

# Interim report 2

## Measles risk assessment, modelling and benefit–cost analysis

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## 1 Abstract

New Zealand has been working towards elimination of endemic (domestic) measles virus transmission, but has suffered from small, but significant outbreaks of measles after measles introductions from abroad. In this interim report we present the results of statistical analyses of risk factors for measles cases since 2007 in New Zealand during outbreaks, provide updated cost analyses measles outbreaks, and include further modelling of measles outbreaks pre- and post different vaccination scenarios, based on alternative situations. We provide preliminary benefit–cost analyses using the results from those simulations, along with a number of alternative vaccination strategies to achieve different vaccination coverage levels. Our key findings were:

- Age is the best predictor of risk of measles infection in multi-variate regression analyses, though some groups such as Pacific people, the less socially deprived, and European and Maori school age children have been more likely to be cases in outbreaks since 2007.
- Estimates of the proportion of the currently naive New Zealand population requiring additional vaccination to ensure measles does not persist range from 0–53%, leading to an additional 0–250,000 additional vaccinations.

- The benefit–cost ratio is dependent on expectations regarding measles transmission: if measles in New Zealand continues to infect the same proportion of secondary cases as in the current 2013–2014 outbreak, additional vaccination is very beneficial, but if outbreaks remained the size of the average outbreaks since 1997, there is no benefit to additional vaccination campaigns.

## 2 Background

As a member of the World Health Organization (WHO) Western Pacific Region, New Zealand is committed to work towards measles elimination, defined as the interruption of endemic (domestic) measles virus transmission. A brief review of the history of measles in New Zealand was provided in our previous interim report. In this report we present regression analyses to determine which populations are most at risk, the likely outcomes of measles infections within New Zealand based on a number of assumptions, and the benefit–cost analyses for vaccination dependent on differing scenarios.

## 3 Risk analysis update

A measles risk assessment has been undertaken by the Ministry of Health to better assess current and future population immunity and high risk groups. Given the current measles outbreak, measles control is a priority for the Ministry and resources are available to control this outbreak and decrease the risk of future outbreaks. In our review of the confidential report to the Western Pacific Regional Verification Commission for Measles Elimination risk assessment provided by the Ministry, titled *Progress Towards Measles Elimination in New Zealand - Final*, found the report to be very thorough, however, we identified additional analyses that might further inform the understanding of risk from measles infection within New Zealand. The additional analyses included in this section are multivariate modelling to account for confounding within the univariate analyses.

### 3.1 Risk analyses methods

We received the raw EpiSurv measles case data from The Institute of Environmental Science and Research Ltd (ESR) on 27 June 2014. Initial analyses of those data (not shown) suggested that denominator data were required to perform multivariate analyses to avoid confounding results due to a lack of independence among risk factors. Specifically we required  $\text{Age} \times \text{Prioritised Ethnicity} \times \text{NZDep}$  data for New Zealand to test whether interactions among case covariates provide additional information on risk over the univariate analyses performed in the *Progress Towards Measles Elimination in New Zealand - Final* report. These  $\text{Age} \times \text{Prioritised Ethnicity} \times \text{NZDep}$  data were provided to us on 3 July 2014 by the University of Otago. We used these denominator data to determine

if there were interactions among specific age categories, prioritized ethnicities, and socioeconomic deprivation indices (NZDep) that might exist among cases allowing better understanding of risk of measles infection.

The University of Otago denominator data provided were not to the same detail as the ESR case data. Notably, the denominator age data were categorised into several classes: 0–5, 6–17, 18–24, 25–64, and 65+ year categories. The ethnicity denominator data were not Prioritized Ethnicity at the Level 1 Ethnic Group Codes, but at the Level 2 Ethnic Group Codes, though with some alternative codes provided that did not match the Level 2 Ethnic codes. After discussions with the University Otago we have provided results based on the best available data, though for smaller ethnic group categories, some results may be unreliable and these are discussed below.

With the 10 NZDep classes, Prioritized Ethnicities, and the age classes above, this led us to have 250 categories. Because for measles cases the very young appear to be disproportionately affected (Figure 1), we split the 0–5 age category into two classes, 0–2 and 3–5 years old, assuming equal numbers of young were born into each age group over the last five years (which is supported by data from NZ statistics [31]).

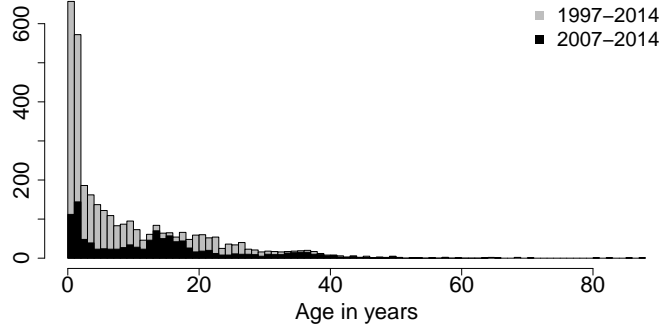


Figure 1: Age of measles cases in years in New Zealand for two periods, 1997–2014 and 2007–2014

This large number of categories, some with small population sizes, lead to both overdispersion and zeroinflation, as there were many categories with zero cases in, particularly in the adult age classes. Furthermore, initial preliminary analyses, including multi- and univariate analyses (not shown) suggested little effect of individual NZDep classifications and several higher order interactions, and therefore we reduced the number of NZDep categories from 1 to 10 to two: 1–5 and 6–10. We also incorporated the 65+ age classes into the 25–64 age category, to make a 25+ age category. By doing so, we reduce the zeroinflation present in the data.

The prioritized ethnicities for cases are: European; Maori; Pacific Peoples;

Table 1: Absolute number of measles cases in specific age, ethnicity and socio-economic deprivation categories from 2007-2014

NZDep	Age	Ethnicity	Cases
1-5	0-2	Asian	11
6-10	0-2	Asian	8
1-5	3-5	Asian	1
1-5	6-17	Asian	11
6-10	6-17	Asian	5
1-5	18-24	Asian	3
6-10	18-24	Asian	5
1-5	25+	Asian	10
6-10	25+	Asian	13
1-5	0-2	European	83
6-10	0-2	European	64
1-5	3-5	European	42
6-10	3-5	European	17
1-5	6-17	European	219
6-10	6-17	European	80
1-5	18-24	European	34
6-10	18-24	European	36
1-5	25+	European	78
6-10	25+	European	51
1-5	0-2	Maori	18
6-10	0-2	Maori	48
1-5	3-5	Maori	7
6-10	3-5	Maori	11
1-5	6-17	Maori	19
6-10	6-17	Maori	92
1-5	18-24	Maori	5
6-10	18-24	Maori	8
1-5	25+	Maori	2
6-10	25+	Maori	6
6-10	0-2	MLA	3
6-10	3-5	MLA	1
6-10	6-17	MLA	1
6-10	18-24	MLA	2
6-10	25+	MLA	6
1-5	0-2	Pacific	5
6-10	0-2	Pacific	58
6-10	3-5	Pacific	3
1-5	6-17	Pacific	5
6-10	6-17	Pacific	22
1-5	18-24	Pacific	1
6-10	18-24	Pacific	8
1-5	25+	Pacific	2
6-10	25+	Pacific	11
1-5	0-2	None	3
1-5	3-5	None	1
1-5	6-17	None	3
6-10	6-17	None	4
1-5	18-24	None	2
6-10	18-24	None	1
1-5	25+	None	5
6-10	25+	None	3

Asian; Middle Eastern/Latin American/African (MELAA); Other Ethnicity; Residual Categories, though for the analyses in this report only the first five are used, as these categories cover the overwhelming number of cases, with only 1.9% (22/1137) of cases having no Prioritized Ethnicity (Table 1).

The numbers of cases per category for the complete data set from 2007-2014 can be seen in Table 2. Subsequent regression analyses (not shown) also suggested that the Middle Eastern/Latin American/African category was over- or underrepresented in per capita rates given the very small sample sizes for this classification (Figure 2, Table 2), leading to very large standard error in regression analyses.

However, there are several issues with the data for Middle Eastern, Latin American and African (MELAA) ethnicities, and along with small population sizes (Table2), and there several issues with estimating the denominator data

Table 2: Absolute number of measles cases in specific age, ethnicity and socio-economic deprivation categories from 2007-2014

NZDep	Age	Ethnicity	Population	Cases 1	Per Capita
1-5	0-2	Asian	6094	11	0.0018
6-10	0-2	Asian	6806	8	0.0012
1-5	3-5	Asian	6094	1	0.0002
6-10	3-5	Asian	6806	0	0.0000
1-5	6-17	Asian	33918	11	0.0003
6-10	6-17	Asian	28905	5	0.0002
1-5	18-24	Asian	22917	3	0.0001
6-10	18-24	Asian	34107	5	0.0001
1-5	25+	Asian	96357	10	0.0001
6-10	25+	Asian	98715	13	0.0001
1-5	0-2	European	57872	83	0.0014
6-10	0-2	European	45445	64	0.0014
1-5	3-5	European	57872	42	0.0007
6-10	3-5	European	45445	17	0.0004
1-5	6-17	European	264330	219	0.0008
6-10	6-17	European	182937	80	0.0004
1-5	18-24	European	107649	34	0.0003
6-10	18-24	European	117840	36	0.0003
1-5	25+	European	1001916	78	0.0001
6-10	25+	European	724317	51	0.0001
1-5	0-2	Maori	10003	18	0.0018
6-10	0-2	Maori	30104	48	0.0016
1-5	3-5	Maori	10003	7	0.0007
6-10	3-5	Maori	30104	11	0.0004
1-5	6-17	Maori	40461	19	0.0005
6-10	6-17	Maori	116640	92	0.0008
1-5	18-24	Maori	15360	5	0.0003
6-10	18-24	Maori	48495	8	0.0002
1-5	25+	Maori	71217	2	0.0000
6-10	25+	Maori	192729	6	0.0000
1-5	0-2	MLA	728	0	0.0000
6-10	0-2	MLA	1290	3	0.0023
1-5	3-5	MLA	728	0	0.0000
6-10	3-5	MLA	1290	1	0.0008
1-5	6-17	MLA	2991	0	0.0000
6-10	6-17	MLA	4539	1	0.0002
1-5	18-24	MLA	1710	0	0.0000
6-10	18-24	MLA	3078	2	0.0006
1-5	25+	MLA	8028	0	0.0000
6-10	25+	MLA	10335	6	0.0006
1-5	0-2	Pacific	2093	5	0.0024
6-10	0-2	Pacific	13124	58	0.0044
1-5	3-5	Pacific	2093	0	0.0000
6-10	3-5	Pacific	13124	3	0.0002
1-5	6-17	Pacific	8541	5	0.0006
6-10	6-17	Pacific	51183	22	0.0004
1-5	18-24	Pacific	3972	1	0.0003
6-10	18-24	Pacific	22098	8	0.0004
1-5	25+	Pacific	18492	2	0.0001
6-10	25+	Pacific	91533	11	0.0001

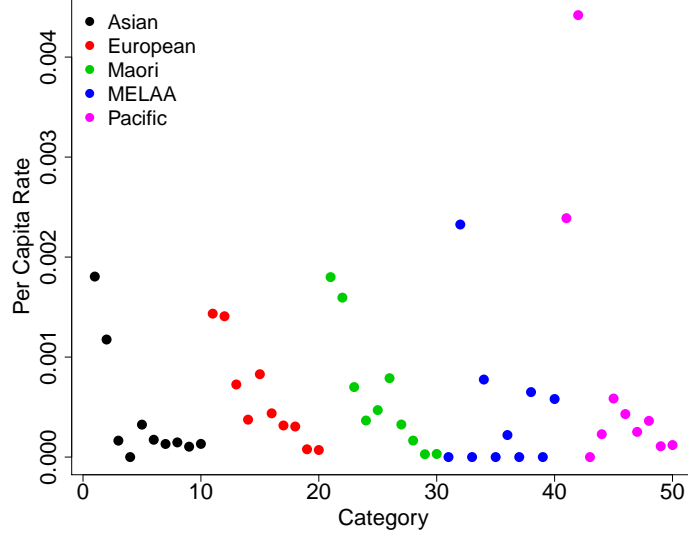


Figure 2: Per capita rates of measles infections broken down by ethnicity, see Table 2 for details

for this group (University of Otago, personal communication). Thus, we removed this grouping for our subsequent analyses and are left with Asian, European, Maori and Pacific as Prioritized Ethnicities. This left us with 1102/1115 (99%) of the measles cases with Prioritized Ethnicity recorded from 2007, and 1102/1137 (97%) of all measles cases recorded since 2007 (Table2).

For all our statistical analyses (including those above not shown) we used a Poisson error structure, but in all cases there was a need to account for overdispersion and thus we used, and present, a quasipoisson regression model. We also account for differences in population sizes by using an offset term, the  $\log(\text{population size})$ . We used a model simplification approach, by beginning our analyses with all terms and all interactions, and simplifying the models through removal of non-significant higher order interaction terms. Thus, the final model that remained with all significant interaction terms had the following linear predictor:

$$\log(y) = \alpha + \beta_a(x_a) + \beta_e(x_e) + \beta_n(x_n) + \beta_{ae}(x_a * x_e) + \log(\text{population}) + \epsilon \quad (1)$$

Where  $\alpha$  is the intercept,  $y$  cases,  $a$  age,  $e$  Prioritized Ethnicity,  $n$  NZDep, and  $\epsilon$  the error term.

### 3.2 Regression analyses results

The distribution of the cases per category used are in Figure fig:histcasecat.

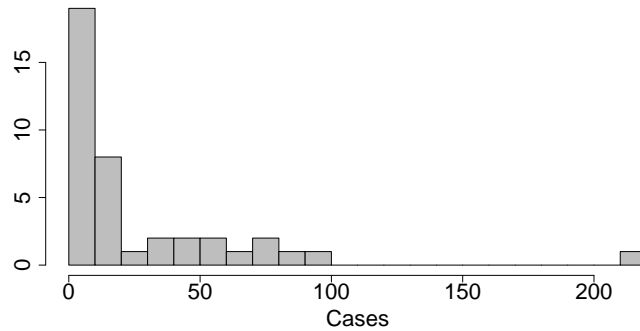


Figure 3: Histogram of cases per category used in the final regression model

The predicted values plotted against the cases are shown in Figure 4, and the residuals are shown in Figure 5.

The significance of the different predictor variables can be seen here, in the ANOVA results:

```
> anova(model3, test="F")
```

Analysis of Deviance Table

Model: quasipoisson, link: log

Response: cases

Terms added sequentially (first to last)

	Df	Deviance	Resid. Df	Resid. Dev	F	Pr(>F)
NULL			39	1453.62		
Age	4	1304.20	35	149.43	183.5795	6.73e-15 ***
Ethnicity	3	20.00	32	129.43	3.7529	0.028500 *
NZDep	1	10.70	31	118.74	6.0236	0.023932 *
Age:Ethnicity	12	81.91	19	36.83	3.8430	0.004459 **

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Signif. codes: 0 '\*\*\*' 0.001 '\*\*' 0.01 '\*' 0.05 '.' 0.1 ' ' 1

A summary of the model with the individual effects and the statistical support for the estimated coefficients can be seen here:

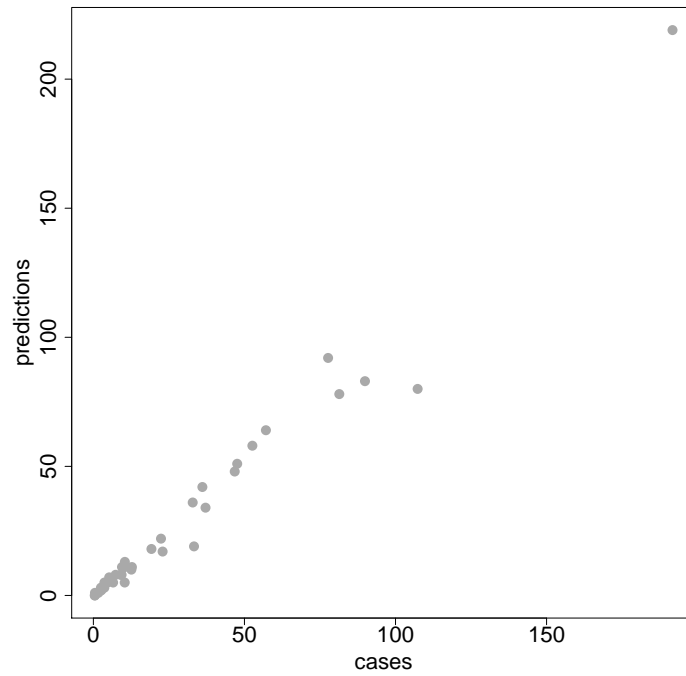


Figure 4: Regression model predictions plotted against the cases (Equation 3)

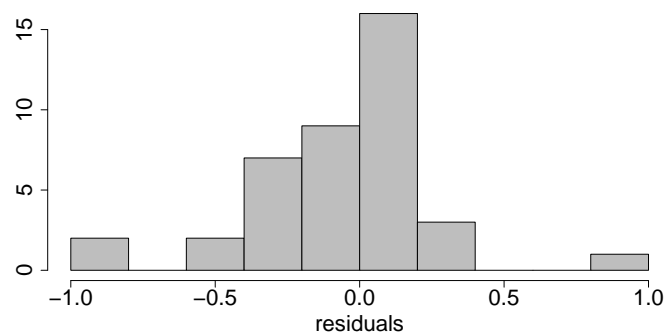


Figure 5: Histogram of residuals from the regression model (Equation 3)

```
> summary(model3)
```



```

Call:
glm(formula = cases ~ Age + Ethnicity + NZDep + Age:Ethnicity +
    offset(log(Popn)), family = "quasipoisson", data = tpsub)

Deviance Residuals:
    Min       1Q   Median       3Q      Max
-2.76316  -0.52409   0.04736   0.49883   1.92918

Coefficients:
                Estimate Std. Error t value Pr(>|t|)
(Intercept)      -6.46738    0.11483  -56.324 < 2e-16 ***
Age3-5            -0.91290    0.20539   -4.445 0.000278 ***
Age6-17          -0.76175    0.13427   -5.673 1.81e-05 ***
Age18-24         -1.50501    0.19366   -7.772 2.57e-07 ***
Age25+           -2.95073    0.16079  -18.352 1.51e-13 ***
EthnicityAsian     0.05304    0.32498    0.163 0.872072
EthnicityMaori     0.21245    0.19935    1.066 0.299919
EthnicityPacific   1.16032    0.20429    5.680 1.78e-05 ***
NZDep6-10         -0.21192    0.08548   -2.479 0.022713 *
Age3-5:EthnicityAsian -2.03154    1.38265   -1.469 0.158112
Age6-17:EthnicityAsian -1.00742    0.47171   -2.136 0.045940 *
Age18-24:EthnicityAsian -0.83115    0.59409   -1.399 0.177917
Age25+:EthnicityAsian  0.42108    0.44334    0.950 0.354143
Age3-5:EthnicityMaori -0.38639    0.40959   -0.943 0.357344
Age6-17:EthnicityMaori -0.08552    0.24685   -0.346 0.732812
Age18-24:EthnicityMaori -0.58278    0.44835   -1.300 0.209209
Age25+:EthnicityMaori -1.04821    0.52418   -2.000 0.060036 .
Age3-5:EthnicityPacific -2.13163    0.81388   -2.619 0.016882 *
Age6-17:EthnicityPacific -1.45411    0.33466   -4.345 0.000349 ***
Age18-24:EthnicityPacific -0.98266    0.51289   -1.916 0.070546 .
Age25+:EthnicityPacific -0.61270    0.43665   -1.403 0.176692
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for quasipoisson family taken to be 1.776063)

Null deviance: 1453.62  on 39  degrees of freedom
Residual deviance:  36.83  on 19  degrees of freedom
AIC: NA

Number of Fisher Scoring iterations: 5

```

The results of the model suggest that, apart from over-representation of some MELAA categories discussed above and not included here, age is a strong predictor of being a measles case. Indeed, all age categories are significantly less likely to be measles cases compared to 0-2 year olds, and the likelihood

decreases with age (Figure 1).

People of Pacific origin are also over-represented ( $\beta = 1.16$ , standard error (SE) = 0.2, p-value < 0.0001), NZDep levels 6-10 under-represented ( $\beta = -0.21$ , SE = 0.085, p-value = 0.02), and there are some other age:ethnicity classes that are significantly less represented in the data compared to Europeans in those ages classes, particularly in the 6–17 age classes.

In later outbreaks (since 2007) there has been a shift in the distribution of ages infected. The very young are still most likely to be infections, but older teenagers are more likely to be represented than the under tens (Figure 1). This pattern suggests that improving vaccination coverage in the young is reducing the burden of measles in those age categories, but interestingly the regression results suggest risk of measles cases in the 6–17 year age category was greater for Europeans and Maori.

### 3.3 Risk analysis discussion

The analyses suggest that age is a particularly strong risk factor for measles. This comes as no surprise to epidemiologists or health care providers. However, our analyses also highlight other groups that are at risk. In particular, Pacific people are at greater risk, as are the more wealthy (NZDep 1–5), and European 6–17 year old children. The results of these analyses are discussed in the benefit–cost section below (Section 5.2). Additional data we have been provided by the Ministry of Health but are yet to incorporate in our risk analyses are finer scale (domicile level) immunisation coverage data from the National Immunisation Register (NIR). A key issue with incorporating spatial immunisation data has been the denominator data, and how to deal with people of greater age than those recorded in the NIR.

### 3.4 Risk analysis summary

- Risk of measles infection decreases significantly with age
- Pacific people are statistically more at risk on a per capita basis
- There is some statistical support for those living in better socio-economic situations being at greater risk of measles
- There is some statistical support for Pacific and Asian children in the 6–17 year age categories being at lower risk than European or Maori children

## 4 Modelling measles epidemics

In this section we briefly review the parts of our previous interim report that are pertinent to this study and include details and new work that is relevant for the benefit–cost analysis (Section 5.2).

A previously-published model of the dynamics of measles infections in New Zealand has been used to evaluate the vaccination strategy in New Zealand of

MMR1 at 15 months and MMR2 before 5 years [27, 26, 32]. The results show that achieving coverage of greater than 90% at both vaccination opportunities is necessary if future epidemics of measles are to be prevented, though herd immunity of approximately 95 percent a homogeneously mixed immune population is recommended to interrupt measles [27, 26]. Thus, while New Zealand immunisation activities have led to measles outbreaks becoming less frequent, with decreasing numbers of cases, outbreaks still occur and the current overall population immunity estimates suggest that approximately 85 to 90 percent of the population is immune to measles, thus the reasons for the ongoing outbreaks are likely due to overall population immunity being less than 95 percent and there being pockets of susceptible, non-immune population remaining. The distribution of the naive population for each age class can be seen in Figure 6, as estimated using the NZ census data [31] and the proportion of each age class immune, based on data provided to us by the Ministry of Health on commencing this project.

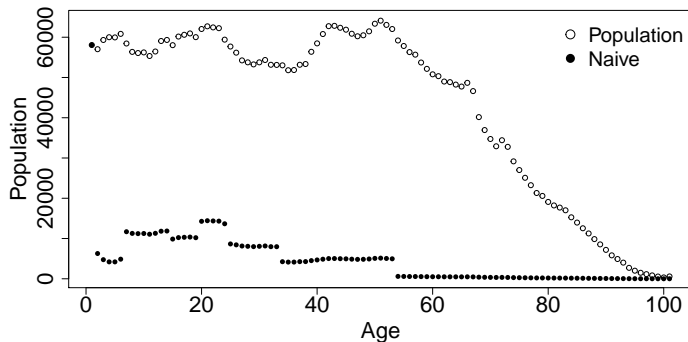


Figure 6: New Zealand population by age and estimates numbers of naive people in each age class

The quantity that determines whether an epidemic will occur is the basic reproduction number of the infection,  $R_0$ . This is defined as the expected number of secondary infections that would arise from a single primary infection introduced into a fully susceptible population [2, 12]. If  $R_0 > 1$  an epidemic will occur following an introduction of infection. The best estimate for measles in New Zealand was  $R_0 = 12.8$  [26]. The basic reproduction number of the infection under vaccination,  $R_v$ , is the expected number of secondary infections that would arise from a single primary infection introduced into a vaccinated population at equilibrium and is a robust indicator of the performance of a vaccination schedule. If  $R_v < 1$  epidemics are prevented. 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

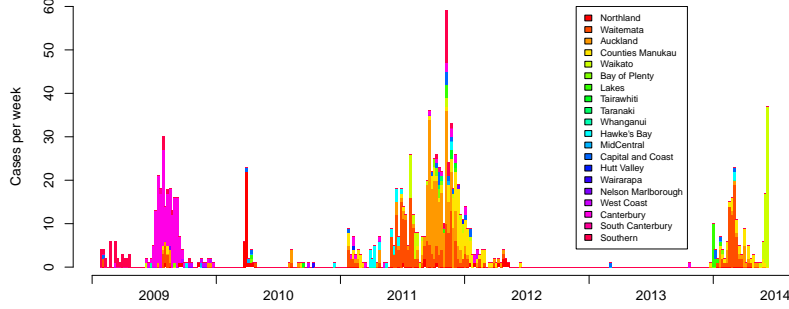


Figure 7: Measles cases by district health board (DHB) from 2009 to 2014

the population who are susceptible.

#### 4.1 Modelling methods

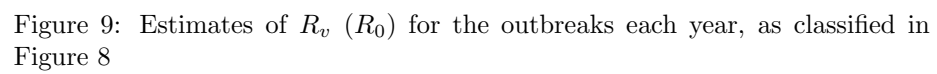
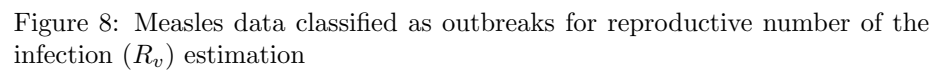
To understand the level of immunity in the population, the transmission dynamics of measles in the partially immune population and how likely an outbreak was of becoming endemic, we estimated  $R_v$  from all the outbreaks in New Zealand since 2009. To do this we estimated  $R_t$ , following an adaptation of the methods in [23, 34]. We were required to compute the generation time for measles to do so. The generation time is the average time an index case infects others after becoming infected. We used a lognormal distribution with mean 12.0 and standard deviation (s.d.) 3.5 from [18]. We then estimated  $R_t$  from the incidence data for each outbreak, defining outbreaks in the dataset given their temporal and geographic correlations (Figure 7). The outbreaks we used in our analyses are shown in Figure 8.

To estimate the proportion of the population requiring vaccination utilising our estimates of  $R_v$ , we make several simplifying assumptions regarding the relationship between the proportion requiring vaccination,  $p_c$ , and  $R_0$ . Specifically, we use the simple relationship:

$$p_c = 1 - (1/R_0) \quad (2)$$

We then assume that the measles epidemics are occurring in a naive population that is the size of the naive population remaining in New Zealand. We estimated this from the national level vaccination coverage data provided by the Ministry of Health for this work (approximately 11%, Figure 6). Thus, the  $p_c$  comes from the naive population in New Zealand and these are the additional vaccinations required to reduce  $R_v$  to one in the overall New Zealand population.

We then used the proportions of the population that were estimated to require vaccination (estimated above), and the proportions of the naive population



per age case from Figure 6 to provide different scenarios to achieve those goals. These are explored and discussed in relation to the risk analyses (Section 3.2) in the benefit–cost analyses section below (Section 5.2).

## 4.2 Modelling results

The estimated  $R_v$  for each outbreak is shown in Figure 9 and in the previous interim report. The probability density of the  $R_v$  estimates for each outbreak all include one, except for the ongoing 2013–2014 outbreak, which has an  $R_v$  well above one. As discussed in the previous interim report, the important caveat to this outbreak analysis is that because this 2013–2014 outbreak is an ongoing outbreak, and not in decline,  $R_0$  is necessarily over one, and so the comparison with others must be cautious. However, the results of these differences are presented in the benefit–cost analysis section (Section 5.2).

These analyses also imply that the regular (approximately yearly) importation of measles is an ongoing process. Given the risk of importation of measles as highlighted in section 3 and our previous report is likely to continue, and we explore the benefit–cost effects of this in Section 5.2.

Again The measles outbreak in 2011–2012 had an  $R_v$  of just greater than one, and yet it persisted for over 12 months. This implies that the current outbreak may persist within the population for a substantial period, given it’s  $R_v$  is approximately twice that of the 2011–2012 outbreak. A caveat to this and other  $R_v$  estimates is that the 2013–2014 outbreak may include some sporadic cases and thus the true basic reproductive numbers may be lower than estimated. However, sub-clinical and underreporting may lower the estimate. The relative contributions of both to our estimates are currently unknown.

To use the results from our modelling exercise to help inform the appropriate measles vaccination coverage. Depending on  $R_v$  the proportion of the national population requiring additional vaccination to make  $R_v < 1$  ranged from 0 ( $R_v = 0.92$ , Figure 9) to an upper limit of 53% for the 2013–2014 outbreak ( $R_v = 2.13$ , Figure 9). These figures can be reached in a number of different ways, and these are discussed in the benefit–cost section (Section 5.2).

## 4.3 Summary of modelling

These results suggest vaccination levels are close to eliminating the possibility of endemic measles transmission, as estimates of  $R_v$  typically include 1 (Figure 9). However, the naive population (Figure 6) and the higher  $R_v$  for the 2013–2014 outbreak (Figure 9) suggests that catch up vaccination may be necessary. In Israel researchers found that vaccinating 85% of susceptible children aged one to seven years at five-yearly intervals would prevent epidemics in Israel [1], but nearly all other studies in Europe suggest no strategies succeeded if coverage rates were below approximately 87%, which the population level immunity in New Zealand has only just reached. Measles vaccination in various regions [1, 5, 13, 16, 33] based on sets of nonlinear differential equation (ODE) models suggest that 85% coverage at MMR1 and MMR2 could be sufficient to prevent

future measles epidemics, but [17] showed that in the Netherlands high overall levels of measles vaccination can obscure pockets of poor coverage, resulting in localised regions with increased risk of infection and effective immunisation is difficult to evaluate. In summary:

- The reproduction number for measles in a partially immune population is often close to one, suggesting increased population level immunity is required to prevent this measles persisting.
- The reproduction number,  $R_v$ , for measles in the current outbreak is well over one, suggesting that this outbreak has the potential to persist for prolonged periods within the population if it is circulating.
- Additional vaccination levels to push  $R_v$  below one among the currently naive population in New Zealand range from 0% ( $R_v < 1$ ) to 53% ( $R_v$  2.13, approximately 250,000 vaccinations), depending on the appropriate reproduction number,  $R_v$ , for measles in New Zealand.

## 5 Cost analyses

In this section we provide a review of the costs of measles from other locations and an analysis of the costs involved with the current measles outbreak. For completeness, we include much of the introduction from the previous interim report, but we have revised some of the figures.

Approximately 50 years ago, approximately 135 million cases and 7–8 million deaths were believed to occur in the world due to measles [9]. Thirty years later, it was estimated there were still approximately 45 million cases of measles occurring annually, including 6 million measles-related fatalities. [36] estimated that in 1999 measles was responsible for more than 30 million disability adjusted life years (DALYs) lost and 12 million in 2005. Similarly, the number of cases was reduced by more than 50% from 43 million in 1999 to approximately 20 million in 2005. They estimated approximately 7.5 million deaths from measles were avoided from 2000–05 due to vaccination. The World Health Organization (WHO) estimated 158,000 deaths from approximately 355,000 measles cases in 2011 [37]. In addition to the substantial losses occurring in measles-endemic countries, a significant impact is felt in heavily measles-vaccinated countries, which may be considered measles-free, due to contact with cases either in the country of origin or in the previously measles-free country.

The annual cost of treating and controlling measles in 11 industrialised countries was estimated to cost more than US\$150 million [8]. The estimated cost for a case ranged from US\$189–344 [8]; however, the average estimated cost of a typical hospital case ranges from US\$967–1,755 [7]. [30] estimated the economic benefits from cases averted due to measles vaccination. They estimated that the expanded vaccination from 2005 to 2015 in 72 of the world’s poorest countries could result in nearly US\$10 billion of costs averted between 2011 and 2020. Ninety-nine percent of these averted costs were the result of lost productivity

due to an estimated 360,000 measles-specific premature mortalities, with the remaining <1% associated with averted treatment costs and reduced caretaker productivity for the nearly 12 million measles cases avoided.

Italy has the highest reported annual cost of measles among industrialised countries [8]. In 2001, it reported losses related to measles of approximately US\$50 million. The economic impact of a large measles outbreak in Italy, 2002–03 examined the costs associated with 5,154 hospitalisations where measles was the main discharge diagnosis. The mean length of hospital stay was 5.2 days (median = 4 days and range = 1 to 303 days). The total cost of these hospitalisations amounted to €8.83 million (€1  $\approx$  NZ\$2.0 in 2002-03), or approximately €1,700 per case. The average cost per non-complicated measles case was €1,429, while the mean cost of a case with complicated measles was €2,721. The average daily cost of a hospital stay was €327.

An outbreak of measles occurred in Sydney, Australia, lasting nearly 2 months in 2011 and resulted in 26 confirmed cases [15]. Seven (27%) of the cases required hospitalisation for more than 1 day and 10 (38%) resulted in management within a hospital emergency department. During this outbreak, a total of 1,395 contacts were identified and managed by a public health unit in western Sydney. The mean number of contacts per case was 54 (median = 28, maximum = 206). The estimated cost to the public health unit for contact management for the epidemic was in excess of AUS\$48,000, with 90% of this being associated with staff time.

Germany implemented a two-dose measles vaccination program in 1991 and has seen the benefits in recent years. In 2001 more than 6,000 cases were reported in Germany but by 2004 this number fell to 122 [35]. However, in 2005 more than 500 cases were reported by the middle of the year in two German states, with the vast majority (>95%) in non-vaccinated children [29]. An economic analysis was performed of the 614 measles cases reported in an 8-month period in Duisburg in the state of North Rhine-Westphalia (NRW). In that study, they estimated the health-care provider costs to be approximately €229,000, or €373 per case. Approximately 78% of these costs were associated with the 95 (15.5%) of the cases that were hospitalised. The mean costs of the hospitalised patients was €1,877, including one patient with encephalitis at a cost of €35,623. In addition to the health-care provider costs, additional costs of €89,400 were incurred by the district public health office, the majority (€85,000, 95.1%) for personnel, €2,300 (2.6%) for vaccination, and €2,100 (2.3%) for serologic testing. Therefore the combined direct costs of these 612 cases amounted to €318,400, or €520 per case. In addition, to determine the total impact, it would be necessary to include the indirect losses associated with lost production of cases and care givers.

Although measles was declared eliminated from the United States in 2000, it remains a concern due to the endemic nature of it around the world [24]. Several studies have been conducted in the United States to assess the economic impact of recent measles outbreaks due to imported measles. [22] estimated the economic impact to public health departments in the US as the result of 16 outbreaks in 2011. The outbreaks lasted an average of 22 days and resulted in



107 confirmed cases; however, from these 107 cases, they estimated between approximately 8,900 and 17,500 contacts with confirmed cases, requiring between 42,600 and 83,100 personnel hours at a cost of between US\$2.7 and 5.3 million. Overall, it was estimated that each contact required 4.7 personnel hours at a cost of US\$298 per contact. It was estimated that for the one week that the Iowa Department of Public Health (DPH) investigated a case in 2004, 2,525 hours were used to identify contacts, set up vaccination clinics, and institute and enforce quarantine orders for those who refused vaccination [11]. In total, it was estimated the direct costs associated with three cases of measles was US\$142,452, or nearly US\$50,000 per case.

The impact of a measles outbreak due to a non-autochthonous case in Indiana was also reported [24], and a total of 34 cases, 94% of which were not vaccinated against measles, were reported in the outbreak. Direct cost information was obtained from approximately 100 public health officers and infection-control officials needed to control the outbreak. Direct cost for those completing a survey showed the outbreak cost at least \$167,685, 83% of which (\$139,023) was for wages, salaries and overhead. This amounted to a direct cost of \$4,932 per measles case. These costs did not include either patient care or indirect costs, which would have made the total and per case cost higher.

The direct medical and public health costs in response to a single case of refugee-imported measles has been reported [10]. Costs included labor, translation and benefits for public health workers. In addition, medical costs were incurred due to vaccination, immunoglobulin, testing for measles immunity, hospitalisation, transportation and diagnosis. In total, 387 hours were associated with this single case, resulting in a cost of US\$11,881. In addition, per-contact costs amounted to US\$264. The cost of hospitalisation for the 3-day stay by the index case was US\$931. Additional costs were associated with physician visits (US\$294), vaccine and immunoglobulin (US\$1,765), mileage (US\$205) and immunologic screening tests for the parents' exposed to measles (US\$240) for a total of US\$23,816.

Economic analyses of measles control programs have shown them to be financially effective. In the Republic of Korea, the economics of alternative measles vaccination programs were compared. All of the alternatives were found to be economically efficient (benefit/cost ratio (B/C) > 1.0), with the alternative using two doses of the MMR program, with a catch-up campaign for measles and rubella being the most favourable (B/C = 1.27).

The purpose of the current study is to estimate the cost of the current measles outbreak in New Zealand. Using this information, we will then evaluate the economics of alternative measles control strategies in order to provide additional information to public health officials and decision makers.

## 5.1 Cost analyses methods

Costs were evaluated as either direct or indirect. Direct costs included physician consultations, hospitalisations, drugs, vaccination, long-term care for chronic sequelae, special education costs. Direct costs can be divided into med-

ical and non-medical [28]. Direct medical costs include costs for diagnosis, treatment, continuing care, rehabilitation and terminal care. Personnel time (investigation and emergency response), materials (phone calls, vaccine), personnel (cost, wages and fringe benefits), overhead costs, public information, and mileage are estimated when calculating direct medical costs. Direct non-medical costs include transportation to and from health care providers.

Indirect costs are productivity losses for the case and/or health care provider, e.g. parent of a school child. Indirect costs included work loss for cases and caregivers. This could also include the economic value of premature life lost, costs associated with permanent disability, e.g. deafness and mental retardation. Commonly the human value approach (HVA) has been used to estimate economic impact of life. The HVA measures the potential future earnings of an individual and discounts it into a present value. Typically this is 3% but 5% has also been used in a sensitivity analysis, which is more compared to non-human life calculations and will tend to reduce the present value of the future earnings (saved by avoiding a case).

Data for the current measles outbreak were obtained from the New Zealand Ministry of Health, from 2008 through June 2014. Data included information on gender of the case, ethnicity and age of the case at discharge from hospital, days spent in the hospital, year of case, number of events, case weight and associated cost.

Cost of the Auckland Regional Public Health Service (ARPHS) for measles response were obtained from the Ministry of Health. Data, for the period January 1 - March 9, 2014, reported salaries for people involved with the measles outbreak management medical team. The costs were reported as direct, additional (above normal budgeting) costs required to enable the management of measles. It includes a breakdown by individual performing the work and whether it was during the normal work schedule (Monday to Friday, M-F) or weekends. Normal work was calculated as  $1.2 \times \text{full time equivalent (FTE)} \times \text{number of days worked}$ . Overtime was calculated as  $1.6 \times \text{FTE (M-F)}$  and  $2.0 \times \text{FTE (weekend)}$ . A full day was considered as 8 hours worked. Salary (hourly) rates were calculated for the following: public health nurse (PHN, \$36), public health assistant (PHA, \$22), data support (\$26), data support (temporary) (\$33), management and programme supervisors (\$40), incident management team (IMT), which had the following work titles: incident controller (\$96), administrator (\$24), planning and intel (\$40), logistics (\$36), communications (\$45), informatics (\$40), operations (\$40), and safety/security officer (SSO) (\$26). In addition, measles operations personnel were calculated at a daily rate of \$600 and operations partners and IMT controller partners at \$729.

Mean wages for New Zealand workers, by age and gender were obtained for the period, 2008–2013 from the New Zealand Income Survey (Statistics New Zealand, 2013). Measles cases were assumed to not work for a period of 5 days. Similarly, a care taker was assumed to not work for 5 days if the case were less than 20 years of age. In order to calculate the wage loss associated with the care taker, it was assumed that the person was a female between the ages of 35–39. Age and gender information for the 192 publicly funded hospital discharges with

Table 3: Estimated costs (NZ\$) for measles management in New Zealand, January 1 – March 9, 2014 (see text for abbreviations)

Category	January	February	March	Total
PHN	55,296	71,175	24,087	150,558
PHA	0	0	2,656	2,656
Data support	0	7,752	4,552	12,304
Supervisors	10,656	10,464	3,232	24,352
IMT	32,918	28,624	7,156	68,698
SSO	0	2,746	1,186	3,932
Measles operations	1,800	10,326	6,678	18,804
Operations partner	2,187	14,580	7,290	24,057
IMT controller partner	2,916	14,580	7,290	24,786
Total	105,773	160,247	64,127	330,147

a measles primary diagnosis from 2008–2013 were matched to the New Zealand wage file to calculate lost wages due to measles.

A regression analysis was performed to test for significant associations between hospital cost and the following explanatory variables: case age at discharge, gender, length of stay (days) and year of case.

## 5.2 Cost analyses results

Direct costs for measles management in New Zealand for the 10-week period, January 1 – March 9, 2014 are shown in Table 3. The reported direct medical costs do not appear to include hospital medical costs, which are reported separately in Table 4.

The total cost for the 293 publicly funded hospital discharges with a measles primary diagnosis that spent 470 nights in hospital was \$550,024 (Table 4). The mean cost per case was \$1,877. The mean cost per day of stay in the hospital was \$1,170.

From 16 December, 2013 through 19 June, 2014 there were 201 confirmed measles cases in New Zealand (note 14 of these occurred before 1 January 2014, so 187 occurred from Jan 2013 – 19 June 2014). The number of cases by age group is shown in Table 5. Of these 201 cases, 34 (17%) were admitted to hospital with the highest proportion occurring in the youngest (< 15 months) and oldest (> 19 years) age groups, 47% and 33%, respectively.

The length of hospital stay for the 293 cases reported between 2000 and 2014 ranged from 0 to 19 days, with a male patient, who was discharged in 2011 at age 57, after a stay of 19 days and a cost of \$8,213 (Figure 10).

Nearly 40% (114/293) of the cases did not spend a night in the hospital, while approximately one-quarter (69/293) spent 1 night and more than three-quarters (222/293) spent less than three nights in the hospital. Only eight cases spent a

Table 4: Number of cases, length of hospital day, cost, cost per case and cost per day for patients with measles as the primary diagnosis, 2000–2014

Year	Cases	Days	Cost	Per.case	Per.day
2000	6	13	8,850	1,475	681
2001	13	18	11,267	867	626
2002	5	2	3,869	774	1,934
2003	9	12	10,241	1,138	853
2004	4	5	4,765	1,191	953
2005	3	11	5,111	1,704	465
2006	1	0	602	602	NC
2007	5	25	82,977	16,595	3,319
2008	3	1	3,038	1,013	3,038
2009	29	38	40,782	1,406	1,073
2010	5	5	6,701	1,340	1,340
2011	132	189	205,303	1,555	1,086
2012	19	12	28,540	1,502	2,378
2013	4	6	5,330	1,333	888
2014	55	133	132,648	2,412	997
TOTAL	293	470	550,024	1,877	1,170

As of 11 July, 2014. NC - not calculated.

Table 5: Frequency of measles cases and number and proportion admitted to hospital by age group, 16 December, 2013 – 19 June, 2014

Age	Cases	Admitted	Proportion
<15 months	21	10	0.47
15 months – 3 years	7	1	0.14
4 – 9 years	8	0	0.00
10 -1 19 years	132	12	0.09
>19 years	33	11	0.33
Total	201	34	0.17

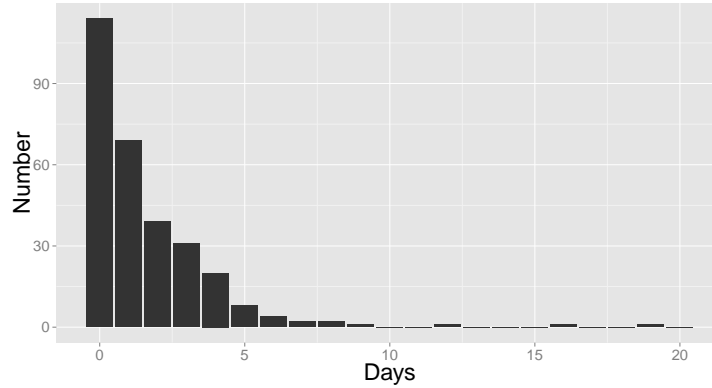


Figure 10: Number of cases attending hospital and stay duration

week or more in the hospital. Due to the small number of cases spending a week or more in the hospital, the regression analysis to determine the association between cost of hospitalisation was limited to the 285 cases hospitalised for seven or fewer days. The number of cases, length of hospital stay, cost, cost per case and cost per day for patients with measles as the primary diagnosis, by year and gender for 2000–2014 appear in Table 6.

Regression analyses showed statistically significant associations between cost of hospitalisation and three variables, length of hospitalisation, case age and year of case, and a less strong association with case gender (Table 7). Results showed the expected hospitalisation costs in 2000 of a female measles patient who did not stay overnight in the hospital was \$582. The cost was \$256 less if the case were a male. It increased of approximately \$406 per night of hospitalisation and \$64 per year over the time period of 2000 - 2014. The cost of a case decreased with the age of the patient by approximately \$8 per year of case age.

Wages lost due to measles were calculated for the period January 2008 – August 2014. Calculations were based on the assumption that 5 days of work were lost for each case; however, individuals under 15 years of age were not assumed to be employed and therefore did not suffer an income loss. If the case were less than 20 years of age, it was assumed there was an income loss of 5 days for the care giver, in addition to the wage loss of the case if 15–19 years of age. Total wage lost for the 247 cases and care givers was estimated to be \$210,436. This consisted of \$107,820 for the cases and \$102,616 for the care giver, but did not include wage losses for cases under 15 years of age. Overall, the cost per case from 2008–2014 was estimated to be \$2,562 (\$852 in forgone wages and \$1,710 in hospital costs).

Table 6: Number of cases, length of hospital stay, cost, cost per case and cost per day for patients with measles as the primary diagnosis, by year and gender, 2000–2014

Year	Gender	Cost	Cases	Length.of.stay	Cost.per.case
2000	F	4,296	2	4	2,148
	M	4,554	4	9	1,139
	Total	8,850	6	13	1,475
2001	F	3,740	5	5	748
	M	7,527	8	13	941
	Total	11,267	13	18	867
2002	F	924	2	0	462
	M	2,945	3	2	982
	Total	3,869	5	2	774
2003	F	9,766	8	12	1,221
	M	475	1	0	475
	Total	10,241	9	12	1,138
2004	F	1,437	1	2	1,437
	M	3,328	3	3	1,109
	Total	4,765	4	5	1,191
2005	F	0	0	0	0
	M	5,111	3	11	1,704
	Total	5,111	3	11	1,704
2006	F	0	0	0	0
	M	602	1	0	602
	Total	602	1	0	602
2007	F	1,930	1	3	1,930
	M	81,046	4	22	20,262
	Total	82,977	5	25	16,595
2008	F	714	1	0	714
	M	2,324	2	1	1,162
	Total	3,038	3	1	1,013
2009	F	11,953	7	15	1,708
	M	28,830	22	23	1,310
	Total	40,782	29	38	1,406
2010	F	5,884	4	5	1,471
	M	817	1	0	817
	Total	6,701	5	5	1,340
2011	F	103,460	66	86	1,568
	M	101,842	66	103	1,543
	Total	205,303	132	189	1,555
2012	F	13,054	8	6	1,632
	M	15,486	11	6	1,408
	Total	28,540	19	12	1,502
2013	F	1,800	1	2	1,800
	M	3,530	3	4	1,177
	Total	5,330	4	6	1,333
2014	F	55,633	2221	46	2,649
	M	77,014	34	87	2,265
	Total	132,647	55	133	2,412
2000-2014	F	335,431	166	284	2,021
	M	214,591	127	186	1,690
	TOTAL	550,022	293	470	1,877

Table 7: Regression results ( $R^2_{\text{adj}} = 0.43$ , p-value  $< 0.001$ ) for measles hospitalisation cost based on length of stay (days), gender, case age and year of case ( $n = 288$ ) in New Zealand, 2000 – 2014

Variable	Coefficient	P.value
Intercept	581.39	$<0.001$
Length of stay (nights)	406.07	$<0.001$
Gender (0 = F, 1 = M)	−255.98	0.006
Case age (years)	−8.23	0.007
Year of case (vs. 2000)	64.35	$<0.001$

### 5.3 Benefit–cost analyses methods

To estimate the benefits from additional vaccinations, as estimated from the above modelling section, we did several things. Primarily, we simulated 1000 measles outbreaks using the estimated  $R_v$  from (Section 4) in the estimated naive population of New Zealand (Figure 6), assuming recovery from infection lead to immunity and thus constantly reducing the population size by the number recovered. We used these values of numbers of predicted cases and the cost figures above to estimate the cost of not vaccinating additional populations. We also simulated what we might expect measles outbreaks to look like following introductions in the population, given that  $R_v$  would be one, though where our estimates for  $R_v$  are already  $< 1$ , we use this. We can therefore estimate the number of cases prevents, and the savings made from the additional vaccinations. We then use the costs of the catch up vaccination schemes and the costs of the expected measles-related costs due to constant introduction of measles and the savings from reduced measles cases to work out the benefit to cost ratio. For our benefit to cost ratio to be beneficial, this must be greater than 1. A value less than one, suggests the costs are higher than the economic benefits. Lastly, because there is a discounting effect with time, we use an 8% discount per year for the costs, as is common for health care discounting, and we calculate these over a 10 year time frame, using a discounting such that:

$$discount/year = cost * 1/1.08^{year-1} \quad (3)$$

Our estimates for the numbers of measles cases are highly variable: if  $R_v$  were greater than one, either the measles outbreak would take off and all the New Zealand population would become infected, or it would stutter after a few infects and fail to take off due to stochasticity. We used the average of 1000 simulations to estimate the mean of these stochastic simulations for our benefit–cost analysis. However, these simulations assume a homogeneously mixed population and thus give large epidemic sizes. We therefore also compared our results to those using the mean number of measles cases seen in New Zealand per year, since 1997. This was 220 cases per year.

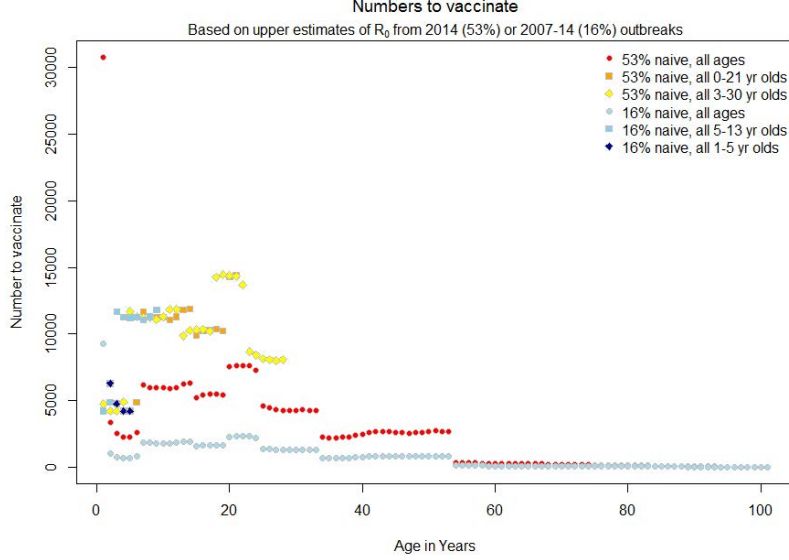


Figure 11: Numbers of the currently naive New Zealand population to ensure  $R_v$  is less than one, and thus all measles introductions will fail to persist within the population.  $R_v$  estimates are from the outbreaks in Figure 8 and shown in Figure 9

The numbers to vaccinate in New Zealand assuming a homogeneously mixed population and using the upper limits of our  $R_v$  estimates are shown in Figure 11.

The expected number of cases in New Zealand, assuming homogenous mixing in a naive population of 11% of the population (the current status) and assuming measles  $R_v$  were 1 is shown in Figure 14. These simulations show that even in scenarios when  $R_v$  is one and thus stochastically should fail to persist for long, large outbreaks can occur. In this modelling exercise, the median value of the 1000 simulations was 2 cases, but the mean 175 and the maximum nearly 25,000 cases.

For the cost analyses we used the values from the above cost section (Section 5.2). Specifically, used the average cost of a case for the analyses to be \$852 lost in wages and \$1710 in hospitalisation costs for those attending hospital, with 17% of cases predicted to be hospitalised (Table 4). We estimated there would be approximately one introduction of measles per year (Section 3). We provide two costs for measles vaccinations for our cost analyses, \$20 and \$50, based on US literature.



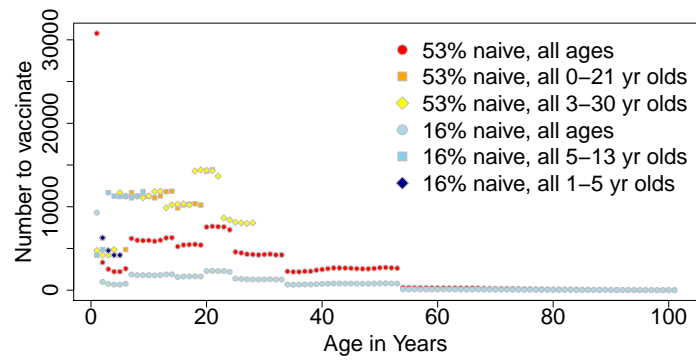


Figure 12: test

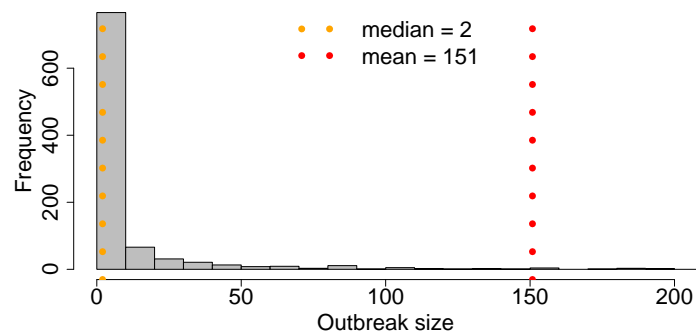


Figure 13: test

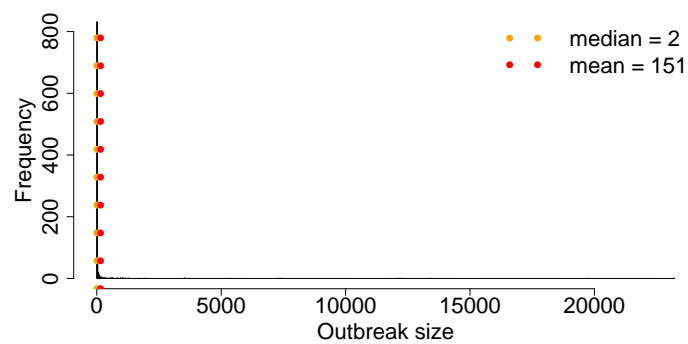


Figure 14: test

Table 8: Cost benefit analyses using simulated epidemic sizes

Years R0 esti- mated from	R0 range esti- mated	R0 for simu- lations	Mean of cases in the popu- lation †	Vaccines required to re- duce R0 to 1	Costs per vaccine	Total vaccine costs (\$)	Total hospi- talised cases (\$)*	Total cases for simu- lations after response	R0 for simu- lations after response	Mean cases in the pop- ulation after catch up †	Total cases over 10 years after action ***	Total hospi- talised cases after action	Total costs for cases after action (\$)	Cases reduced due to action	Savings (\$)	Benefit- cost ratio
2009- 2014	0.92- 1.19	0.92	13	0	0	2	10765	0.92	13	130	22	107053				
2009- 2014	0.92- 1.19	1.19	128901	80000	20	1159502	21913	147295173	1	175	1750	298	1449178	127151	105293982	40.36
2009- 2014	0.92- 1.19	1.19	128901	80000	50	2898755	21913	147295173	1	175	1750	298	1449178	127151	105293982	24.22
2013- 2014	1.82- 2.13	1.82	340032	208153	20	3016923	57805	388554566	1	116	1160	197	960598	338872	280620541	70.55
2013- 2014	1.82- 2.13	1.82	340032	208153	50	7542307	57805	388554566	1	116	1160	197	960598	338872	280620541	33
2013- 2014	1.82- 2.13	2.13	382074	252561	20	3660563	64953	436595960	1	116	1160	197	960598	380914	315435600	68.26
2013- 2014	1.82- 2.13	2.13	382074	252561	50	9151406	64953	436595960	1	116	1160	197	960598	380914	315435600	31.19

† 1000 simulations

\* Proportion of cases hospitalised 0.17

\*\* Wage losses per case \$852 and cost per hospitalised case \$1710

\*\*\* Based on 10 introductions of measles, one per year

Table 9: Cost benefit analyses using simulated epidemic sizes

Years R0 esti- mated from	R0 range esti- mated	R0 for simula- tions	Vaccines required to re- duce R0 to 1	Costs per vaccine (\$)	Total vaccine costs (\$)	Expected number of cases ex- pected based on av- erage since 1997 ***	Total hospi- talised cases*	Total costs for cases (\$)**	R0 for simu- lations after catch up	Mean number of cases in the popu- lation after action simula- tions)	Total cases over 10 years after action ***	Total hospi- talised cases after action	Total costs for cases after action (\$)	Cases reduced due to action	Savings (\$)	Benefit- cost ratio
2009- 2014	0.92- 1.19	0.92	0		0	2200	374	1821824	0.92	13	130	22	107653			
2009- 2014	0.92- 1.19	1.19	80000	20	1159502	2200	374	2513940	1	175	1750	298	1449178	450	372646	0.14
2009- 2014	0.92- 1.19	1.19	80000	50	2898755	2200	374	2513940	1	175	1750	298	1449178	450	372646	0.09
2013- 2014	1.82- 2.13	1.82	208153	20	3016923	2200	374	2513940	1	116	1160	197	960598	1040	861226	0.22
2013- 2014	1.82- 2.13	1.82	208153	50	7542307	2200	374	2513940	1	116	1160	197	960598	1040	861226	0.1
2013- 2014	1.82- 2.13	2.13	252561	20	3660563	2200	374	2513940	1	116	1160	197	960598	1040	861226	0.19
2013- 2014	1.82- 2.13	2.13	252561	50	9151406	2200	374	2513940	1	116	1160	197	960598	1040	861226	0.09

† 1000 simulations

\* Proportion of cases hospitalised 0.17

\*\* Wage losses per case \$852 and cost per hospitalised case \$1710

\*\*\* Based on 10 introductions of measles, one per year

## 5.4 Benefit–cost analyses results

The benefit–cost results are in Table 8 and Table 9. The results in the two tables show two alternative trends. In scenarios where we simulate the expected outbreaks in a homogeneously mixed population and  $R_v$  is above 1 the benefits of vaccination are always substantially greater than the costs of the increased supplementary vaccination (Table 8). However, if the previous recent history of cases since 1997 is the ‘status quo’ and what we may expect in the future then the *additional* effort to vaccinate the naive population of New Zealand based on  $R_v$  estimates that were greater than one (Figure 9) is not a cost effective exercise (Table 9).

It is worth noting that vaccination strategies that target the very young (<1 year old) may be less effective, as our analyses of the vaccinated cases suggests a substantial proportion of vaccinated cases that were vaccinated (Figure 15) and that they were vaccinated with a single vaccine at a very young age (Figure 16).

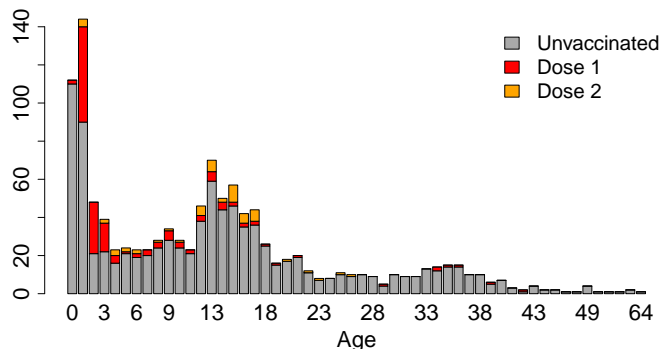


Figure 15: Age and vaccination status of cases

## 5.5 Benefit–cost analysis discussion

The results presented here are based on available data, and only a 10 week period for the 2013–2014 outbreak. The majority of the cost analyses were discussed in our previous interim report and though some details have changed, we will focus here on the benefit–cost analyses. However, for all analyses more detailed costs of all aspects of hospitalisation would be beneficial. So too would information of the cost of measles vaccination in New Zealand.

We have used standard discounting from healthcare of 8% per annum, but again there may be official New Zealand discounting rates that we are unaware of. For our benefit–cost analyses we have not included measles outbreak management costs, though these were provided for the period of January 1 – March 9, 2014 and are included in our benefit–cost analyses. It is likely to be unreal-

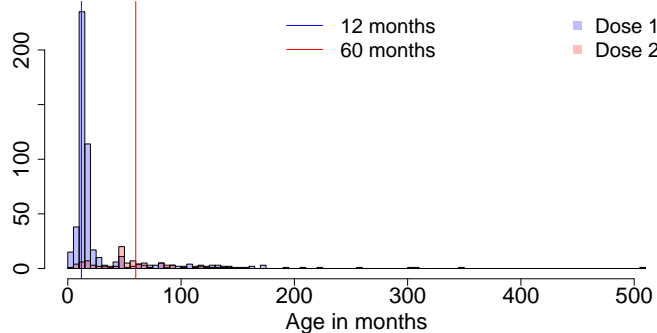


Figure 16: Age of vaccination of vaccinated measles cases

istic to assume that these costs would be linearly related with the number of measles cases, making it difficult to extrapolate these costs outside the reported period for 2014.

In other outbreaks, the average cost per measles case was estimated to be US\$254, US\$276, and US\$307 for Canada, the Netherlands, and the UK, respectively [7]. In our analyses if we include loss of earnings and hospitalisation costs, our estimates are higher, around US\$959 per case. This figure is from NZ\$ 852 for loss of wages and  $0.17 \times \text{NZ \$ } 1710$  for costs related to attending hospital. However, costs can vary widely, with the containment of a single case and two secondary cases of measles in 2004 in Iowa, USA, estimated to cost US\$142,542 alone [11].

Our estimates for the benefit–cost ratio of catch up vaccination are also much higher than those in some studies, if we presume the  $R_v$  is greater than 1 and measles will continue to circulate amongst the naive New Zealand population until everyone is infected. Estimates in Korea suggest catch up vaccination schemes have a benefit–cost ratio of just over one [6]. However, if we presume that in a totally naive population  $R_0$  for measles is around 12, and sometimes estimates to be more than 18 (i.e. 1 case infects 18 others on average, [2]) then the majority of naive people becoming infected is not unrealistic given some of our  $R_v$  estimates (Figure 9) and the benefits of catch up vaccination are clear (Table 8). If measles continues to cause smaller outbreaks, and/or  $R_v$  is less than one (Figure 9), then there is little financial benefit in additional vaccination (Table 8 and Table 9), though there may be medical and other benefits relating to maintaining measles free status that we have not included in our report.

Finally, our model of measles introductions is a simple one, and more complex models may predict smaller outbreaks depending on contact structure and other scenarios, such as the size of the local naive population. Whatever happens, however, it is clear that there will be ongoing costs to maintain New

Zealand free of endemic measles and introductions occurring on an annual basis (see previous report) may produce some large and costly outbreaks, even if vaccination cover is high and  $R_v$  is less than one (Figure 14).

## 5.6 Benefit–cost analysis summary

- The mean wage losses per measles case is estimated to be \$852
- The mean cost per measles case attending hospital is estimated to be \$1710
- Approximately 17% of measles cases attend hospital
- For  $R_v$  values estimated for the 2013–2014 outbreak and the upper bounds estimated for all outbreaks since 2009, the benefits of catch up vaccination strategies are clear ( $>1$  B/C ratio).
- For  $R_v$  values at the lower bounds of the estimates for all outbreaks since 2009, the benefits of catch up vaccination strategies are not clear and may not be cost effective ( $<1$  B/C ratio).
- Large outbreaks, with a mean size of approximately 175 cases per year, median of 2, but peak size of up to many thousands, may occur regularly due to importation, despite  $R_v$  being below one and the epidemic predicted to die out without additional interventions.

## 6 Summary of key findings

- Risk of measles infection decreases significantly with age
- Pacific people are statistically more at risk on a per capita basis, as are those living in better socio-economic situations
- Pacific and Asian children in the 6–17 year age categories have been at lower risk than European or Maori children of the same age
- Additional vaccination levels to push  $R_v$  below one among the currently naive population in New Zealand range from 0% ( $R_v < 1$ ) to 53% ( $R_v$  2.13, approximately 250,000 vaccinations), depending on the appropriate reproduction number,  $R_v$ , for measles in New Zealand.
- The mean wage losses per measles case is estimated to be \$852
- The mean cost per measles case attending hospital is estimated to be \$1710, and approximately 17% of measles cases attend hospital
- For  $R_v$  values estimated for the 2013–2014 outbreak and the upper bounds estimated for all outbreaks since 2009, the benefits of catch up vaccination strategies are clear ( $>1$  B/C ratio).

- For  $R_v$  values at the lower bounds of the estimates for all outbreaks since 2009, the benefits of catch up vaccination strategies are not clear and may not be cost effective ( $<1$  B/C ratio).
- Large outbreaks, with a mean size of approximately 175 cases per year, median of 2, but peak size of up to many thousands, may occur regularly due to importation, despite  $R_v$  being below one and the epidemic predicted to die out without additional interventions.

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## References

- [1] Agur, Z., L. Cojocaru, G. Mazor, R. M. Anderson and Y. L. Danon (1993). Pulse mass measles vaccination across age cohorts. *Proceedings of the National Academy of Sciences USA*, 90, 11698–11702.
- [2] Anderson, R. M. and R. M. May (1991). *Infectious diseases of humans: dynamics and control*. Oxford: Oxford University Press.
- [3] Anon. (2002a). *Immunisation handbook* Wellington: Ministry of Health. pp. 131–146.
- [4] Anon. (2002b). *Infectious diseases in livestock* The Royal Society. pp. 68.
- [5] Babad, H. R., D. J. Nokes, N. J. Gay, E. Miller, P. Morgan-Capner, and R. M. Anderson (1995). Predicting the impact of measles vaccination in England and Wales: model validation and analysis of policy options. *Epidemiology and Infection*, 114, 319–344.
- [6] Bae, G. R, Y. J. Choe, U. Y. Go, Y. I. Kim, and J. K. Lee (2013). Economic analysis of measles elimination program in the Republic of Korea, 2001: A cost benefit analysis study. *Vaccine*, 31, 2661–2666.
- [7] Carabin, H., W. J. Edmunds, U. Kou, S. van den Hof, and V. H. Nguyen (2002). Measles in industrialized countries: a review of the average costs of adverse events and measles cases. *BMC Public Health*, 2, 22.
- [8] Carabin, H., W. J. Edmunds, M. Gyldmark, P. Beutels, D. Levy-Bruhl, H. Salo, U. K. and Griffiths (2003) The cost of measles in industrialised countries. *Vaccine*, 21, 4167–4177.

- [9] Clements, C. J. and G. D. Hussey (2004). Chapter 4: Measles. In *The Global Epidemiology of Infectious Diseases*, Murray, C., A. D. Lopez, and C. D. Mathers, (eds.), Geneva. World Health Organization, pp. 391.
- [10] Coleman, M. S., L. Garbat-Welch, H. Burke, M. Weinberg, K. Humbaugh, A. Tindall, and J. Cambron (2012). Direct costs of a single case of refugee-imported measles in Kentucky. *Vaccine*, 30,317–321.
- [11] G. H. Dayan, I. R. Ortega-Sanchez, C. W. LeBaron, M. P. Quinlisk, and the Iowa Measles Response Team (2005). The cost of containing one case of measles: the economic impact on the public health infrastructure - Iowa, 2004. *Pediatrics*, 116:e1; DOI:10/1542/peds.2004-2512.
- [12] Diekmann, O. and J. A. P. Heesterbeek (2000). *Mathematical epidemiology of infectious diseases: model building, analysis and interpretation*. Chichester: Wiley.
- [13] Edmunds, W. J., N. J. Gay, M. Kretzschmar, R. G. Pebody and H. Wachman (2000). The pre-vaccination epidemiology of measles, mumps and rubella in Europe: implications for modelling studies. *Epidemiology and Infection*, 125, 635–650.
- [14] Fila, A., A. Brenna, A. Pana, G. M. Cavallaro, M. Massari and M. L.C. degli Atti (2007). Health burden and economic impact of measles-related hospitalization in Italy, 2002-2003. *BMC Public Health*, 7,169
- [15] Flego, K. L., D. A. Belshaw, V. Sheppeard, and K. M. Weston (2013). Impacts of a measles outbreak in western Sydney on public health resources. *Communicable Diseases Intelligence Quarterly Report*, 37, E240–245.
- [16] Gay, N. J., L. Pelletier, and P. Duclos (1998). Modelling the incidence of measles in Canada: an assessment of the options for vaccination policy. *Vaccine*, 16, 794–801.
- [17] Glass, K., J. Kappey, and B. T. Grenfell (2004). The effect of heterogeneity in measles vaccination population immunity. *Epidemiology and Infection*, 132, 675–683.
- [18] Klinkenberg, D. and H. Nishiuraa (2011). The correlation between infectivity and incubation period of measles, estimated from households with two cases. *Journal of Theoretical Biology*,284, 52–60
- [19] Koopmanschap, M. A. (1998). Cost-of-illness studies: useful for health policy? *Pharmacoeconomics*, 14, 143–148.
- [20] Larg, A. and J. R. Moss (2011). Cost-of-illness studies: a guide to critical evaluation. *Pharmacoeconomics*, 29,653–671.
- [21] Mansoor, O., A. Blakely, M. Baker, M. Tobias, and A. Bloomfield (1998). A measles epidemic controlled by immunisation. *New Zealand Medical Journal*, 111, 467–471.



- [22] Ortega-Sanchez, I. R., M. Vijayaraghavan, A. E. Barskey, and G. S. Wallace (2014). The economic burden of sixteen measles outbreaks on United States public health departments in 2011. *Vaccine*, 32,1311–1317.
- [23] Obadia, T., R. Haneef and P-Y. Boelle The R0 package: a toolbox to estimate reproduction numbers for epidemic outbreaks. *BMC Medical Informatics and Decision Making*, 2012, 12–147.
- [24] Parker, A. A., W. Staggs, G. H. Dayan, I. R. Ortega-Sanchez, P. A. Rota, L. Lowe, P. Boardman, R. Teclaw, C. Graves, and C. W. LeBaron (2006). Implications of a 2005 measles outbreak in Indiana for sustained elimination of measles in the United States. *The New England Journal of Medicine*, 355, 447–455.
- [25] Prouty, R.W., G. Smith and K. C. Lakin (2001). Residential services for persons with developmental disabilities: status and trends through 2000. *Minneapolis: Institute on Community Integration*, University of Minnesota, pp. 179, rtc.umn.edu/risp00.
- [26] Roberts, M. (2004). A mathematical model for measles vaccination. Wellington: Ministry of Health.
- [27] Roberts, M. G. and M. I. Tobias (2000). Predicting and preventing measles epidemics in New Zealand: Application of a mathematical model. *Epidemiology and Infection*, 124, 279–287.
- [28] Saha, S. and U. G. Gerdtham (2013). Cost of illness studies on reproductive, maternal, newborn, and child health: a systematic literature review. *Health Economics Review*, doi:10.1186/2191-1991-3-24.
- [29] Siedler, A., A. Tischer, A. Mankertz, and S. Santibanez (2006). Two outbreaks of measles in Germany 2005. *Eurosurveillance* 2006;11(4) article 5, www.eurosurveillance.org, accessed 14 June 2014.
- [30] Stack, M. L., S. Ozawa, D. M. Bishai, A. Mirelman, Y. Tam, L. Niessen, D. G. Walker, and O.S. Levine (2011). Estimated economic benefits during the 'decade of vaccine' include treatment savings, gains in labor productivity. *Health Affairs*, 30,1021–1028.
- [31] *Statistics New Zealand* (2014). <http://nzdotstat.stats.govt.nz/>, accessed 17 June 2014.
- [32] Tobias, M. I. and M. G. Roberts (1998). Predicting and preventing measles epidemics in New Zealand: Application of a mathematical model. Wellington: Ministry of Health.
- [33] Wallinga, J., D. Levy-Bruhl, N. J. Gay, and C. H. Wachman (2001). Estimation of measles reproduction ratios and prospects for elimination of measles by vaccination in some Western European countries. *Epidemiology and Infection*, 127, 281–295.

- [34] Wallinga, J., and P. Teunis (2004). Different Epidemic Curves for Severe Acute Respiratory Syndrome Reveal Similar Impacts of Control Measures. *American Journal of Epidemiology*, 160, 509.
- [35] Wichmann, O., A. Siedler, D. Sagebiel, W. Hellenbrand, S. Santibanez, A. Mankertz, G. Vogt, U. van Treeck, and G. Krause (2009). Further efforts needed to achieve measles elimination in Germany: results of an outbreak investigation. *Bulletin of the World Health Organization*, 87, 108–115.
- [36] Wolfson, L. J., P. M. Strebel, M. Gacic-Dobo, E. J. Hoekstra, J. W. McFarland, and B. S. Hersh (2007). Has the 2005 measles mortality reduction goal been achieved? A natural history modelling study. *Lancet*, 369, 191–200.
- [37] World Health Organisation measles media centre, January (2013) Geneva: World Health Organization. [www.who.int](http://www.who.int), accessed July 1, 2014.
- [38] Zhou, F, S. Reef, M. Massoudi, M. J. Papania, H. R. Yusuf, B. Bardenheier, L. Zimmerman, and M. M. McCauley (2004). An economic analysis of the current universal 2-dose measles-mumps-rubella vaccination program in the United States. *Journal of Infectious Diseases*, 189, S131–45.