a population density of 96,300 persons per square mile, for a total of around 36,000 persons between them. This extremely high-density situation undoubtedly contributed to the size and rapid spread of the outbreak.

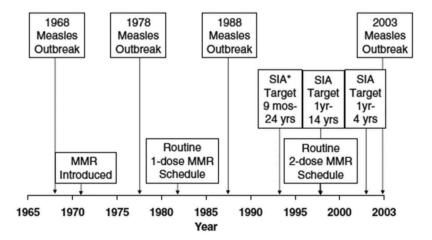


Figure 4. Timeline of the measles SIA and history of measles outbreaks in RMI. Reproduced from Hyde TB, Dayan GH, Langidrik JR, Nandy R, Edwards R, Briand K et al. Measles outbreak in the Republic of the Marshall Islands, 2003. Int J Epidemiol 2006;35:299–306. doi:10.1093/ije/dyi222 with permission from Oxford University Press [71]. mos: months; yrs: years.

During the outbreak, Marin et al. [72] concluded that measles vaccine effectiveness was high; thus, diminished vaccine effectiveness was not the main cause of the outbreak [73].

18. Resurgence

As reported to WHO, there has been a decline in funding for measles-control activities since 2008 [74]. For instance, financial support to the Measles and Rubella Initiative decreased from US \$150 million in 2007 to slightly more than US\$ 50 million in 2009 (Measles and Rubella Initiative, unpublished data, 2009) [75]. Even those countries designated as 'priority' have struggled to raise the desired 50% of operational costs for SIAs. The impact of insufficient resources was measured modeling two scenarios; the worst case scenario assumed that routine MCV-1 coverage in the 47 priority countries remained at 2008 levels during 2009-2013 and that none of these countries carried out nationwide SIAs during 2010-2013. The status guo scenario assumed that routine MCV-1 coverage increased 1% per year among priority countries, with less than 90% coverage in 2008, and that SIAs were conducted during 2010-2013 in 46/47 priority countries. The results indicated that if the 47 priority countries were unable to keep up currently recommended strategies during 2010–2013, deaths from measles might rebound. This could mean an estimated 1.7 million measlesrelated deaths (Figure 5). If the priority countries (excluding India) implemented high-quality SIAs and continued to increase routine coverage of MCV-1, projected global mortality during 2010-2013 might remain at 2008 levels, resulting in approximately 0.6 million measles-related deaths.

Concerns that priority countries may not be able to maintain improvements in routine immunization and SIAs are quantified by the above data, suggesting that there could be as many as 1.1 million additional measles deaths during the following 4 years under a worst case scenario.

Although measles was eliminated from Brazil in 2000, it was not protected from resurgence. An outbreak occurred in Ceará in the North East of the country in 2014. It was probably imported directly from Europe. The capital experienced measles mostly in young children while elsewhere, the disease was more common in persons 15–29 years of age [76]. Extrapolating to the Pacific environment, the islands are not only vulnerable to outbreaks in any areas with currently low coverage, but even cohorts of older individuals whose protection is inadequate, making the population vulnerable to resurgence.

This danger of reintroduction and resurgence is no less real in the Pacific. Table 6 shows the number of confirmed measles cases in the previous 12 months in other countries in the Western Pacific Region – the Pacific Islands' nearest neighbors.

19. Discussion

The forgoing review helps to define the issues relating to the use of SIAs and measles control. Consistent with other parts of the world, positive results have accrued from well-executed SIAs in the Pacific. In 1999, 14 PICTs implemented coordinated SIAs with the result that measles transmission virtually stopped for several years. But the 2012, SIA in Solomon Islands, targeting children less than 5 years of age did not prevent a subsequent outbreak of measles mostly among older persons from occurring within 2 years.

In contrast, countries such as French Polynesia with a strong health infrastructure underpinning immunization services accomplished high coverage with MCV-1 and MCV-2 without resorting to an SIA.

There is a basic epidemiological question to address – can SIAs prevent epidemics of measles? The answer is complex. The outbreaks in 2014 in Solomon Islands and FSM showed how SIAs were not successful in boosting the immune profile sufficiently before importation of cases occurred. This was at least in part because cases occurred in older cohorts that had not been targeted by the SIAs. On the other hand, the 2013 SIA in Vanuatu was able to contribute to preventing widespread transmission following the importation of measles virus in 2014 [77].

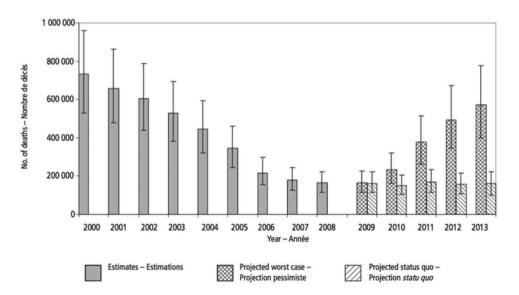


Figure 5. Estimated number of measles deaths worldwide, 2000–2008 and projections of possible resurgence in measles deaths worldwide, 2009–2013. Source: Global reductions in measles mortality 2000–2008 and the risk of measles resurgence. *Wkly Epidem Rec* 4 December 2009, No. 49, 2009, 84, 505–516 [74].

Table 6. Confirmed measles cases by month of onset, June 2014–May 2015, WHO WPR.

				2014						2015		
Country	Jun	Jul	Aug	Sept	Oct	Nov	Dec	Jan	Feb	Mar	Apr	May
Australia	34	32	23	2	17	5	14	10	6	11	9	0
Brunei Darussalam	0	0	0	0	0	0	0	0	0	0	0	0
Cambodia	0	0	0	0	0	0	0	0	0	0	0	0
China	6113	3779	2007	1033	778	755	1356	2359	4312	5767	7937	7035
China, Hong Kong SAR	4	7	3	3	1	0	0	0	1	1	2	2
China Macao SAR	1	0	0	0	0	0	0	0	0	0	0	0
Japan	38	12	19	5	2	6	2	1	2	3	10	2
Lao DPR	0	0	0	28	36	1	0	0	2	0	0	0
Malaysia	18	19	19	17	23	7	13	16	25	46	68	39
Mongolia	0	0	0	0	0	0	0	0	0	159	262	124
New Zealand	98	31	5	0	1	3	0	0	2	2	2	3
PNG	640	259	64	29	10	37	21	34	4	7	2	0
Philippines	1260	1305	1386	957	448	204	45	150	190	133	54	12
Republic of Korea	44	25	3	2	1	0	0	0	0	4	1	0
Singapore	6	12	9	0	2	0	2	2	3	2	7	1
Viet Nam	457	257	210	170	155	38	10	38	14	12	19	8
PICTs	128	114	9	3	2	0	0	3	2	7	0	0
WPR Total	8841	5852	3757	2249	1476	1056	1463	2613	4563	6154	8373	7226

Values in bold for PICTs. WPR: Western Pacific Region; PICTs: Pacific island countries and territories; PNG: Papua New Guinea; SAR: Special Administrative Region; DPR: Democratic People's Republic.

Source: Case-based and aggregated data reports to the WHO Western Pacific Regional Office by 20 June 2015.

As can be seen from Figure 6, the frequency of SIAs conducted in PICTs has been variable over the last decade. If anything, they have become less frequent, with only six reported since 2010. The driving forces previously have been the need to protect against or react to measles outbreaks and identifying age cohorts of under-immunized individuals that have been the result of low coverage in previous years. The SIA in Solomon Islands was following an outbreak of measles. The ones in Vanuatu were in response to low routine coverage AND outbreaks of measles. The 2013 SIA was also used to introduce the rubella component of the MMR vaccine. The 2011 SIA in Fiji was in response to an outbreak of rubella, and the remaining ones were for correcting low coverage. Only countries with low coverage have been using SIAs as a quick way to raise coverage.

It is important to consider whether there remains a risk of outbreaks in the Pacific Islands. The answer is an unequivocal YES. Countries such as Vanuatu have MCV-1 coverage low enough to sustain measles transmission. And these countries have not yet introduced a second routine dose. Added to this is the knowledge that measles has been transmitted in the past from one island to another, the lower performing countries undoubtedly placing all other islands at some level of risk. To their credit, many countries have already achieved high MCV-1 and MCV-2 coverage, and any cases arriving in those countries would likely have minimal impact.

Samoa has noted that it experienced a period of low coverage between 2007 and 2011 and is considering a one-off follow-up SIA for those age groups that have resulting low protection. Countries that have had high routine coverage are not undertaking SIAs and are not experiencing measles cases. It is clearly important to conduct effective (high coverage) SIAs; these will help protect against outbreaks, but poorly executed SIAs may not prevent an outbreak in the next few years.

It is important how nonimmunes are distributed in the population. In the smaller islands, there will be such small numbers of nonimmune children that the unimmunized pose only a minimal risk. But larger islands such as Fiji will accumulate large numbers of nonimmunes very quickly after an SIA if their routine coverage levels for MCV-1 and MCV-2 are not very high. What matters is the absolute number of susceptible people that are relatively well connected (e.g. same island, some age group, same social group). If these nonimmunes/susceptibles are mostly in one place, they pose a greater risk. It therefore makes strategic sense here to

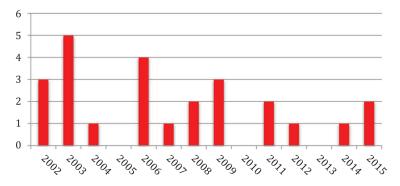


Figure 6. Number of SIAs in PICTs, 2002-2015. Source: Data compiled from WHO Western Pacific Regional Office, Fiji

consider SIAs on a regular basis, particularly for islands with large populations and whose immunization services are performing less well.

The logistics of reaching far-flung islands with vaccine and personnel are huge. Ferry, outboard motorboat or canoe constitute the main methods of reaching distant islands; inter-island flights are very expensive and therefore of limited use. Various factors combine to prevent or delay immunization - brutal terrain reducing accessibility to remote populations, nonavailability of transport, and travel logistics and costs [78]. Similarly, there is a wide range of population densities, with some countries (e.g. Kiribati) covering huge areas and having very isolated populations. The island environment tests even the most robust equipment. Metal soon corrodes in salt-laden air. Remoteness of access delays repair and replacement. The cold chain generally has adequate capacity but is of varying quality and is being replaced with solar technology, especially in more remote locations. The decision to undertake an SIA, therefore, must not be taken lightly, and consideration needs to be given to the expense, opportunity cost, and the considerable difficulties in mounting such an exercise in the Pacific environment.

20. Expert commentary

The literature and the country reviews reported here suggest that regular SIAs combined with high coverage with one dose of measles vaccine given in the routine system will control measles. Better still, a second dose in the routine system should obviate the need for an SIA unless one is needed to capture those who were too old to benefit from the introduction of the second dose. By 2015, only two PICTs had so far failed to introduce a second dose. The remainder should be largely protected from outbreaks *if their coverage for both doses is high enough*. However, a number of countries are not yet reaching high routine coverage with their MCV-2 dose, and this should be the preferred method of controlling measles, resorting to SIAs only as a second option.

21. Five-year view

While high coverage with two doses of MCV provided in a well-functioning health system is the preferred strategy, SIAs can play a critical role in closing immunity gaps. When SIAs are indicated, they should be well designed to meet specific needs, must be carried out effectively and safely with very high coverage, and include other public health interventions as appropriate to make them more cost-effective. However, benefits are likely to be limited following a poorly executed SIA.

Smaller, more affluent islands are likely to focus on raising routine coverage (especially MCV-2), but larger islands with relatively large populations are likely to continue using SIAs to reach hard-to-reach populations that would otherwise be missed.

Alternative presentations of measles vaccine such as the micro-needle patch [79] that are more heat-stable and easier to administer are now under development and will hopefully make it easier to administer the vaccine, especially in locations such as remote Pacific islands.

It is not currently clear precisely how SIAs should be evaluated [80]. This should be clarified by a South African group that is planning a systematic review of SIAs, focusing on whether this strategy improves vaccine coverage, prevents outbreaks, and what is its impact on service delivery [81].

Key issues

- MCV coverage varies considerably across PICTs.
- Few countries have high MCV-2 coverage
- Measles outbreaks continue to occur in nearby large countries, and remain an ongoing potential source of infection for PICTs.
- PICTs remain at risk from measles outbreaks
- SIAs will become less necessary in PICTs overall, but will continue to be used as a strategy for measles control, at least for the near future, especially in some larger island nations.

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Declaration of interest

The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

References

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

- 1. Cliff A, Haggett P, Smallman-Raynor M. Measles. An historical geography of a major human viral disease. Blackwell, UK; 1993. p. 129.
- Breakwell L, Moturi E, Helgenberger L, et al. Measles outbreak associated with vaccine failure in adults - federated states of Micronesia, February-August 2014. MMWR Morb Mortal Wkly Rep. 2015 Oct 2;64(38):1088–1092. DOI:10.15585/mmwr. mm6438a7
- •• It is one of the few published papers documenting measles epidemiology in the Pacific.
- 3. Measles vaccine. WHO position paper. Wkly Epidem Rec. 2 Apr 2004. 2004;79(14):129–144.
- World Health Organization (2012). Retrospective measles data on supplementary activities 2000_2010. Available from: http://www.who.int/_ monitoring/data/Summary_Measles_SIAs_2000_to_2011.xls
- 5. Castillo-Solorzano C, Ruiz Matus CR, Flannery B, et al. The Americas: paving the road toward global measles eradication. J Infect Dis. 2011;204:S270–S278.

- Otten M, Kezaala R, Fall A, et al. Public health impact of accelerated measles control in the WHO African Region 2000-03. Lancet. 2005 Sep 3–9;366(9488):832–839.
- Wichmann O, Hellenbrand W, Sagebiel D, et al. Large measles outbreak at a German public school, 2006. Pediatr Infect Dis J. 2007;26:782–786. DOI:10.1097/INF.0b013e318060aca1
- van Boven M, Kretzschmar M, Wallinga J, et al. Estimation of measles vaccine efficacy and critical vaccination coverage in a highly vaccinated population. J R Soc Interface. 2010;7:1537– 1544. DOI:10.1098/rsif.2010.0086
- Anders JF, Jacobson RM, Poland GA, et al. Secondary failure rates of measles vaccines: a meta-analysis of published studies. Pediatr Infect Dis J. 1996 Jan;15(1):62–66.
- 10. World Health Organization. Measles vaccines: WHO position paper. Wkly Epidem Rec. 2009;84:349_60.
- 11. Field guide for planning and implementing supplemental activities for measles and rubella. Copenhagen: WHO European Office; March 2004. http://www.euro.who.int/en/health-topics/communicable-diseases/ measles-and-rubella/publications/pre-2009/field-guide-for-planningand-implementing-supplemental-activities-for-measles-and-rubella
- 12. Measles & Rubella Initiative. Global Measles and Rubella Strategic Plan 2012-2020. http://measlesrubellainitiative.org/learn/the-solu tion/the-strategy/
- 13. Global reductions in measles mortality. 2000–2008 and the risk of measles resurgence. Wkly Epidemiol Rec. 2009(84):509–516.
- WHO/Europe calls for scaled-up vaccination against measles. http:// www.euro.who.int/en/media-centre/sections/press-releases/2015
- External Evaluation of the Regional IVD Strategic Plan: 2009-2013. WHO Regional Office for Africa. Brazzaville, Congo; 2013.
- Maurice J. Measles outbreak in DR Congo an "epidemic emergency". Lancet. 386, 9997, 943, 5 Sep 2015;DOI:10.1016/S0140-6736(15)00115-45
- 17. Measles Facts Sheet. http://www.who.int/mediacentre/factsheets/ fs286/en/
- Panagiotopoulos T, Antoniadou I, Valassi-Adam E, et al. Increase in congenital rubella occurrence after immunisation in Greece: retrospective survey and systematic review. How does herd immunity work? BMJ. 1999;319(December (7223)):1462–1467.
- Cutts FT, Lessler J, Metcalf CJ. Measles elimination: progress, challenges and implications for rubella control. Expert Rev Vaccines. 2013 Aug;12(8):917–932. DOI:10.1586/14760584.2013.814847
- Simons E, Ferrari M, Fricks J, et al. Assessment of the 2010 global measles mortality reduction goal: results from a model of surveillance data. Lancet. 2012;379:2173_8.
- It documents the global progress of measles control up to 2010.
- Verguet S, Johri M, Morris SK, et al. Controlling measles using supplemental activities: a mathematical model to inform optimal policy. Vaccine. 2015 Mar 3;33(10):1291–1296. DOI:10.1016/j. vaccine.2014.11.050
- Lessler J, Moss WJ, Lowther SA, et al. Maintaining high rates of measles in Africa. Epidemiol Infect. 2011 Jul;139(7):1039–1049. Epub 2010 Oct 5. DOI:10.1017/S0950268810002232
- Wolfson LJ, Strebel PM, Gacic-Dobo M, et al. Has the 2005 measles mortality reduction goal been achieved? A natural history modelling study. Lancet. 2007 Jan 20;369(9557):191–200.
- Black FL, Berman LL, Liberl M, et al. Inadequate immunity to measles in children vaccinated at an early age: effect of revaccination. Bull WHO. 1984;62:315–319.
- 25. Vitek CR, Aduddell M, Brinton MJ, et al. Increased protections during a measles outbreak of children previously vaccinated with a second dose of measles-mumps-rubella vaccine. Pediatr Infect Dis J. 1999;18:620–623.
- It documents the importance of a second dose of vaccine in controlling measles.
- Erdman DD, Heath JL, Watson JC, et al. Immunoglobulin M antibody response to measles virus following primary and secondary vaccination and natural virus infection. J Med Virol. 1993;41:44–48.
- McBean AM, Foster SO, Herrmann KL, et al. Evaluation of a mass measles campaign in Yaoundé, Cameroun. Trans R Soc Trop Med Hyg. 1976;70(3):206–212.

- Kearney M, Yach D, Van Dyk H, et al. Evaluation of a mass measles immunization campaign in a rapidly growing peri-urban area. S Afr Med J. 1989;76:157–159.
- 29. Berry DJ, Yach D, Hennink MHJ. An evaluation of the national measles vaccination campaign in the new shanty areas of Khayelitsha. S Afr Med J. 1991;79:433–436.
- Abdool Karim SS, Abdool Karim Q, Dilraj A, et al. Unsustainability of a measles immunization campaign–rise in measles incidence within 2 years of the campaign. S Afr Med J. 1993 May;83(5):322–323.
- It documents the lack of success of early SIAs.
- Cliff J, Simango A, Augusto O, et al. Failure of targeted urban supplemental measles vaccination campaigns (1997-1999) to prevent measles epidemics in Mozambique (1998-2001). J Infect Dis. 2003 May 15;187(Suppl 1):S51–7.
- Yaméogo KR, Perry RT, Yaméogo A, et al. Migration as a risk factor for measles after a mass vaccination campaign, Burkina Faso, 2002. Int J Epidemiol. 2005 Jun;34(3):556–564. Epub 2005 Jan 19.
- Weldegebriel GG, Gasasira A, Harvey P, et al. Measles resurgence following a nationwide measles vaccination campaign in Nigeria, 2005-2008. J Infect Dis. 2011 Jul;204(Suppl 1):S226–31. DOI:10.1093/ infdis/jir136
- Murakami H, Van Cuong N, Van Tuan H, et al. Epidemiological impact of a nationwide measles campaign in Viet Nam: a critical review. Bull World Health Organ. 2008;86:948–955.
- 35. Pourabbas B, Ziyaeyan M, Alborzi A, et al. Efficacy of measles and rubella vaccination one year after the nationwide campaign in Shiraz, Iran. Int J Infect Dis. 2008 Jan;12(1):43–46. Epub 2007 Oct 18
- Gao J, Chen E, Wang Z, et al. Epidemic of measles following the nationwide mass campaign. BMC Infect Dis. 2013;13:139. DOI:10.1186/1471-2334-13-139
- Doumtsop JG, Malano ER, Diallo IT, et al. An evaluation of the 2012 measles mass vaccination campaign in Guinea. Pan Afr Med J. 2014 Jan 8;17. 4. eCollection 2014. DOI:10.11604/ pamj.2014.17.4.2475
- Tricou V, Pagonendji M, Manengu C, et al. Measles outbreak in Northern Central African Republic 3 years after thelast national campaign. BMC Infect Dis. 2013 Feb 26;13: 103. DOI:10.1186/1471-2334-13-103
- Ent M, Gupta SK, Hoekstra E. Two doses of measles vaccine reduce measles deaths. Indian Pediatrics. 2009 November 17;46:933–938.
- 40. Millennium Project. http://www.unmillenniumproject.org/goals/
- Munyoro MN, Kufa E, Biellik R, et al. Impact of nationwide measles vaccination campaign among children aged 9 months to 14 years, Zimbabwe, 1998-2001. J Infect Dis. 2003 May 15;187 (Suppl 1):S91–6.
- 42. Vijayaraghavan M, Martin RM, Sangrujee N, et al. Measles supplemental activities improve measles vaccine coverage and equity: evidence from Kenya, 2002. Health Policy. 2007 Sep;83(1):27–36. Epub 2006 Dec 14.
- It documents the ability of SIAs to improve equity.
- Koehlmoos TP, Uddin J, Sarma H. Impact of measles eradication activities on routine immunization services and health systems in Bangladesh. J Infect Dis. 2011;204(Suppl):S90–S97. DOI:10.1093/infdis/ jir086
- It documents the impact of SIAs on health services.
- Onyeka IN, Ilika AL, Ilika FN, et al. Experiences from polio supplementary immunization activities in Anambra State, Nigeria. Niger J Clin Pract. 2014;17:808–813.
- Nationwide measles vaccination campaign for children aged. 6 months-12 years - Afghanistan, 2002. MMWR Morb Mortal Wkly Rep. 2003 Apr 25;52(16):363–366.
- Dadgar N, Ansari A, Naleo T, et al. Implementation of a mass measles campaign in central Afghanistan, December 2001 to May 2002. J Infect Dis. 2003 May 15;187(Suppl 1):S186–90.
- Zuber PL, Conombo KS, Traoré AD, et al. Mass measles vaccination in urban Burkina Faso, 1998. Bull World Health Organ. 2001;79 (4):296–300.
- Goodson JL, Sosler S, Pasi O, et al. Impact of a measles outbreak response campaign: Maroua, Cameroon, 2009. J Infect Dis. 2011 Jul;204(Suppl 1):S252–9. DOI:10.1093/infdis/jir151

- 49. Aylward RB, Clements CJ, Olivé JM. The impact of immunization control activities on measles outbreaks in middle and low-income countries. Int J Epidemiol. 1997;26(3):662–669.
- 50. Johri M, Sharma JK, Jit M, et al. Use of measles supplemental activities (SIAs) as a delivery platform for other maternal and child health interventions: opportunities and challenges. Vaccine. 2013 Feb 18;31(9):1259–1263. Epub 2012 Oct 5. DOI:10.1016/j. vaccine.2012.09.044
- 51. Vince JD, Datta SS, Toikilik S, et al. Integrated package approach in delivering interventions during immunization campaigns in a complex environment in Papua New Guinea: a case study. Vaccine. 2014 Aug 6;32(36):4614–4619. Epub 2014 Apr. DOI:10.1016/j. vaccine.2014.04.056
- 52. Verguet S, Waasila Jassat W, Bertram MY, et al. Supplementary immunization activities (SIAs) in South Africa: comprehensive economic evaluation of an integrated child health delivery platform. Glob Health Action. 2013. DOI:10.3402/gha.v6i0.20056
- 53 Weiss WM, Rahman MD, Solomon R, et al. Determinants of performance of supplemental immunization activities for polio eradication in Uttar Pradesh, India: social mobilization activities of the Social mobilization Network (SM Net) and Core Group Polio Project (CGPP). BMC Infect Dis. 2013 Jan 17;13: 17. DOI:10.1186/1471-2334-13-17
- Helleringer S, Frimpong J, Adelwahab J, et al. Supplementary polio immunisation activities and prior use of routine immunisation services in non-polio-endemic sub-Saharan Africa. Bull World Health Organ. 2012;90(7):495–503.
- Sutter RW, Maher C. Mass vaccination campaigns for polio eradication: an essential strategy for success. Curr Top Microbiol Immunol. 2006;304:195–220.
- 56. Fields R Using measles SIAs to strengthen routine immunization. 11th Annual Meeting, The Measles and Rubella Initiative, John Snow, Inc.; 2012
- 57. Schreuder B, Kostermans C. Global health strategies versus local primary health care priorities–a case study of national immunisation days in Southern Africa. S Afr Med J. 2001;91(3):249–254.
- Verguet S, Jassat W, Bertram MY, et al. Impact of supplemental immunisation activity (SIA) campaigns on health systems: findings from South Africa. J Epidemiol Community Health. 2013 Nov 1;67(11):947–952. Epub 2013 Aug 23. DOI:10.1136/jech-2012-202216
- 59. Verguet S, Jassat W, Hedberg C, et al. Measles control in Sub-Saharan Africa: South Africa as a case study. Vaccine. 2012 Feb 21;30(9):1594– 1600. Epub 2012 Jan 9. DOI:10.1016/j.vaccine.2011.12.123
- 60. Hanvoravongchai P, Mounier-Jack S, Oliveira Cruz V, et al. Impact of measles elimination activities on immunization services and health systems: findings from six countries. J Infect Dis. 2011 Jul;204(Suppl 1):S82–9.
- It documents the impact of SIAs on health services.
- 61. Better Use of Public Health Campaigns for Child Survival: the Impact and Operations of Papua New Guinea's Supplementary Immunization Activity 2003-05. Australia: Centre for International Health, The Burnet Institute; Oct 2009. A research monograph by Child Health and Research Institute (CHRI) 2009. https://www.burnet.edu.au/system/ publication/file/1264/MORGAN_0874306001257243452-Better_Use_ of Public Health Campaigns-03.11.09.pdf
- Kaucley L, Levy P. Cost-effectiveness analysis of routine immunization and supplementary immunization activity for measles in a health district of Benin. Cost Eff Resour Alloc. 2015;13:14. DOI:10.1186/s12962-015-0039-7
- 63. Verguet S, Jassat W, Bertram MY, et al. Supplementary immunization activities (SIAs) in South Africa: comprehensive economic

evaluation of an integrated child health delivery platform. Glob Health Action. 2013 Mar 1;6: 1–9. DOI:10.3402/gha.v6i0.20056

- 64. Shu M, Liu Q, Wang J, et al. Measles vaccine adverse events reported in the mass vaccination campaign of Sichuan province, China from 2007 to 2008. Vaccine. 2011 Apr 18;29(18):3507–3510. Epub 2009 Nov 10. DOI:10.1016/j.vaccine.2009.10.106
- Pless RP, Bentsi-Enchill AD, Duclos P. Monitoring vaccine safety during measles mass campaigns: clinical and programmatic issues. J Infect Dis. 2003 May 15;187(Suppl 1):S291–8.
- 66. Measles Elimination Field Guide. http://www.wpro.who.int//docu ments/measles_elimination_field_guide_2013/en/
- 67. World Health Organization Regional Committee for the Western Pacific. Resolution no. WPR/RC54.R3 (Expanded Programme on Immunization: measles and hepatitis B). Manila: WHO Regional Office for the Western Pacific; 2003.
- 68. Secretariat to the Pacific Community. http://www.spc.int/
- Hilman I Mission report. Measles-Rubella Supplementary Activities in the Solomon Islands. UNICEF Consultant. 17 Sep–28 Nov 2014; Suva, Fiji.
- •• It is one of the few published papers documenting measles epidemiology in the Pacific.
- 70. WHO/UNICEF Joint Reporting Form
- 71. Hyde TB, Dayan GH, Langidrik JR, et al. Measles outbreak in the republic of the Marshall Islands, 2003. Int J Epidemiol. 2006;35:299–306.10.1093/ije/dyi222
- •• It is one of the few published papers documenting measles epidemiology in the Pacific.
- 72. Marin M, Nguyen HQ, Langidrik JR, et al. Measles transmission and vaccine effectiveness during a large outbreak on a densely populated island: implications for vaccination policy. Clin Infect Dis. 2006;42:315–319.
- •• It is one of the few published papers documenting measles epidemiology in the Pacific.
- McIntyre RC, Preblud SR, Polloi A, et al. Measles and measles vaccine efficacy in a remote island population. Bull World Health Organ. 1982;60:767–775.
- •• It is one of the few published papers documenting measles epidemiology in the Pacific.
- Global reductions in measles mortality 2000–2008 and the risk of measles resurgence. Wkly Epidem Rec. 4 December, 2009;84 (49):505–516.
- 75. The Measles Initiative. http://www.measlesrubellainitiative.org/
- 76. Leite RD, Barreto JL, Sousa AQ. Measles re-emergence in Ceará, Northeast Brazil, 15 years after elimination. Emerg Infect Dis. 2015 September;21(9):DOI:10.3201/eid2109.150391
- 77. WHO Vaccine-preventable diseases: monitoring system. 2015 global summary. http://apps.who.int/immunization_monitoring/global summary/incidences?c=VUT
- Health Service Delivery Profile, Solomon Islands. 2012. Developed in collaboration between WHO and the MHMS. http://www.wpro.who. int/health_services/service_delivery_profile_solomon_islands.pdf
- 79. Micro-needle patch for measles could be a game-changer. CDC Newsroom. http://www.cdc.gov/media/releases/2015/p0427-micro needle-patch.html
- Dietz V, Cutts F. The use of mass campaigns in the expanded program on immunization: a review of reported advantages and disadvantages. Int J Health Serv. 1997;27(4):767–790.
- 81. Kagina BM, Wiysonge CS, Machingaidze S, et al. The use of supplementary immunisation activities to improve uptake of current and future vaccines in low-income and middle-income countries: a systematic review protocol. BMJ Open. 2014 Feb 18;4(2):e004429. DOI:10.1136/bmjopen-2013-004429