Has the 2005 measles mortality reduction goal been achieved? A natural history modelling study

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Summary

Background In 2002, the UN General Assembly Special Session on Children adopted a goal to reduce deaths owing to measles by half by the end of 2005, compared with 1999 estimates. We describe efforts and progress made towards this goal.

Methods We assessed trends in immunisation against measles on the basis of national implementation of the WHO/UNICEF comprehensive strategy for measles mortality reduction, and the provision of a second opportunity for measles immunisation. We used a natural history model to evaluate trends in mortality due to measles.

Results Between 1999 and 2005, according to our model mortality owing to measles was reduced by 60%, from an estimated 873 000 deaths (uncertainty bounds 634 000–1 140 000) in 1999 to 345 000 deaths (247 000–458 000) in 2005. The largest percentage reduction in estimated measles mortality during this period was in the western Pacific region (81%), followed by Africa (75%) and the eastern Mediterranean region (62%). Africa achieved the largest total reduction, contributing 72% of the global reduction in measles mortality. Nearly 7·5 million deaths from measles were prevented through immunisation between 1999 and 2005, with supplemental immunisation activities and improved routine immunisation accounting for 2·3 million of these prevented deaths.

Interpretation The achievement of the 2005 global measles mortality reduction goal is evidence of what can be accomplished for child survival in countries with high childhood mortality when safe, cost-effective, and affordable interventions are backed by country-level political commitment and an effective international partnership.

Lancet 2007; 369: 191–200

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Introduction

Measles was the single most lethal infectious agent before the licensure in 1963, and subsequent widespread use, of live attenuated measles vaccine. In the early 1960s, as many as 135 million cases of measles and over 6 million measles-related deaths are estimated to have occurred yearly.[1] The immunosuppressive nature of measles reduces patients' defences against complications such as pneumonia, diarrhoea, and acute encephalitis. Pneumonia, either a primary viral pneumonia or a bacterial superinfection, is a contributing factor in about 60% of measles-related deaths.[2,3] The introduction of routine measles vaccination in most developing countries during the 1980s as part of the Expanded Programme on Immunization had a major effect on global measles mortality. By 1987, WHO estimated that the number of deaths from measles worldwide had been reduced to 1·9 million.[4]

Global measles vaccination activities can be characterised into three broad phases. The first phase involved the introduction of routine vaccination against measles in almost every country in the world through the Expanded Programme on Immunization, beginning in 1974,[5] and the UNICEF-led initiative for Universal Childhood Immunization by 1990.[6] In this phase the recommendation was for one dose of measles vaccine to be administered at or shortly after 9 months of age to at least 80% of children in every country. During the second phase from 1990 to 1999, routine measles vaccination levelled off in the 70–80% coverage range[7] and many industrialised countries introduced a second routine dose, usually at or around the time of school entry, to protect children who did not respond to the first dose.[8] Also during this period, the Pan American Health Organization (PAHO) implemented a strategy that included a second opportunity for measles immunisation for all children to stop endemic measles transmission in the Americas.[9]

The third phase began around 2000 with the realisation that despite the availability of a safe, effective, and relatively inexpensive measles vaccine for over 40 years, measles remained a leading cause of childhood mortality, especially for children living in developing countries.[10] To address this problem, WHO and UNICEF began to target 45 priority countries (panel), together accounting for more than 90% of estimated global measles deaths, to implement a comprehensive strategy for accelerated and sustained reduction in mortality due to measles. The strategy emphasised the PAHO approach to provide all children with a second opportunity for measles immunisation.[11] At present 47 countries are targeted for measles mortality reduction, because Yemen and Timor Leste have been added to the list of priority countries.

The WHO/UNICEF comprehensive strategy for measles mortality reduction has four components: achieving and maintaining high coverage (>90%) for routine measles immunisation in every district; ensuring that all children receive a second opportunity for measles immunisation; effective surveillance for cases of measles,

Panel: WHO and UNICEF 45 priority countries

Afghanistan, Angola, Bangladesh, Benin, Burkina Faso, Burma, Burundi, Cambodia, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Djibouti, Equatorial Guinea, Eritrea, Ethiopia, Gabon, Ghana, Guinea, Guinea-Bissau, India, Indonesia, Kenya, Lao People's Democratic Republic, Liberia, Madagascar, Mali, Mozambique, Nepal, Niger, Nigeria, Pakistan, Papua New Guinea, Rwanda, Senegal, Sierra Leone, Somalia, Sudan, Togo, Uganda, Tanzania, Vietnam, Zambia

including monitoring of immunization coverage; and assuring appropriate clinical management of patients with measles, particularly the provision of vitamin A.[10,11]

Achieving high immunisation coverage for all birth cohorts is the foundation of the strategy for accelerated and sustained measles mortality reduction. Because about 15% of infants who receive measles vaccine at 9 months of age do not develop lasting immunity, even high coverage with a single-dose vaccination policy will result in a substantial proportion of children who remain susceptible to the disease.[9] Since measles is highly infectious, the risk of an outbreak increases over time through an accumulation of susceptible children in the population. The ongoing strengthening of routine immunisation services at the district level alone will not result in a rapid reduction in deaths from measles. To obtain a timely reduction of measles deaths, a critical component of the strategy is to provide all children with a second opportunity for measles immunisation. This approach aims to protect children who did not previously receive measles vaccine, as well as those who were vaccinated but failed to develop an immune response.

The second opportunity for measles immunisation can be delivered either through a routine two-dose schedule (in which immunisation services achieve and sustain high coverage), or through periodic supplementary immunisation activities where routine coverage is low to moderate. Supplementary immunisation activities are mass vaccination campaigns that target all children in a defined age group and wide geographical area regardless of previous disease or vaccination history. They use a range of additional strategies (eg, outreach to remote areas, door-to-door canvassing, additional clinic hours, mobile vaccination teams) that reach children who do not routinely access health services and thereby achieve very high vaccination coverage. Catch-up campaigns are one-time only events generally targeting children aged 9 months to 14 years with a goal of rapidly increasing population immunity among pre-school and school-age children.[12] The specific target age group depends on the age-specific susceptibility in the population.

To maintain high population immunity in pre-school-age children over time, follow-up campaigns, generally targeting all children aged 9 months to 4 years, are periodically done every 3–5 years. The interval between follow-up campaigns is a function of routine immunisation coverage (the higher the routine coverage, the longer the interval between campaigns). By contrast, in countries that have achieved and maintained high routine vaccination coverage, the second opportunity for measles immunisation can also be provided through implementation of a routine two-dose measles vaccination schedule. This appproach usually involves administration of a second dose of measles vaccine at age 12–18 months of age or at school entry.[13]

In May, 2003, the World Health Assembly endorsed a resolution urging member states to achieve the goal adopted by the UN General Assembly Special Session on Children (2002) to halve the number of deaths due to measles by the end of 2005, compared with 1999 estimates.[14,15] We report the achievement of this goal, and outline remaining challenges to reduce mortality further and prospects for the eventual global eradication of measles.

Methods

Measuring vaccination coverage

By July of each year, all Member States of WHO and UNICEF are requested to submit information on routine measles vaccination coverage, supplementary measles immunisation activities, and reported measles cases from the previous year to WHO and UNICEF. WHO/UNICEF estimates of national routine coverage[16] with one dose of measles vaccine are based on a review of coverage data from administrative records, surveys, national reports, and consultation with local and regional experts. Coverage achieved during supplementary immunisation activities is calculated by dividing the number of administered doses that are recorded on tally sheets by the estimated target population. Additionally, coverage surveys done after supplementary immunisation activities are often used by countries to revise their administrative coverage estimates. Regional and global coverage were estimated for the routine first dose of measles vaccine and supplementary activities by applying the national WHO/UNICEF coverage estimates and reported supplementary coverage to the UN Population Division estimates of the relevant target populations (surviving infants for routine first-dose coverage, and the specified age groups for supplementary activities).[17]

A country was defined as providing a second opportunity for measles immunisation if it either had a routine two-dose measles immunisation schedule or had undertaken a nationwide supplementary immunisation activity with coverage of 90% or greater within the previous 5 years.

Estimating measles deaths

A major challenge in measuring progress towards the 2005 measles mortality reduction goal has been the absence of complete and reliable mortality surveillance data from many countries, particularly those with the highest disease burden. Deaths from measles are not routinely reported to WHO, and cases of measles are substantially under-reported even in industrialised countries.[18] To advise WHO on the best methods to monitor global progress towards the 2005 goal, an expert advisory group was convened on Jan 12–13, 2005. The group noted the strengths and weaknesses of various methods for estimating measles mortality but endorsed the approach described in this paper that makes use of surveillance data where reliable, and where surveillance data are unreliable employs a natural history model, which accounts for recent changes in vaccination coverage and is therefore best suited to monitor trends in measles incidence and mortality.[19]

To estimate and monitor trends in yearly numbers of deaths from measles worldwide, a modification of a model proposed by Stein and others[20] was used. In this model the total numbers of cases are estimated and allocated to age groups, and then age-specific case-fatality ratios are applied to the numbers of cases to estimate the numbers of deaths per year.

For countries with good disease reporting (method 1) and routine measles vaccination coverage greater than 80%, the number of cases was derived by dividing by an estimated notification efficiency (5%, 20%, or 40%, as appropriate), representing the proportion of cases that are captured and reported through routine surveillance. The reporting efficiency was assigned to groups of countries using published estimates of reporting efficiency for one or more countries in the group.[20]

For the remaining countries (ie, those where average measles vaccination coverage over the past decade has been <80%) an assumption was made that the average yearly number of cases was equal to the number of children in the birth cohort who did not become immune through vaccination (method 2). Because of the highly infectious nature of measles, as well as results from serological surveys showing that by early adulthood most people have immunological evidence of either immunisation or infection-derived immunity,[21–24] it can be concluded that all individuals who are not effectively immunised are eventually infected with measles.[25–27] Thus, the average number of cases per year, if immunisation were only given through routine services, would be equivalent to the number of those in the birth cohort who did not become immune through vaccination (although distributed across different age groups).

The number of cases per year was reduced if children received a second routine dose, or if the country had recently used supplementary immunisation activities. A discounting function was then used to calculate the effect of supplementary activities (100%, 90%, 80%, 50%, and 25% for 1, 2, 3, 4, and 5 years after the activity, respectively), on the basis of the observation that such strategies have an effect for about 5 years, and the longer the time since the campaign, the less the effect on reducing the number of cases. This is consistent with the observed effect of mass measles campaigns in 14 countries in the African region during 1998–2001.[28] These average percentage reductions are assumed to apply to countries using similar campaigns in other regions. This static model assumes all the epidemiological parameters remain the same over a 5-year period, and thereby removes the cyclical variations in measles incidence and reflects an average smoothed annual number of cases and deaths. The cases are then distributed across age groups using the age distributions reported by Stein and others[20] (see also webappendix[20,29,30]). Age-specific case-fatality rates are then applied to these estimates of case numbers to estimate the number of deaths.

See Online for webappendix

Data sources for the model included the estimated yearly routine first and second dose measles coverage by country,[7,16] coverage of supplementary immunisation activities by country (WHO-IVB database, extracted Sept 1, 2006), and population data.[17] Vaccine effectiveness was assumed to be 85% if given before age 1 year and 95% if given to older children.[31,32] Further details about the model are given in the webappendix.

On the basis of a review of published work,[20] case-fatality ratios for children aged 1–4 years were used as the reference. The values used ranged from 0·05% in industrialised countries of Europe and North America, 0·1% in the industrialised Pacific and South and Central America, 0·8% in the remainder of Asia and the Pacific, and (on average) 3% in Africa, ranging up to 6% in the least developed countries (eg, Sierra Leone). For more than 86% of the world's population, the case-fatality ratio applied to children aged 1–4 years was less than 3%.[19,31] We assume that the ratio in children younger than 1 year is larger than that in children aged 1–4 years, which in turn is larger than that in children aged 5–9 years. The case-fatality ratio for children aged 10 years and older is assumed to be 0 (this simplifying assumption has the effect of including any deaths in children older than 10 years in the deaths in the 5–9 age group).[20]

To derive lower and upper bounds for the annual mortality estimates, the output from Markov[33] simulation models implemented in the S-Plus (version 6.1) software package applied to mortality estimates for the year 2000 was reviewed. A series of distributions, including beta, Dirichlet, and multivariate normal distributions were chosen as appropriate,[30] depending on whether the parameters were univariate (beta) or multivariate (multinomial) proportions, or were continuous in nature, to represent the uncertainty in the input parameters (routine immunisation coverage, supplementary activity coverage, reported incidence rates, notification efficiency, vaccine effectiveness, distribution of cases across age groups, and age-specific case-fatality ratios). Some variables had a correlation structure imposed on them (for example, the age-specific case-fatality ratios within a specific country were assumed to vary together, whereas vaccine efficacy and case fatality ratios were assumed to be independent). When distributions had been assessed, by use of the prior sample size method (see webappendix),[30] 10 000 samples were taken from the input distributions and propagated through the model. The 95% uncertainty intervals for the estimates in the year 2000 were found to vary from –33% to 33% of the point estimate.

The model was found to be most sensitive to two variables: case-fatality ratios and routine measles vaccination coverage. Because it is simpler to implement and more transparent to explain, a deterministic approximation was used; coverage was allowed to vary by plus or minus 5% (absolute) and case-fatality ratios by plus or minus 20% (relative), to derive the lower and upper bounds for the estimates, which for the base year of 1999 yielded a range of approximately plus or minus 33%.

The model was then used to derive yearly estimates of measles cases, deaths, and disability adjusted life years (DALYs), as well as estimates of cases, deaths, and DALYs averted.

Results

During the 1980s, worldwide coverage of routine measles vaccination increased to about 70%, and then levelled off during the 1990s. Between 1999 and 2005, coverage of routine immunisation increased from 71% to 77%, with substantial variation across geographical regions (table 1). Moreover, we noted a marked increase in the proportion of countries providing children with a second opportunity for measles immunisation either through a routine two-dose schedule or a nationwide supplementary immunisation activity. In 2005, of 192 countries, 171 (89%) offered children a second opportunity nationally and seven (4%) sub-nationally, compared with 125 (65%) nationally in 1999 (figure 1).

Calculations based on WHO/UNICEF coverage estimates and the estimated number of surviving infants[17] showed that more than 29 million 1-year-old children worldwide had not received a dose of measles vaccine through routine immunisation services (table 2). The southeast Asian region had the largest number of unvaccinated 1-year-old children and of children aged 9 months to 14 years without a second opportunity for measles immunisation.

From 2000 to 2005, more than 362 million children aged 9 months to 14 years received measles vaccine through supplementary immunisation activities in the 47 priority countries.[11] Of the total doses administered, 84% were given in catch-up campaigns and 16% in follow-up campaigns. Of the priority countries, 34 (72%) had completed nationwide campaigns and 11 (23%) had undertaken subnational campaigns during this period. Reported coverage for supplementary immunisation activities in the priority countries ranged from 65% to 99% (median 96%). By the end of 2005, 45 of the 47 priority countries had completed or begun implementation of a measles catch-up campaign.

Since 1980, implementation of global measles control activities has resulted in about 60% of the worldwide population aged younger than 15 years being protected by routine vaccination (figure 2). Provision of a second opportunity for measles immunisation through supplementary activities or a routine second dose started in the late 1980s and has accelerated since 2000, resulting in protection of an additional 20% of the population younger than 15 years (figure 2).

Starting in 2000, supplementary immunisation activities and improvements in routine coverage accelerated the decline in mortality due to measles (figure 2). Based on results from surveillance data and the natural history model, overall global measles mortality decreased 60% from 873 000 deaths (uncertainty bounds 634 000–1 140 000 deaths) in 1999 to 345 000 deaths (247 000–458 000) in 2005 (table 1, figure 3). The largest percentage reduction in estimated mortality due to

	1999				2005				Relative decrease in measles deaths 1999–2005
	Routine measles vaccine first-dose coverage	Estimated number of measles deaths (uncertainty bounds)	Births (millions)*	Mortality rate per 1000 livebirths*	Routine measles vaccine first-dose coverage	Estimated number of measles deaths (uncertainty bounds)	Births (millions)*	Mortality rate per 1000 livebirths*	
Africa	50%	506 000 (370 000–658 000)	26	177	65%	126 000 (93 000–164 000)	29	168	75%
Americas	92%	<1000	16	32	92%	<1000	16	26	..
Eastern Mediterranean	73%	102 000 (75 000–132 000)	14	105	82%	39 000 (26 000–53 000)	16	94	62%
Europe	90%	<1000	10	27	93%	<1000	10	25	..
Southeast Asia	59%	237 000 (171 000–310 000)	38	98	65%	174 000 (126 000–233 000)	38	82	27%
Western Pacific	85%	27 000 (18 000–38 000)	26	44	87%	5000 (3000–8000)	24	37	81%
Total	71%	873 000 (634 000–1 140 000)	130	90	77%	345 000 (247 000–458 000)	133	82	60%

Difference between total and regional total due to rounding up to 1000. *World Population Prospects: The 2004 Revision. Population database. Population Division, Department of Economic and Social Affairs, UN Secretariat.

Table 1: **Routine measles vaccine coverage, estimated number of deaths from measles, and basic demographic characteristics by WHO region, 1999 and 2005**

measles during this period was in the western Pacific region (81%), followed by Africa (75%) and the Middle East (62%).

In children younger than 5 years, we estimated that worldwide mortality due to measles decreased from 791 000 (573 000–1 032 000) in 1999 to 311 000 (222 000–415 000) in 2005. Notably, three-quarters of the reduction in measles mortality among children younger than 5 years occurred in Africa, where estimated measles mortality in this age group fell from 459 000 (335 000–597 000) to 114 000 (83 000–148 000). Evidence suggests that case-fatality ratios are reduced in individuals with measles who have been vaccinated but have not become immune[34] and in individuals who receive vitamin A supplementation[35] during supplementary immunisation activities. The model, which assumed that the case-fatality ratio remained constant between 1999 and 2005, might thus have underestimated the reduction in mortality due to measles.

We estimated that measles was responsible for more than 30 million DALYs lost in 1999, falling to 12 million in 2005, and that the number of cases fell from more than 43 million in 1999 to just over 20 million in 2005 (table 3). Cumulatively, from 2000 to 2005, nearly 7·5 million measles deaths had been prevented through immunisation. Given 1999 coverage levels, 2·3 million of these deaths had been prevented through intensified efforts to raise routine coverage and provision of a second opportunity for measles immunisation. Moreover, worldwide distribution of mortality due to measles has drastically shifted. In 1999, 58% of all deaths from measles were estimated to occur in the African region,

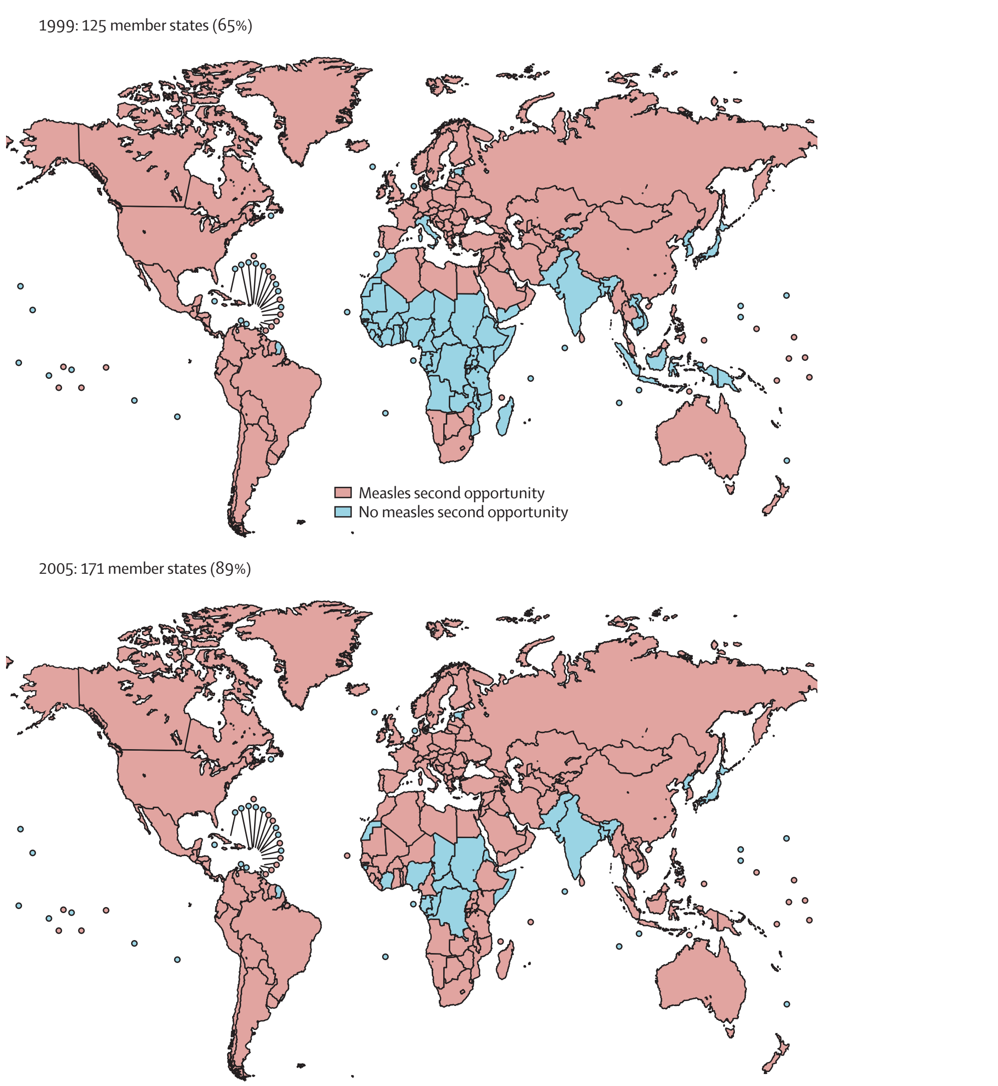

***Figure 1:* Availability of second opportunity for measles vaccination, 1999 and 2005**

	Number (%) of children younger than 1 year unvaccinated with first dose	Number (%) of children younger than 15 years without second opportunity
Africa	9055 (31%)	102 280 (17%)
Americas	1216 (4%)	..
Eastern Mediterranean	2547 (9%)	84 512 (14%)
Europe	694 (2%)	..
Southeast Asia	12 611 (43%)	413 457 (67%)
Western Pacific	3187 (11%)	17 885 (3%)
Total	29 311 (100%)	618 133 (100%)

The difference between total and regional total is due to rounding up to 1000.

Table 2: **Estimated number (thousands) and percentage distribution of children not reached with first dose of measles vaccine and without second opportunity for measles immunisation in 2005, by WHO region**

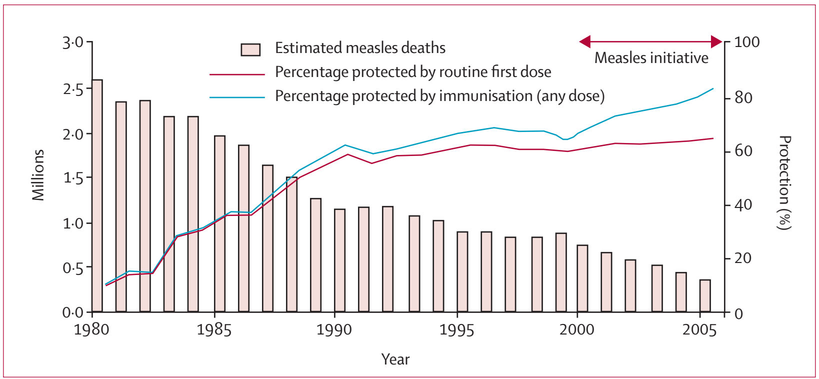

Figure 2: **Estimated trends in worldwide mortality due to measles, 1980–2005**
Shown with proportion of population younger than 15 years protected by routine first-dose measles vaccination and all sources of vaccination. "Any dose" includes effect of second opportunity for measles immunisation either as a routine second dose or through supplementary immunisation activities.

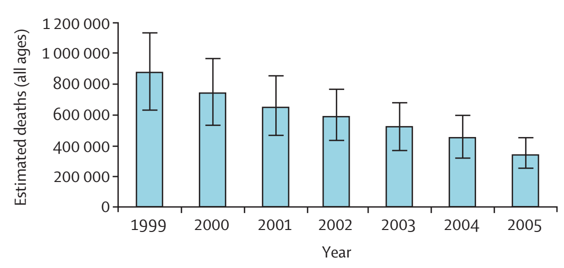

Figure 3: **Estimated worldwide mortality due to measles, 1999–2005**
Bars are uncertainty bounds

and 27% in southeast Asia. However, by 2005, 50% of all deaths from measles occurred in southeast Asia and only 37% in Africa.

Discussion

Intensified large-scale vaccination efforts, particularly in priority countries with the highest burden of measles, have substantially decreased reported incidence of measles and the estimated number of deaths from measles worldwide. Although difficult to quantify, the widespread administration of vitamin A through supplementary immunisation activities against polio and measles and through routine services has also probably contributed to the reduction of measles mortality. Based on modelled estimates, the goal to reduce worldwide measles mortality by 50% between 1999 and 2005 has been met with a 60% decrease, mainly driven by the gains achieved in the African region. Although other published point estimates of measles mortality in children younger than 5 years[36–38] for 2000–03 differ from those presented in this report, the remarkable progress in reaching more children with measles immunisation and the effect this improvement has had on reported cases of measles[39] suggests that the estimated 60% decline in measles mortality has indeed occurred.

Published estimates of worldwide measles mortality using different modelling approaches vary, but all have wide uncertainty bounds that overlap. Investigators who examined the proportional causes of worldwide child mortality in 42 countries in the year 2000, based on data obtained from verbal autopsies in 18 countries, estimated that deaths from measles represented about 3% (with wide uncertainty bounds) of the more than 10 million yearly deaths in children younger than 5 years.[36] This point estimate is significantly less than our modelled estimate of 6%, or 669 000 (uncertainty bounds: 485 000–877 000), for the same year, but the estimates are not entirely inconsistent, in view of the wide uncertainty intervals for both approaches. The approach of Morris and others[36] has two important weaknesses for investigating mortality due to measles where a highly effective intervention is being rapidly scaled-up. First, it is based on a retrospective cross-sectional rather than a

	1999						2005					
	Estimated DALYs lost	Estimated number of measles deaths	Estimated number of measles cases	Estimated DALYS averted	Estimated deaths averted	Estimated cases averted	Estimated DALYs lost	Estimated number of measles deaths	Estimated number of measles cases	Estimated DALYS averted	Estimated deaths averted	Estimated cases averted
Americas	8	<1	408	307	8	15 366	<1	<1	<1	318	8	15 910
Europe	35	<1	501	730	20	9802	9	<1	170	752	21	10 139
Western Pacific	961	27	6660	3058	86	18 975	180	5	1139	3768	106	22 720
Eastern Mediterranean	3573	102	4448	3375	96	9200	1383	39	2009	6303	179	12 755
Southeast Asia	8352	237	18 085	9133	260	18 307	6125	174	14 057	11 213	319	22 039
Africa	17 746	506	13 222	13 578	387	10 961	4419	126	3382	30 536	871	23 511
Total	30 675	873	43 324	30 181	857	82 611	12 116	345	20 757	52 890	1504	107 074

Table 3: **Estimated cases, deaths, and DALYS (thousands) occurring and averted, 1999 and 2005, by WHO region**

cohort approach to examining mortality, and is thus unsuited to monitoring yearly or short-term trends in mortality. Second, the model[36] showed systematic bias towards underestimation of diseases that represent small proportions (<10%) of total child mortality.

Our mortality estimates based on the natural history model are corroborated by data from countries that have implemented the recommended vaccination strategies and have strengthened measles surveillance. An analysis of the effect of intensified vaccination efforts in 19 African countries showed a 92% reduction in reported measles cases.[28] Additionally, only one country (Burkina Faso) experienced a large outbreak after completing a catch-up supplementary immunisation activity. This outbreak was carefully investigated and was largely caused by large scale population migration as a result of civil unrest in neighboring Côte d'Ivoire.[40] Countries in Asia that have implemented the WHO/UNICEF strategy have shown similar results. Cambodia implemented a catch-up supplementary immunisation activity against measles from 2000 to 2003, together with rebuilding of its routine immunisation programme, resulting in a fall in the number of reported measles cases from 12 237 in 2000 to 264 cases in 2005.[41] In Vietnam, the number of reported measles cases decreased by more than 95% (from 16 512 cases in 2000 to 410 cases in 2005[41]) after nationwide supplementary activities aimed at all children aged 9 months to 10 years in 2002–03. In all these countries measles is no longer a public health problem, and in some measles transmission may have been interrupted altogether.

Following a recommendation from an expert review of methods to estimate measles mortality,[19] we attempted to validate the results by comparing this model with surveillance data, as discussed above, and by examining a single-cause proportional mortality model to validate levels of measles mortality in children younger than 5 years for the year 2000.

A systematic review of published studies reporting community-based measures of measles mortality between 1980 and 2000, and overall child mortality, found 28 studies[42–77] in 16 countries that met the inclusion criteria: that the total number of deaths in each study was greater than 50, and that the proportion of deaths due to measles was less than 20% (to ensure that non-representative studies and outbreak settings were excluded). A weighted logistic regression model[78–80] was fitted in S-Plus using the total number of deaths in each study as the weights, and using measles vaccination coverage and the proportion of the population that was rural as explanatory variables, with separate slopes against coverage for African and non-African countries. The final model fit these data well (R^2=92%), and when applied to current vaccination coverage figures by country, yielded an estimate of 625 000 (95% CI 209 000–1 378 000) deaths in children younger than 5 years for the year 2000, remarkably consistent with our modelled estimate of 669 000 (uncertainty intervals 485 000–877 000).

The natural history method described in this paper has limitations. First, it is a simplification of the actual transmission dynamics, and does not always capture herd immunity effects well, especially in high-coverage settings. Second, the approach to deriving age-specific estimates would be better done in proper cohort-type susceptible-exposed-infected-recovered (SEIR) transmission models.[81–84] Third, better quality surveillance data and additional field studies for key model inputs are essential to more precisely estimate trends in measles mortality in the future.[19]

The availability of a safe, effective, and inexpensive measles vaccine for more than 40 years has been essential for effective measles control. Additionally, a vaccine delivery strategy that reaches more than 90% of all children is needed. The approach of providing all children with a second opportunity for measles immunisation (using supplementary immunisation activities where necessary) together with ongoing strengthening of routine immunisation services, has proven to be extremely effective in rapidly and sustainably reducing numbers of deaths from measles. A very aggressive implementation of this strategy has interrupted the circulation of indigenous measles virus in the Americas.[85]

A key factor contributing to progress in reducing measles mortality in Africa has been the support of the Measles Initiative. This partnership, which was formed in 2001 and spearheaded by the American Red Cross, the US Centers for Disease Control and Prevention, the United Nations Foundation, UNICEF, and WHO, has played a critical role in supporting African countries in their efforts to reduce measles mortality. With additional resources from the Global Alliance for Vaccines and Immunization and most recently the International Finance Facility for Immunization,[86] the Measles Initiative is expanding its support to high-burden countries in the eastern Mediterranean, southeast Asian, and western Pacific regions of WHO. Every organisation in the Measles Initiative shares the goal of rapidly reducing measles mortality through implementation of the WHO/UNICEF recommended strategies. Additional principles for an effective partnership have included strong country ownership and commitment to measles control, appreciation of the specific role each partner can play, and the need for contributions of all partners to be recognised.

For the **Measles Initiative** see http://www.measlesinitiative.org

WHO and UNICEF together with its partners have developed the global immunisation vision and strategies for the period 2006–15.[87,88] This document was welcomed by the 2005 World Health Assembly and includes ambitious—but appropriate—targets of achieving 90% coverage with measles vaccine in every district, and a 90% reduction in worldwide measles mortality, between 2000 and 2010, as an important component of the child survival Millennium Development Goals. Important challenges still exist to achieve the 2010 goal for reduction of measles mortality. First, activities need to be fully implemented in large countries that still have a high measles burden such as India, Pakistan, and Indonesia. Second, to sustain the reductions in measles deaths in the 47 priority countries, enhanced efforts are needed to improve immunisation systems to ensure that at least 90% of infants are vaccinated against measles before their first birthday. Third, the priority countries will need to continue to carry out follow-up supplementary immunisation activities every 2–4 years until their routine immunisation systems are capable of providing two doses of measles vaccine to a very high proportion of every birth cohort. Fourth, field surveillance with laboratory confirmation of suspected measles outbreaks will need to be extended to all priority countries to allow programmes to be effectively monitored.

The proven effectiveness of measles vaccine in preventing disease, and of the comprehensive measles immunisation strategy in reducing deaths from measles and interrupting transmission in many countries, has prompted calls for establishment of a global goal for measles eradication.[89–92] Indeed, four of the six WHO regions have already established regional measles elimination goals—the Americas (2010), Europe (2010), the eastern Mediterranean region (2010), and the western Pacific (2012).

At first glance, measles seems to satisfy most of the five indicators for determining whether a disease is a candidate for eradication.[93] First, an effective intervention (ie, measles vaccine) exists to interrupt transmission of the agent. Second, sensitive and specific surveillance and laboratory methods exist to detect and confirm cases. Third, man is the only known natural host of measles virus. Fourth, interruption of measles transmission has been achieved across wide geographic areas over time. Fifth, measles is perceived as an international public-health priority in many (but not all) countries.

Despite these characteristics, developed countries have shown little interest in launching another global eradication initiative, especially since efforts to eradicate poliovirus have not yet been completed.[94] Even if transmission of measles virus could be interrupted throughout the world, the threat of reintroduction of the virus, either intentionally (eg, as a biological weapon) or unintentionally (eg, in a laboratory accident) makes the possibility that measles vaccination with at least a one-dose schedule could ever be stopped unlikely.[95,96]

The success of efforts to reduce measles mortality by 50% between 1999 and 2005 has led to a further goal: to reduce mortality due to measles by 90% between 2000 and 2010.[87,88] The second opportunity for measles vaccination is one of the most cost-effective child-health interventions available today,[31] and international commitments to funding the initiative indicate both the effectiveness and the cost-effectiveness of the measure.[86,97] If political will and financial commitments to achieving this goal are maintained, and innovative strategies for linking delivery of measles vaccine with other child survival interventions are used (eg, insecticide treated bednets),[88,98] there is good reason to believe that this new target can be met, accelerating progress towards achieving one of the targets of Millennium Development Goal 4, to reduce child mortality by two-thirds.[99]

The Measles Initiative

The following institutions are partners in the Measles Initiative: American Red Cross, Becton Dickinson, Bill and Melinda Gates Foundation, Canadian International Development Agency, The Church of Jesus Christ of Latter-day Saints, Exxon Mobil, Global Alliance for Vaccines and Immunization, International Federation of Red Cross and Red Crescent Societies, Izumi Foundation, United Nations Foundation, UNICEF, US Centers for Disease Control and Prevention, Vodafone Foundation, and the World Health Organization.

Contributors

L J Wolfson was the lead author in the overall conceptualisation and design of the article and in drafting and revising the text, developed the mathematical models, and prepared the tables and figures. All authors participated in the overall conceptualisation and design of the article, and in revising and editing the text. P M Strebel assisted in drafting the text and in coordinating inputs from co-authors, and participated in development of the original mathematical model used to estimate the global burden of measles. M Gacic-Dobo collected data, prepared databases needed for the estimates, and prepared tables and maps. E J Hoekstra and J W McFarland participated in drafting the text. B S Hersh provided technical advice related to measles epidemiology, and until his transfer to Cambodia, provided overall supervision for the article.

Conflict of interest statement

We declare that we have no conflict of interest.

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