Cost-benefit analyses of supplementary measles immunisation in the highly immunized population of New Zealand

D.T.S. Hayman [a,*], J.C. Marshall [a], N.P. French [a], T.E. Carpenter [b], M.G. Roberts [c], T. Kiedrzynski [d]

[a] mEpiLab, Infectious Diseases Research Centre, Massey University, Palmerston North 4442, New Zealand
[b] EpiCentre, Infectious Diseases Research Centre, Massey University, Palmerston North 4442, New Zealand
[c] Infectious Diseases Research Centre, Institute of Natural & Mathematical Sciences, New Zealand Institute for Advanced Study, Massey University, Private Bag 102 904, North Shore Mail Centre, Auckland, New Zealand
[d] Ministry of Health, Wellington, New Zealand

ARTICLE INFO

ABSTRACT

As endemic measles is eliminated from countries through increased immunisation, the economic benefits of enhanced immunisation programs may come into question. New Zealand has suffered from outbreaks after measles introductions from abroad and we use it as a model system to understand the benefits of catch up immunisation in highly immunised populations. We provide cost-benefit analyses for measles supplementary immunisation in New Zealand. We model outbreaks based on estimates of the basic reproduction number in the vaccinated population (R_v, the number of secondary infections in a partially immunised population), based on the number of immunologically-naïve people at district and national levels, considering both pre- and post-catch up vaccination scenarios. Our analyses suggest that measles R_v often includes or exceeds one (0.18–3.92) despite high levels of population immunity. We calculate the cost of the first 187 confirmed and probable measles cases in 2014 to be over NZ$1 million (~US$864,200) due to earnings lost, case management and hospitalization costs. The benefit-cost ratio analyses suggest additional vaccination beyond routine childhood immunisation is economically efficient. Supplemental vaccination-related costs are required to exceed approximately US$66 to US$1877 per person, depending on different scenarios, before supplemental vaccination is economically inefficient. Thus, our analysis suggests additional immunisation beyond childhood programs to target naïve individuals is economically beneficial even when childhood immunisation rates are high.

© 2017 Published by Elsevier Ltd.

1. Introduction

Increased measles immunisation is eliminating endemic measles. As the risk of measles declines, it may be difficult for policymakers to determine the most cost-effective immunisation programs. Integration of measles data through modelling and benefit-cost analyses can help inform policy decisions [1].

The incidence of measles cases globally was reduced by >50% from 43 million in 1999 to approximately 20 million in 2005, and by 75% from 2000 to 2015, with elimination announced for the Americas in 2016 [2,3]. Various case fatality ratios have been used, but it has been estimated that approximately 7.5 million deaths from measles were avoided from 2000 to 2005 due to vaccination [4] and the decrease in measles mortality (79%, 651,600 to 134,200) reflected the decline in measles incidence (75%, 146 to 36 cases per million persons) from 2000 to 2015 [3].

The societal benefits for measles vaccination have been estimated to be significant. The combined annual economic cost of measles during the 1996–2000 period in 11 industrialized countries was estimated to be ~US$150 million in 2001 [6]. The economic benefits from cases averted due to measles vaccination in 72 of the world's poorest countries was predicted to result in nearly US$10 billion of losses averted between 2011 and 2020 [7]. Ninety-nine percent of these averted costs were the result of preventing lost productivity due to preventing an estimated 360 thousand measles-specific premature mortalities. The remaining savings were associated with averted treatment costs and reduced caretaker productivity for the nearly 12 million measles cases it was estimated were avoided [7]. Return on investment for averting measles through two routine immunisation doses and outreach campaigns was estimated at 58 times the cost (uncertainty range: 28–105) [8].

In addition to societal losses occurring in measles-endemic countries, a significant impact is felt in highly measles-vaccinated countries (e.g. having a two-dose routine vaccination

* Corresponding author.
 E-mail address: D.T.S.Hayman@massey.ac.nz (D.T.S. Hayman).

schedule for measles containing vaccines, and approaching or achieving 95% childhood vaccination coverage [9]) due to imported measles cases. Studies in the United States have assessed the economic impact of recent measles outbreaks due to imported cases, following endemic measles elimination in 2000 [10]. The economic impact to public health departments as the result of 16 outbreaks in 2011, lasting an average of 22 days and resulting in 107 confirmed cases, was assessed. These 107 cases had an estimated 8900–17,500 contacts, requiring between 42,600 and 83,100 personnel hours, at a cost of between US$2.7 and US$5.3 million. Overall, it was estimated that each contact required 4.7 personnel hours at a cost of US$298 per contact [11], highlighting the potential costs of measles post-elimination.

Economic analyses of measles control programs have shown them to be economically effective [1,12]. Benefit-cost ratios (B/C) in the range 10.8–54.2 have been estimated for measles, mumps, and rubella (MMR) vaccination generally in the USA [13]. In the Republic of Korea, different measles vaccination strategies were found to be economically efficient (B/C > 1.0), with the strategy using two doses of the MMR vaccine, with a catch up campaign for measles and rubella being the most favorable (B/C = 1.3) [14]. However, the generality of the benefits of catch up immunisation campaigns in highly immunised populations is unclear though the risk of resurgence in highly immune populations has been assessed [15].

As a member of the WHO Western Pacific Region, New Zealand is committed to measles elimination. New Zealand immunisation programs have led to the cessation of endemic measles, but have changed considerably over time [17]. In 1969 measles vaccine was introduced for 10 months to five year old children and children up to 10 years old at special risk. In 1974 immunisation at 12 months old was recommended and in 1978 a five year measles elimination program was implemented, before a single dose MMR was introduced (MMR1) in 1990. A second MMR dose (MMR2) was introduced in 1992 for 11 year olds. In 1996 MMR1 was given at 15 months to allow immunisation to be given alongside diphtheria, tetanus, pertussis and *Haemophilus influenzae* type b booster vaccines. A mathematical model for the dynamics of measles in New Zealand prepared in 1996 [18] successfully predicted an epidemic in 1997, which was curtailed by a mass vaccination campaign [19,20]. This targeted immunisation of children under 10 years old was performed in the face of an epidemic and the MMR1 schedule was changed to 12 months nationally with two doses at 6–11 months and 15 months in Auckland. The last widespread epidemic was in 1997, but New Zealand has suffered smaller outbreaks due to measles importation [16]. Subsequent extension of the modelling work was used to show that the previously recommended schedule of MMR1 at 15 months and MMR2 at 11 years was insufficient to prevent further epidemics [19] and in 2001 MMR2 was scheduled at four years nationally and another school catch up program focused on providing MMR2 to children aged five to 10 years. Between 2002 and 2008 laboratory confirmed or epidemiologically linked case numbers were low (less than five cases) and separated by months and since 2009 all cases were linked to importations by epidemiological links and/or, genotyping.

Numerous models for measles vaccination strategies [22–26] based on sets of nonlinear ordinary differential equations (ODEs) have been proposed, and all suggest that it is necessary to maintain high coverage rates in order to prevent future epidemics [1]. The differences in the models have been in the details of the representation of the infectious period, and in the ways in which the age and contact structures of the population have been specified. While analyses suggest that 85% coverage at MMR1 and MMR2 could be sufficient to prevent future measles epidemics in some scenarios [22,25], in the Netherlands analyses showed that high overall levels of measles vaccination can obscure pockets of poor coverage, resulting in localized regions with increased risk of infection [27]. No such models exist for New Zealand currently. However, the key parameter that determines whether an epidemic will occur, the basic reproduction number R_0, has been estimated. R_0 is defined as the expected number of secondary infections that would arise from a single primary infection introduced into a fully susceptible population [28,29]. If $R_0 > 1$ an epidemic will occur following an introduction of infection. The best estimate for measles in New Zealand was $R_0 = 12.8$ [30]. A modification of R_0 is the basic reproduction number of the infection under vaccination, R_v. R_v is the expected number of secondary infections that would arise from a single primary infection introduced into an immunised population at equilibrium and is an indicator of the performance of a vaccination schedule. If $R_v < 1$ outbreaks will die out.

Here we provide a quantitative assessment of the economic benefits of catch up immunisation programs in the highly immunised population of New Zealand. To do so we estimate the cost of the most recent measles outbreaks in New Zealand. Using this information, we evaluate the economic benefits of additional measles immunisation from a societal perspective [13], including the financial costs related to measles control and prevention, as well as costs related to lost earnings, to provide information for public health officials and decision makers.

2. Methods

2.1. Data summary

We performed an observational study of measles case notification data provided by the New Zealand Ministry of Health (MoH). We used different data sets to estimate per case costs based on the best data available. Significant outbreaks of measles have occurred in New Zealand since 2009 [16] (Fig. S1) and our study was initiated during a large measles outbreak in mid-2014. We estimated R_v from all the outbreaks, defined as local transmission including 2 or more cases, in New Zealand since 2009. Measles case notifications and national hospitalization cost data were available for the period 1st January 2000 to 12th June 2014 and to 11th July 2014 respectively. Per capita income in New Zealand has increased substantially since 2000, so wages lost due to measles are calculated for the period 1st January 2008 – 31st August 2014, which accounts for wages over the period during which most cases occurred. Detailed public health management costs were only available for the period 1st January 2014 to 9th March 2014 and provided by Auckland Regional Public Health Service (ARPHS). The total costs were therefore estimated for the first 187 measles cases in 2014 in New Zealand. Population immunity levels for vaccination were estimated using nationwide serology and vaccination data to 2013 [16]. All costs are given in US$ using the mean 2014 exchange rate of 0.83 NZ$ to US$ (Reserve Bank of New Zealand, www.rbnz.govt.nz/statistics). Further details are below.

2.2. Basic reproduction number modelling methods

To understand the transmission dynamics of measles in the partially immunised population we estimated R_v from all the outbreaks in New Zealand since 2009. To do this we estimated R_t, the case reproduction number of the infection at time *t*. R_t is the expected number of secondary infections that arise from a single infection at a particular *time* and depends on the number in the population who are susceptible, which we estimated following an adaptation of published methods [21,31]. In order to calculate R_t, we are required to compute the generation time for measles; i.e. the time between infection of a primary case and infection of secondary cases caused by the primary case. We used a lognormal