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Achieving measles control: lessons from the 2002–06 measles control strategy for Uganda

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Background The 2002–06 measles control strategy for Uganda was implemented to strengthen routine immunization, undertake large-scale catch-up and follow-up vaccination campaigns, and to initiate nationwide case-based, laboratory-backed measles surveillance. This study examines the impact of this strategy on the epidemiology of measles in Uganda, and the lessons learnt.

Methods Number of measles cases and routine measles vaccination coverage reported by each district were obtained from the National Health Management Information System reports of 1997 to 2007. The immunization coverage by district in a given year was calculated by dividing the number of children immunized by the projected population in the same age category. Annual measles incidence for each year was derived by dividing the number of cases in a year by the mid-year projected population. Commercial measles IgM enzyme-linked immunoassay kits were used to confirm measles cases.

Results Routine measles immunization coverage increased from 64% in 1997 to 90% in 2004, then stabilized around 87%. The 2003 national measles catch-up and 2006 follow-up campaigns reached 100% of children targeted with a measles supplemental dose. Over 80% coverage was also achieved with other child survival interventions. Case-based measles surveillance was rolled out nationwide to provide continuous epidemiological monitoring of measles occurrence. Following a 93% decline in measles incidence and no measles deaths, epidemic resurgence of measles occurred 3 years after a measles campaign targeting a wide age group, but no indigenous measles virus (D_{10}) was isolated. Recurrence was delayed in regions where children were offered an early second opportunity for measles vaccination.

Conclusion The integrated routine and campaign approach to providing a second opportunity for measles vaccination is effective in interrupting indigenous measles transmission and can be used to deliver other child survival interventions. Measles control can be sustained and the inter-epidemic interval lengthened by offering an early second opportunity for measles vaccination through other health delivery strategies.

Keywords Measles control, developing countries, mass campaigns, surveillance, Uganda

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KEY MESSAGES

- Wide age-group (6 months–14 years) supplemental measles campaigns interrupted indigenous measles transmission in Uganda.
- Supplemental measles immunization campaigns can be used to deliver, just as they can be delivered by, other child survival intervention programmes.
- The majority of measles-like illnesses in areas of measles control are due to unknown etiology.

Background

Prior to 2001, measles was a major cause of illness and death in children in Uganda. As in Kenya and Tanzania, over 10 000 cases were reported to WHO/UNICEF annually (WHO 2008). In Uganda, measles contributed substantially to the overall under-five mortality rate of 152 deaths per 1000 live births (Uganda Bureau of Statistics and ORC Macro 2001). Even after a series of measles immunization campaigns for children under 5 years of age phased over 3 years (1999–2001), measles was still ranked third among the diseases of epidemic potential reported (Ministry of Health 2002), and almost two-thirds (64%) of cases reported by the Health Management Information System (HMIS) continued to occur among children under 5 years of age. Nanyunja *et al*. (2003) reported that this accelerated measles control strategy (1999–2001) prevented an estimated 97 284 cases of measles, reducing the annual measles incidence by 39% and measles-related deaths by 63% compared with 1997 levels. However, these achievements fell short of the goal of 90% reduction in morbidity and 95% reduction in mortality.

With routine measles immunization coverage stagnating at around 60% from 1999 to 2001 (WHO 2007a), and an assumed measles vaccine efficacy of 85% when given at 9 months (Kearney *et al*. 1989; Bautista-Lopez *et al*. 2001; Gans *et al*. 2003), almost half of children would have remained unprotected through routine vaccination in each annual birth cohort. There would thus have been a rapid build-up in the number of susceptible children, sufficient to sustain measles transmission and increase the likelihood of re-introducing the virus to susceptible infants and young children (Hanratty *et al*. 2001).

In line with World Health Organization (WHO) recommendations (WHO 2001), the 2002–06 measles control strategy for Uganda was developed based on experiences from seven southern African countries (Biellik *et al*. 2000) and lessons from the roll-out implementation of the 1999–2001 accelerated measles control plan. The goal of this strategy was to reduce measles incidence and deaths by 90% by the year 2006, compared with 2001 levels. The objectives of measles control in Uganda were: (1) to vaccinate at least 80% of children with one dose of measles vaccine at 9 months of age, through routine immunization, by 2006; (2) to vaccinate at least 95% of all children aged 6 months to 14 years during a nationwide measles vaccination campaign in 2003; (3) to provide vitamin A supplementation to at least 90% of children aged 6–59 months during measles campaigns; and (4) to establish effective case-based laboratory surveillance for measles nationwide by 2003.

Routine immunization was strengthened through expansion of primary health care grants to districts (Mugyenyi *et al*. 2006), the introduction of hepatitis B and Hib vaccines in 2002 (Lewis *et al*. 2008), implementing the 'Reaching Every District' (RED) approach from 2003 onwards (Mugyenyi *et al*. 2006; WHO 2007b), and other strategies. Under RED, training was provided to all district health teams, and each year, selected poorly performing districts were given additional technical and financial support. Uganda progressed in measles vaccination to be among 17 countries in the African region with coverage of 80% or more by 2004 (Arevshatian *et al*. 2007).

A nationwide immunization campaign implemented in 5 days from 15–19 October 2003 offered supplemental measles vaccination to all children aged 6 months to 14 years of age. A follow-up supplemental measles vaccination campaign was conducted nationwide between August and November 2006, for children aged 6–59 months of age. In addition, in February 2005, children aged 9–23 months received supplemental measles vaccine in the 15 districts of northern Uganda during sub-national polio immunization days. In these high-risk districts, this strategy provided a second opportunity for measles vaccination to all children not yet born or eligible in October 2003, regardless of immunization status. During the second round of polio immunization in April 2005, all children aged 9–59 months were again screened for immunization status and offered missed antigens.

In all campaigns, vitamin A was given to all children aged 6–59 months, and albendazole for deworming to all children 5–14 years. In selected districts, additional interventions such as supplemental tetanus immunization for girls and women of child-bearing age or praziquantel for schistomiasis were provided in a fully integrated manner. A second integrated, nationwide, follow-up measles vaccination campaign is planned for October 2009. Case-based, laboratory-backed measles surveillance was initiated in four districts in November 2002 and rolled out to all districts of Uganda during preparations for the under-15 measles vaccination campaign in October 2003. The roll-out plan included adaptation of pilot-tested, case-based surveillance tools; training of all operational health workers; and supply of field and laboratory commodities nationwide. This study analysed the impact and lessons learnt from implementation of the 2002–06 measles control strategy for Uganda.

Methods

To determine the impact of the measles control strategy for 2002–06, immunization coverage (routine and campaign),

descriptive epidemiological analysis (time, place and person) and case-based measles surveillance data were reviewed. The cost per child vaccinated in the 2003 'catch-up' and 2006 'follow-up' campaigns was also assessed. The Ministry of Health approved the use of their routine HMIS and case-based surveillance databases for this study.

Study population

In 2003, the projected population of Uganda, based on the 2002 national housing and population census, was 25 401 451. The estimated number of children under 15 years of age was 12 957 380, 51% of the total population (Uganda National Bureau of Statistics 2002). This population was projected to increase to 28 158 686 by the year 2006, in line with the annual growth rate of 3.4%.

Immunization coverage and programme costs

The routine immunization coverage for each district in a given year was calculated by dividing the number of children aged less than 1 year immunized in that district by the number of surviving infants (4.3% of the total projected population). The number of children immunized is provided monthly by each District Health Team through the HMIS.

The campaign coverage was calculated by dividing the number of children aged 6 months to 14 years or 6–59 months immunized by the projected population in the same age category, for the 2003 'catch-up' and 2006 'follow-up' campaigns, respectively. The number of children immunized was obtained from each district through the collation and consolidation of tally sheets used at each immunization post during the campaigns.

The crude cost per child vaccinated during the campaign was obtained by dividing the total direct costs of vaccines, supplies and operational costs by the total number of children aged 6 months to 14 years or 6–59 months vaccinated through the 2003 and 2006 campaigns, respectively. Indirect costs such as cost of travel for children and mothers to the vaccination stations, opportunity costs and direct costs of de-worming tablets and vitamin A were not included.

Measles surveillance

Measles surveillance in Uganda is implemented within the Integrated Disease Surveillance and Response (IDSR) framework. A suspected measles case is defined as any person with fever, a generalized skin rash lasting at least 3 days, and at least one of the following: cough, coryza or conjunctivitis. A confirmed measles case was defined as any suspected case (meeting the standard case definition) with a positive IgM or measles virus isolation and no history of vaccination in the 4 weeks prior to sample collection, or any suspected case that is epidemiologically linked in time, person and place to a laboratory-confirmed measles case or outbreak (WHO 1999).

Any case that satisfies the suspected measles case-definition criteria is recorded in the health facility HMIS outpatients register. As with other epidemic-prone diseases, the investigating health unit maintains a line-list of suspected measles cases investigated. A weekly epidemiological surveillance report (including all suspected measles cases) is compiled from the health facility line-list of epidemic-prone diseases. At the end of each month, all suspected measles cases are aggregated in the monthly HMIS reports sent by all health facilities of the country, through health sub-districts and district health teams, to the national health databank.

Following the initial pilot in four districts (2002) and the vaccination campaign (2003), case-based laboratory-backed measles surveillance was rolled out nationwide to improve measles surveillance. For case-based surveillance, all suspected measles cases meeting the standard case definition are investigated by filling an investigation form and obtaining a serum sample for laboratory confirmation. For each suspected measles case, detailed epidemiological information is obtained, including age, sex, vaccination status (vaccinated or not vaccinated against measles, and date of vaccination if child health card available), outcomes and serological markers (measles and rubella IgM). In outbreak settings, suspected measles cases have a throat swab and/or urine sample collected for measles virus isolation. At the health unit, case-based data is included in the monthly HMIS reports. The completed case-based measles investigation forms are transmitted to the Uganda National Expanded Programme on Immunization (UNEPI) along with serum samples (and throat swab or urine specimen) for testing at the Uganda Virus Research Institute (UVRI) Expanded Program on Immunization (EPI) laboratory.

Laboratory methods

Whole blood specimens obtained from an investigated suspected measles case are put into a vacutainer and allowed to stand for 30–60 minutes for blood clots to retract. The vacutainer containing clotted blood is allowed to sit at an angle for about 4–6 hours for serum to separate. The separated serum is stored in cryovials and transported at between 2–8°C (in a specimen carrier with frozen icepacks) to the UVRI/EPI laboratory within 72 hours of collection (Uganda National Expanded Programme on Immunization 2004). All sera are tested with commercial enzyme-linked immunoassay kits for measles IgM, and specimens negative or indeterminate for measles are tested for rubella IgM (Dade Behring, Germany). Measles virus is isolated from urine and throat swabs using Vero/SLAM cell culture, and detected from culture isolates by polymerase chain reaction (PCR). Virus genotyping is carried out as previously reported by Muwonge *et al*. (2005).

Data analysis

Data from the HMIS databank, UNEPI database for case-based measles surveillance and UVRI laboratory database for measles (including outbreak investigated cases) that are routinely entered in EpiInfo-based databases were collated and analysed. The aggregated number of measles cases and routine measles vaccination coverage reported by each district was obtained from the national HMIS reports of 1997–2007. Completeness of monthly HMIS reports was calculated by multiplying the proportion of health units reporting in each district by the proportion of districts reporting to the national level.

The annual measles incidence was estimated by dividing the estimated number of cases (monthly HMIS reported cases divided by completeness of reporting) by the projected

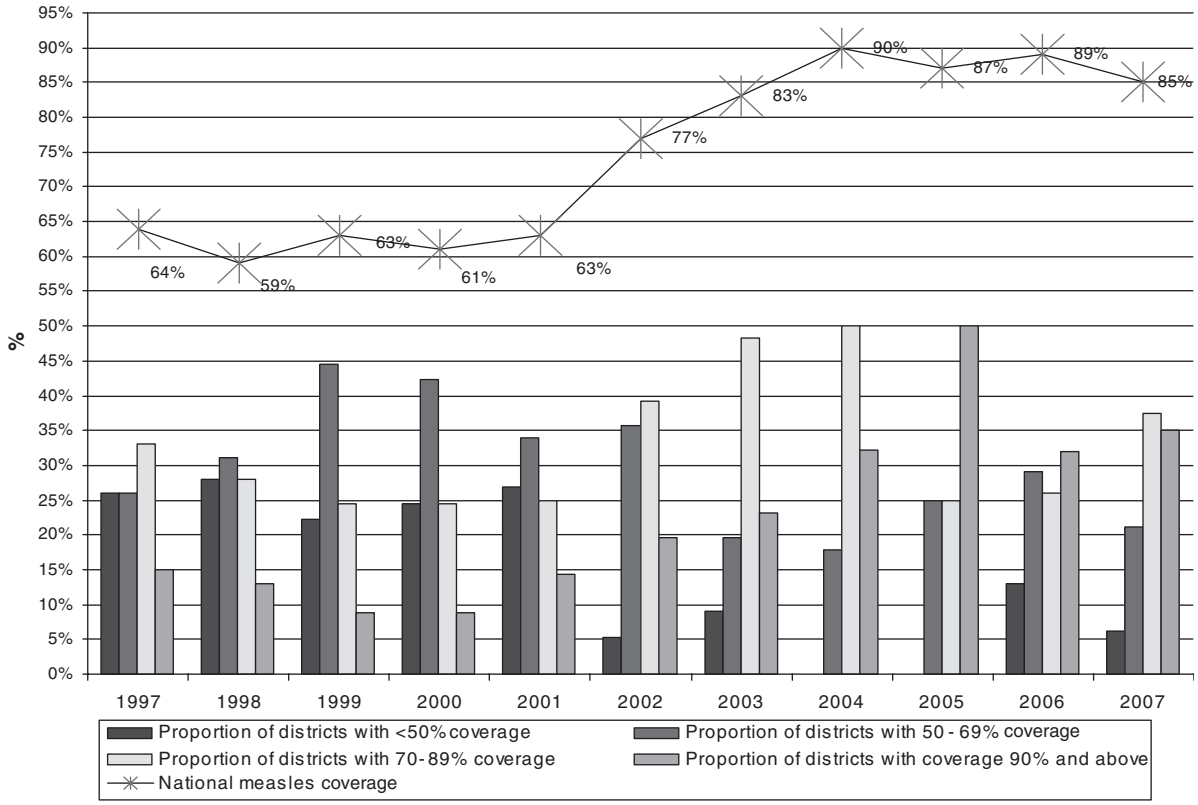

Figure 1 Routine measles vaccination performance indicators for Uganda, 1999–2007

population for that year. The population data used for calculation of pre-campaign incidence rates were official projections from the 1991 census. Projections from the 2002 census were used to calculate post-campaign incidence rates. The age distribution of measles cases before the campaign was obtained for confirmed cases in the case-based measles surveillance database for the period prior to 30 October 2003. Post-campaign age and geographic distribution of measles cases was obtained for the confirmed cases from 1 November 2003 to 31 December 2006.

Results

Measles immunization coverage and cost analysis

The reported routine measles vaccination coverage rose from 63% in 2001 to 90% in 2004, falling slightly to 85% in 2007 (Figure 1). Analysis of measles coverage by district shows variations in performance. The proportion of districts attaining routine measles vaccination coverage above 90% increased from 14% in 2001 to 50% in 2005 before falling to 32% and 35% in 2006 and 2007, respectively (Figure 1). The proportion and number of districts reporting less than 50% measles vaccination coverage decreased from 27% (15 of 56) in 2001 to 0% in 2004 and 2005, before rising to 13% (9 of 69) and 6% (5 of 80) in 2006 and 2007, respectively.

During the catch-up vaccination campaign in October 2003, measles vaccine was administered to 13 475 675 children under 15 years of age, compared with the target of 12 957 380, resulting in campaign coverage of 104%. District disaggregated data indicated that coverage ranged from 52% in Kalangala to 130% in Mayuge districts. Of 56 districts, 47 (84%) attained coverage of 95% or higher (Figure 2). However, post-campaign coverage verification surveys in districts with coverage of less than 90% showed that actual coverage was higher than administrative coverage and had reached the target (data not shown). The low administrative coverage in these areas was thought to be primarily a result of over-estimated population figures due to inter-district demographic variations, while cross-border movements in districts with international boundaries explained coverage above 100%. The campaign also reached 100% of children aged 6–59 months with a supplemental dose of vitamin A and 87% of children aged 5–14 years with a single de-worming dose of albendazole.

The supplemental measles vaccination carried out in February 2005 in 15 northern districts (integrated with polio sub-national immunization days to prevent polio importation from South Sudan) reached 557 868 children. Vaccination coverage by age group showed that through this strategy, 100% (275 272) of children aged 9–23 months not born or eligible for measles vaccine in October 2003 received their second opportunity for measles vaccination 18 months ahead of the planned national follow-up campaign in 2006. An additional 282 596 children aged 24–59 months were given measles vaccine in the absence of proof of prior immunization.

The follow-up measles vaccination campaign carried out between August and November 2006 reached 5 239 221 children aged 6–59 months compared with the target of 5 263 090,

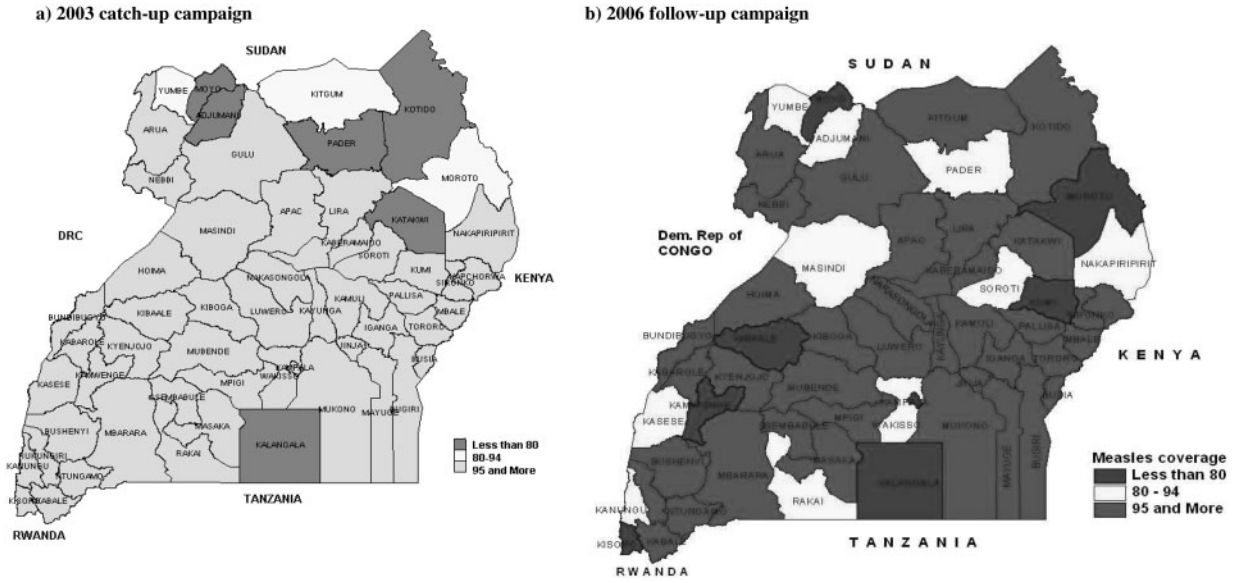

Figure 2 Mass measles immunization coverage by district of Uganda

resulting in a national coverage of 99.5%, with variations in coverage by district. Of 80 districts operational in November 2006, 56 (70%) attained coverage of 95% or higher (Figure 2). The follow-up campaign also reached 95% (5 092 070 of the 5 357 305) and 99% (5 189 712 of 5 263 090) of children targeted with oral polio vaccine (OPV) and Vitamin A, respectively.

The direct cost of the catch-up mass measles campaign in October 2003 was US$9 704 553. The direct cost per child immunized with measles vaccine was therefore US$0.72, with US$0.33 having been spent on vaccines and injection materials alone. The cost per child vaccinated in the follow-up measles campaigns was US$1.00, including US$0.15 per child for procurement of OPV.

Epidemiology of measles

Based on the 1999–2001 HMIS reported data, the annual average number of reported measles cases was 53 049. In 2001 alone, 48 301 measles cases were reported through the HMIS. Following the October 2003 mass measles campaign covering children 6 months to 14 years old, the number of HMIS reported measles cases declined to 1697 and 5736 cases in 2005 and 2006, respectively (Figure 3). The estimated annual incidence of suspected measles (adjusted for completeness of HMIS reporting) dropped from 331 cases per 100 000 inhabitants in 2001 to a record low of 7 cases per 100 000 in 2005, before increasing to 22 cases per 100 000 population in 2006.

Of the 48 301 measles cases reported in 2001 through the HMIS, 63% (43,983) were children below 5 years. The proportion of HMIS reported measles cases occurring in children under 5 years in the post-campaign years of 2004, 2005 and 2006 was 54% (4197 of 7836), 63% (1202 of 1905) and 74% (4219 of 5736), respectively.

Following the 2003 campaign, measles occurred sporadically, although more cases were confirmed in the central districts of the country where routine immunization coverage was lower than the national average (data not shown). There was no confirmed measles death reported in the post-campaign period of 1 November 2003 to 31 December 2006.

Laboratory results

From 1999 to 30 October 2003, UVRI/EPI laboratory received 1667 serum specimens from outbreaks and districts piloting the case-based measles surveillance system. Of these, 936 were positive for measles IgM (excluding those positive within 4 weeks of vaccination), giving a pre-campaign positive predictive value (PPV) of 56% for the clinical diagnosis of suspected measles. However, specimens from outbreaks showed a PPV of 96% (860 out of 896).

From 1 November 2003 to 31 December 2007, 6661 serum samples were received from the nationwide case-based measles surveillance. Of these, 983 tested positive for measles IgM and were classified as confirmed measles; 92 were classified as related to measles immunization as the specimens had been collected within 30 days of vaccination. The post-campaign PPV for the measles case definition was 4%, 1%, 34% and 7% in the completed years of 2004, 2005, 2006 and 2007, respectively (Figure 4). Of laboratory-confirmed measles cases, 56% (550 of 983) were aged less than 5 years. The proportion of measles IgM negative and indeterminate samples that tested positive for rubella was 10% (73 of 731) before the campaign and 22% (1715 of 6661) following the under-15 campaigns. No indigenous measles virus (genotype D_{10}) was isolated over the review period (data not shown).

Discussion

Uganda's measles control strategy for the period 2002–06, including the measles vaccination campaign for children under 15 years, follow-up campaigns and rising routine immunization coverage, led to a dramatic (93%) reduction in measles incidence and a 100% decline in measles mortality in the 4

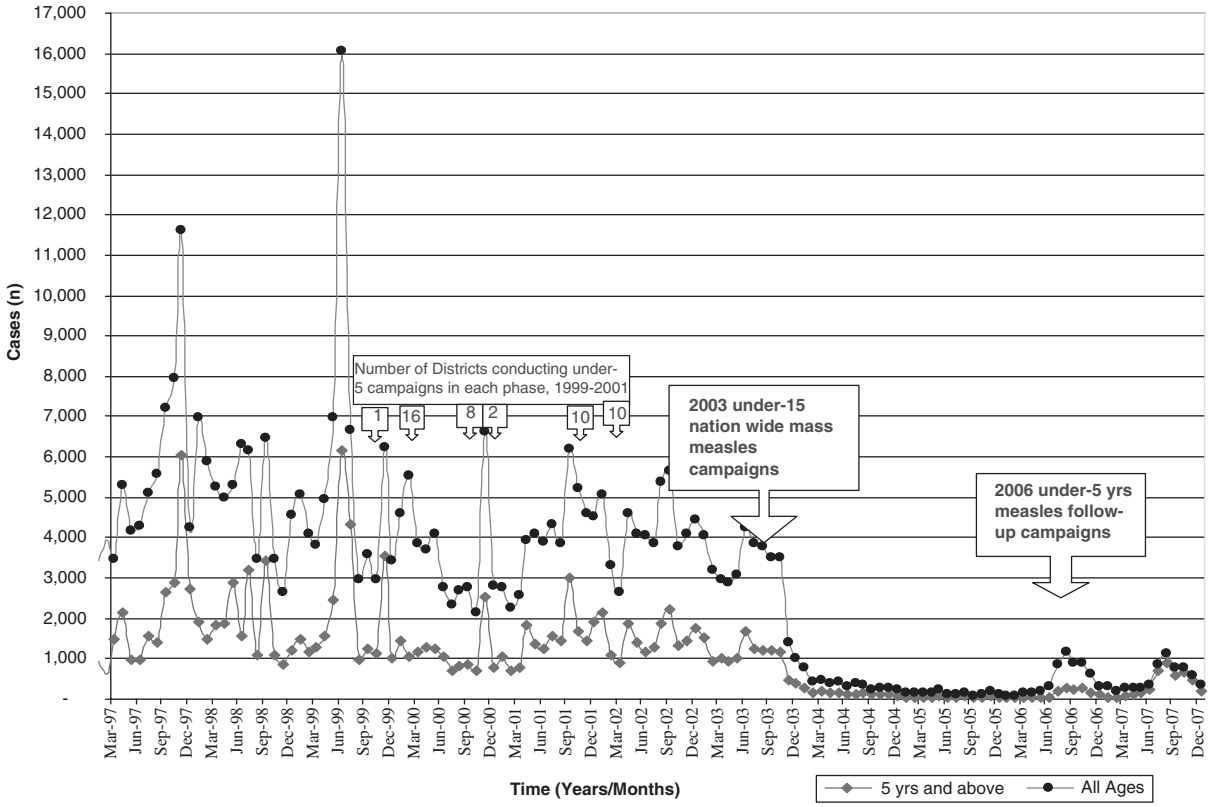

Figure 3 HMIS reported measles cases in Uganda, 1997–2007

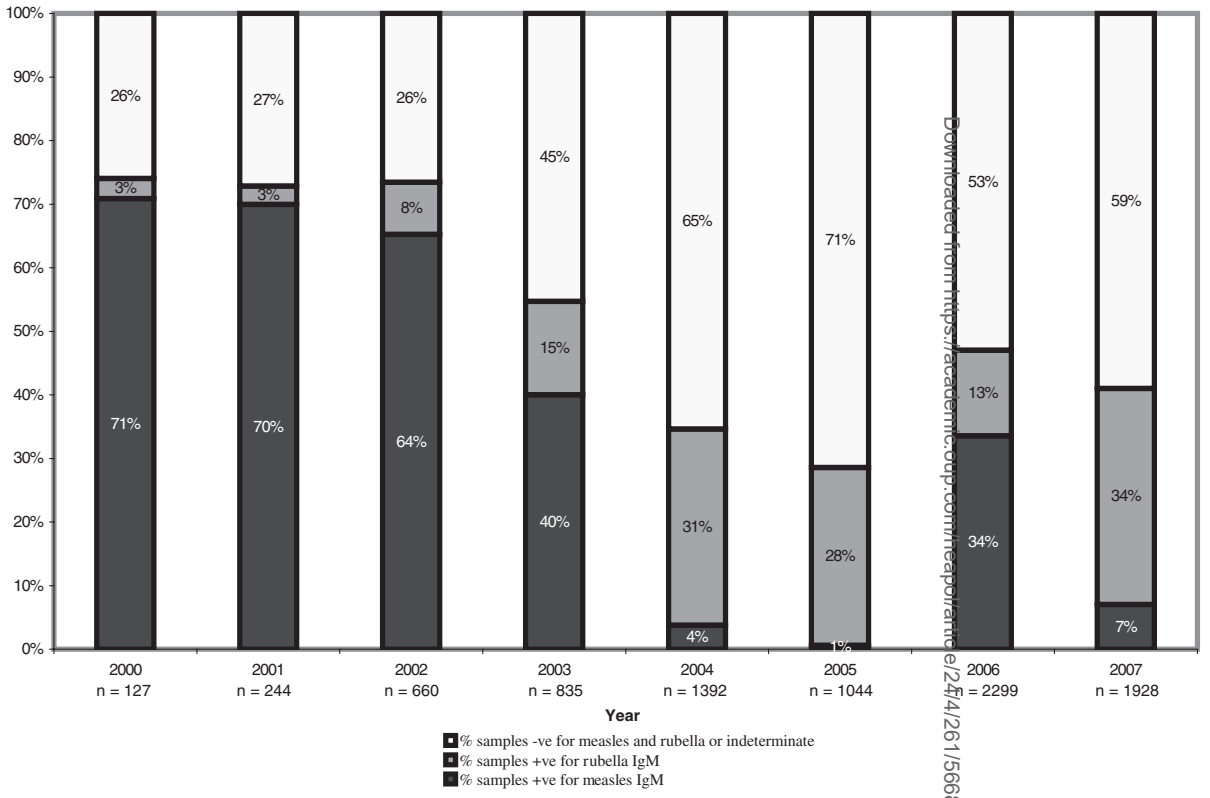

Figure 4 Total laboratory samples and measles/rubella IgM predictive values in Uganda, 2001–07

years following the October 2003 campaign. This experience is similar to that reported in Brazil (Prevots *et al*. 2003) and seven southern African countries (Biellik *et al*. 2002). Contrary to the estimated impact in Africa (Wolfson *et al*. 2007), Uganda exceeded the targeted 90% reduction in measles incidence and 95% reduction in measles mortality. Secondly, the campaign interrupted indigenous measles virus transmission (Muwonge *et al*. 2005). The present study suggests that the interruption of measles transmission lasted less than 3 years with an inter-epidemic interval of 32–34 months. Nationwide follow-up vaccination for children aged less than 5 years was adequate to arrest re-establishment of measles virus transmission. These findings are consistent with other experiences using this strategy (Biellik *et al*. 2002; Munyoro *et al*. 2003; Prevots *et al*. 2003; Otten *et al*. 2005; Nshimirimana *et al*. 2006).

Uganda enjoyed a 'measles-free honeymoon' with fewer than 10 sporadic measles cases confirmed in the 30 months following the campaign. The earliest confirmed measles outbreak occurred in June 2006, and within months, outbreaks were confirmed in 23 of Uganda's 69 districts, almost all in central and southern parts of the country. Therefore, despite the short post-campaign observation time, we conclude that measles transmission could be re-established within 3 years following a wide age-group (under 15 years) measles vaccination campaign in Uganda, where routine immunization coverage is still less than 90% in many districts. We postulate that the innovation to provide a second vaccination opportunity to children aged 9–23 months in high-risk districts in 2005 effectively contributed to limiting the number of sporadic measles cases and delayed the appearance of outbreaks in those regions. Due to the nationwide follow-up campaigns scheduled for 2006, it was not possible to document how much longer the second vaccination opportunity would have delayed resurgence and re-establishment of measles transmission in the high-risk districts.

Case-based, laboratory-confirmed measles surveillance showed that measles virus does not cause the majority of clinically suspected measles cases reported in the HMIS of Uganda following the mass measles campaigns. This finding is also consistent with what was documented in South Africa following their 1996–97 campaigns (WHO Regional Office for Africa 2002). The proportions of suspected measles cases confirmed to be rubella or testing negative for both measles and rubella have increased. This raises the need to study the epidemiology of rubella and define other causes of rash-like illnesses in Uganda, such as varicella, parvovirus, roseola and others. Studies on stored serum samples would help sustain the collaboration of clinicians and clients for measles surveillance and their confidence in the UVRI/EPI laboratory results of measles and rubella IgM.

Contrary to what was documented elsewhere in Africa (Biellik *et al*. 2002; Munyoro *et al*. 2003; Otten *et al*. 2005; Nshimirimana *et al*. 2006), the HMIS and case-based surveillance data did not reveal a shift in age distribution of suspected or confirmed measles following the mass measles vaccination campaigns for under-15s in Uganda. Possible reasons for this variation could be short duration of observation, small numbers of confirmed measles cases and bias arising from self-selection of cases detected at health facilities, as younger children are more likely to be ill and brought for care. In Uganda, low population immunity due to low routine immunization coverage and lower vaccine efficacy associated with measles vaccination at 9 months can also explain the continued occurrence of sporadic measles in children under 5 years (Mupere *et al*. 2006).

This study illustrates that even with the poor economies and weak health systems of developing countries, it is possible for mass vaccination campaigns to be highly effective and implemented in a manner that strengthens routine immunization services delivery, as suggested by Bonu *et al*. (2004) and Dietz and Cutts (1997). Improvements in routine immunization coverage during the study period may in part be a result of the spillover benefits of the campaign, such as raised public awareness due to advocacy and social mobilization, renewed immunization programme infrastructure, retraining of health personnel and extended partnerships. Involvement of political, religious and traditional leaders in mobilization activities for the campaigns, and the resulting rapid reduction in measles cases, helped to build public confidence in immunization services and in health services in general. Mass campaign planning skills, updated population data, new vaccination posts and revived community links have been applied to the planning and implementation of routine immunization outreach in poorly performing districts. Integration of albendazole for de-worming of children was found to be a 'crowd puller' during the 2003 measles vaccination campaign, and is now promoted in all routine immunization services. This integrated approach to the 2003 campaign, similar to the experience in Ghana (Grabowsky *et al*. 2005), set the stage for inclusion of child survival interventions in other service delivery strategies such as child health days and primary health care outreach programmes, now recommended for accelerating progress towards Millennium Development Goals in Africa (Clements *et al*. 2008).

Positive gains in health systems strengthening have resulted from the training of primary health care personnel, of front-line supervisors, the hands-on experience that is gained from the planning and management of logistics and financial resources for the campaign, and the extensive partnerships with tribal, religious and political leaders. Consequently, national immunization coverage indicators have improved and the proportion of districts attaining measles vaccination coverage above the 90% coverage required for effective measles control has also increased.

While interpreting the results presented in this study, the following limitations were considered. The completeness of HMIS-based measles reporting from health facilities varied during the review period. For this reason, the results presented here are adjusted for completeness of HMIS reporting. Secondly, diagnosis of measles in the routine surveillance system for the years up to October 2003 was mainly clinical. Clinical case definitions for measles have a high sensitivity and relatively low specificity, although evidence from laboratory investigation of outbreaks suggested that the diagnosis was correct 96% of the time. Conversely, as Ferson *et al*. (1995) and Brown *et al*. (1994) reported, this study may have underestimated the post-campaign decline in measles morbidity based on HMIS-reported cases, as only a small fraction of

suspected cases (less than 10%) following the campaigns were true measles. Thirdly, not all cases meeting the clinical case definition are detected by the health-facility-based HMIS and case-based measles surveillance systems. Nevertheless, Kintu *et al*. (2005) document that the HMIS of Uganda is adequate in providing overall trends in disease incidence, and the observed changes in measles epidemiology are corroborated by case-based surveillance data.

To sustain low measles transmission, strategies to prevent accumulation of susceptible children are critically important. Sustaining high routine immunization coverage in all areas (districts) of the country forms the basis for the RED strategy (WHO 2007b) and remains the foundation for measles control. In addition, targeted immunization policies can prevent or control outbreaks in high-risk settings. Developing countries should consider targeted measles vaccination for (1) outbreak settings (American Academy of Pediatrics 2006), (2) people who work in health care facilities, given the high risk of infection and transmission to patients and co-workers (Atkinson *et al*. 1991; Lewis *et al*. 2006), and (3) HIV-infected children (Moss *et al*. 1999).

Routine immunization coverage and measles surveillance data should be used to review national immunization policy, with a view to including a 'second opportunity' for measles vaccine on a regular basis and more frequently than through national campaigns. The WHO-recommended two-dose routine measles vaccination policy should be adapted for lower coverage countries where strategies can be developed to delay resurgence of measles outbreaks, extend the time between supplemental immunization campaigns, and reduce costs. In northern Uganda, we demonstrated the effectiveness of sub-national risk assessment and provision of a follow-up measles vaccination opportunity within 18 months of a major catch-up campaign, and experience has shown that child health days successfully extend routine services to hard-to-reach populations. We therefore propose that a flexible two-dose measles immunization policy could include offering two doses of measles vaccine through routine immunization services in high coverage districts or sub-national population groups, and a 'second opportunity' in lower coverage areas through locally developed service delivery strategies other than mass campaigns, such as child health days. As child health days reach more children than routine immunization outreaches, a second opportunity could be recorded as measles-containing vaccine 1 (MCV1) if a child has no documented proof of the first dose, and MCV2 if the child has already received the first dose. This policy would raise the profile and coverage of measles vaccination generally, including the first and second routine doses; strengthen routine immunization as the main delivery mechanism for the second opportunity; and specifically create incentives for special initiatives and innovations to raise the coverage of the first routine measles vaccination dose.

Conclusion

This study confirms what has been shown in other countries; that offering a second opportunity for measles vaccination is effective in achieving measles control. The wide age-group measles vaccination campaign in Uganda led to a 93% decline in measles morbidity, interrupted indigenous measles virus transmission and benefited routine immunization. The campaign approach to providing a second opportunity for measles vaccination is demonstrably effective, and can be used to offer other child survival interventions, but must be repeated every 3 years in countries or sub-national regions where routine first-dose coverage is lower than 90%. In developing countries with limited resources, the costs of repeating such massive vaccination exercises may not be affordable. For optimal efficiency and maximum impact, future mass vaccination campaigns in Uganda and other measles-endemic countries should offer other child survival interventions. The impact could be sustained, the inter-epidemic interval lengthened and outbreaks averted by offering a second opportunity for measles vaccination through other established routine or innovative health service delivery strategies. Before considering a measles elimination goal, countries should ensure adequate efforts are in place to sustain the morbidity and mortality reductions achieved.

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No conflict of interest is reported.

References

Abdool Karim SS, Absool Karim Q, Chamane M. 1999. Impact of measles immunization campaign on measles admissions to Natal Hospital. *South African Medical Journal* **80**: 579–81.

American Academy of Pediatrics. 2006. Measles. In: Pickering LK (ed.). *2006 Red book: Report of the Committee on Infectious Diseases*. 27th edition. Elk Grove Village, IL: American Academy of Pediatrics, pp. 441–52.

Arevshatian L, Clements CJ, Lwanga SK *et al.* 2007. An evaluation of infant immunization in Africa: is a transformation in progress? *Bulletin of the World Health Organisation* **85**: 421–500.

Atkinson WL, Markowitz LE, Adams NC, Seastrom GR. 1991. Transmission of measles in medical settings, 1985–1989. *American Journal of Medicine* **91**(Suppl 3B): 320S–324S.

Baughman AL, Williams WW, Atkinson WL *et al.* 1994. The impact of college pre-matriculation requirements on risk for measles outbreaks. *Journal of American Medical Association* **255**: 1127–32.

Bautista-Lopez NL, Vaisberg A, Kanashiro R *et al.* 2001. Immune response to measles vaccine in Peruvian Children. *Bulletin of the World Health Organisation* **79**: 1038–46.

Biellik R, Madema S, Taole A *et al.* 2002. First 5 years of measles elimination in Southern Africa: 1996–2000. *The Lancet* **359**: 1564–8.

Bonu S, Rani M, Razum O. 2004. Global public health mandates in a diverse world: the polio eradication initiative and the expanded programme on immunisation in sub-Saharan Africa and South Asia. *Health Policy* **70**: 327–45.

Brown DWG, Ramsey MEP, Richards AF, Miller E. 1994. Salivary diagnosis of measles: a study of notified cases in the United Kingdom, 1991–9. *British Medical Journal* **308**: 1015–17.

Clements CJ, Nshimirimana D, Gasasira A. 2008. Using immunization delivery strategies to accelerate progress in Africa towards achieving the Millennium Development Goals. *Vaccine* **26**: 1926–933.

Cutts FT, Henderson RH, Clements CJ *et al.* 1991. Principles of measles control. *Bulletin of the World Health Organisation* **69**: 1–7.

Dietz V, Cutts F. 1997. The use of mass campaigns in the expanded program on immunization: a review of reported advantages and disadvantages. *International Journal of Health Services* **27**: 767–90.

Durrheim DN, Harris BN, Spear R, Billinghurst K. 2001. The use of hospital based nurses for the surveillance of potential disease outbreaks. *Bulletin of the World Health Organisation* **78**: 22–27.

Ferson MJ, Young LC, Robertson PW, Whybin LR. 1995. Difficulties in clinical diagnosis of measles: Proposal for modified clinical case definition. *Medical Journal of Australia* **163**: 364–66.

Gans H, Yasukawa L, Rinki M *et al.* 2003. Immune response to measles and mumps vaccination of infants at 6, 9, and 12 months. *Journal of Infectious Diseases* **187**: 817–26.

Grabowsky M, Nobiya T, Ahum M *et al.* 2005. Distributing insecticide-treated bednets during measles vaccination: a low cost means of achieving high and equitable coverage. *Bulletin of the World Health Organisation* **83**: 195–201.

Hanratty T, Holt T, Duffell E *et al.* 2000. UK measles outbreak in non-immune anthroposophic communities: the implications for the elimination of measles from Europe. *Epidemiology and Infection* **125**: 377–83.

Kearney M, Yach D, Van Dyk H, Fisher SA. 1989. Evaluation of a mass measles immunisation campaign in a rapidly growing peri-urban area. *South African Medical Journal* **76**: 157–9.

Kintu P, Nanyunja M, Nzabanita A, Magoola R. 2005. Development of HMIS in Poor Countries: Uganda as a case study. *Health Policy and Development Journal* **3**: 46–53.

Lewis RF, Braka F, Mbabazi W *et al.* 2006. Exposure of Ugandan health personnel to measles and rubella: Evidence of the need for health worker vaccination. *Vaccine* **24**: 6924–9.

Lewis RF, Kisakye A, Gessner B *et al.* 2008. Action for child survival: Elimination of *Haemophilus influenzae* type b meningitis in Uganda. *Bulletin of the World Health Organisation* **86**: 292–301.

Ministry of Health, Uganda. 2002. Annual Health Sector Performance Report. Financial Year 2001/2002. Ministry of Health, Kampala.

Moss WJ, Cutts F, Griffin D. 1999. Implications of the human immunodeficiency virus epidemic for control and eradication of measles. *Clinical Infectious Diseases* **29**: 106–12.

Mugyenyi P, Braka F, Makumbi I *et al*. 2006. Uganda routine immunization performance improvement initiatives. In: Report of the Task Force on Immunization in Africa, 13th Annual Meeting, Brazzaville, Congo, 28 Feb–3 March 2006, p.66. Online at: http://www.afro.who.int/ddc/vpd/tfi2006/reports/tfi_report_2005_english.pdf, accessed 10 September 2008.

Munyoro MN, Kufa E, Biellik R, Pazvakavamba IE, Cairns KL. 2003. Impact of nationwide measles vaccination campaign among children aged 9 months to 14 years, Zimbabwe, 1998–2001. *Journal of Infectious Diseases* **187**: S91–6.

Mupere E, Karamagi C, Zirembuzi G *et al.* 2006. Measles vaccination effectiveness among children under 5 years of age in Kampala, Uganda. *Vaccine* **24**: 4111–5.

Muwonge A, Nanyunja M, Rota PA *et al.* 2005. New Measles Genotype, Uganda. *Emerging Infectious Diseases Journal* **11**: 1522–6.

Nanyunja M, Lewis RF, Makumbi I *et al.* 2003. Impact of mass measles campaigns among children less than 5 years old in Uganda. *Journal of Infectious Diseases* **187**: S63–8.

Uganda Bureau of Statistics. 2002. Uganda 2002 population and housing census main report. Entebbe: Uganda Bureau of Statistics. Online at: http://www.ubos.org/, accessed 11 September 2008.

Nshimirimana D, Masresha BG, Maumbe T, Dosseh A. 2006. Effects of measles-control activities—African Region, 1999–2005. *Morbidity and Mortality Weekly Report* **55**: 1017–21.

Otten M, Kezaala R, Fall A *et al.* 2005. Public health impact of accelerated measles control in the WHO African Region 2000–2003. *The Lancet* **366**: 832–9.

Prevots DR, Parise MS, Segatto TCV *et al.* 2003. Interruption of measles transmission in Brazil, 2000. *Journal of Infectious Diseases* **187**: S111–208.

Uganda Bureau of Statistics and ORC Macro. 2001. *Uganda Demographic and Health Survey 2000–2001*. Calverton, MD: UBOS and ORC Macro, pp. 99.

Uganda National Expanded Programme on Immunization. 2004. EPI surveillance field guide. First Edition. Entebbe: Ministry of Health.

WHO. 1999. *Guidelines for epidemic preparedness and response to measles outbreaks*. EMC/CDS/CSR/1SR/99.1. Geneva: World Health Organization.

WHO. 2001. *Measles mortality reduction and regional elimination, strategic plan, 2001–2005*. WHO/V&B/01.13. Geneva: World Health Organization.

WHO. 2007a. Immunization surveillance, assessment and monitoring. Reported estimates of measles containing vaccine coverage. Geneva: World Health Organization. Online at: http://www.who.int/immunization_monitoring/en/globalsummary/timeseries/tscoveragemcy.htm, accessed 15 January 2007.

WHO. 2007b. The RED Strategy. Geneva: World Health Organization. Online at: http://www.who.int/immunization_delivery/systems_policy/red/en/index.html, accessed 30 October 2007.

WHO. 2008. Immunization surveillance, assessment and monitoring. Reported measles cases. Geneva: World Health Organization. Online at: http://www.who.int/immunization_monitoring/en/globalsummary/timeseries/tsincidencemea.htm, accessed 15 September 2008.

WHO Regional Office for Africa. 2002. *Southern Africa Integrated Disease Surveillance Network Feedback Bulletin* **2**(4) and **3**(1). Harare.

Wolfson LJ, Strebel PM, Gacic-Dobo M *et al.* for the Measles Initiative. 2007. Has the 2005 measles mortality reduction goal been achieved? A natural history modelling study. *The Lancet* **369**: 191–200.