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 for the measles outbreaks in New Zealand, 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 model 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 multivariate regression analyses, though some groups, such as people of Pacific ethnicity, 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 extremely 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 were 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*, we 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 regression 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 Age $\times$ Prioritised Ethnicity $\times$ 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 Age $\times$ Prioritised Ethnicity $\times$ 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 [32]).

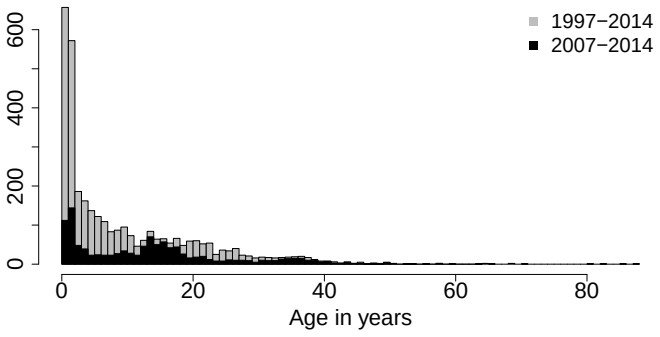

Figure 1: Age of measles cases in years in New Zealand for two periods, 1997–2014 and 2007–2014

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: NZDep 1–5 and NZDep 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 (MLA); 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 (see "None", 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 numerous issues with the data for Middle Eastern, Latin American and African ethnicities category, and along with small population sizes (Table2), and there several issues with estimating the denominator data for this

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

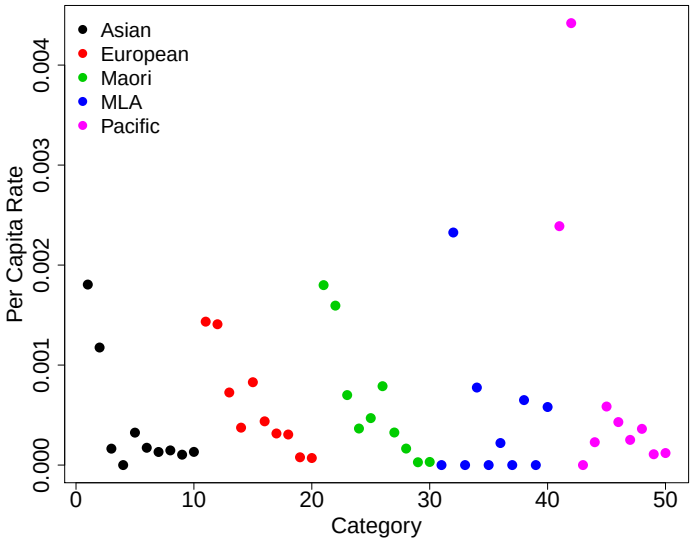

Figure 2: Per capita rates of measles infections broken down by ethicity, see Table 2 for details

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 the results of a quasipoission regression model. We also account for differences in population sizes by using an offset term, the log(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:

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

Where α is the intercept, y cases, $_a$ age, $_e$ Prioritized Ethnicity, $_n$ NZDep, and ϵ the error term.

3.2 Regression analyses results

The distribution of the cases per category used in the regression analyses are in Figure 3.

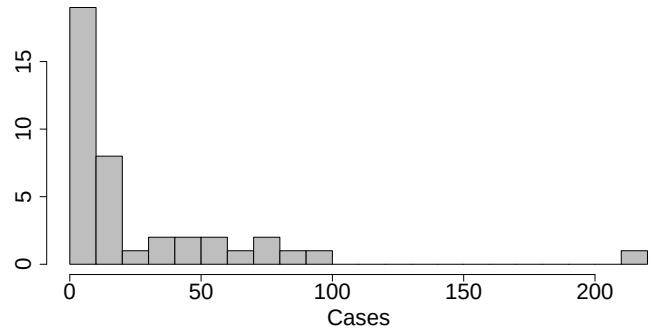

Figure 3: Histogram of cases per category used in the final regression model

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

The significance of the different predictor variables can be seen 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 **
---
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:

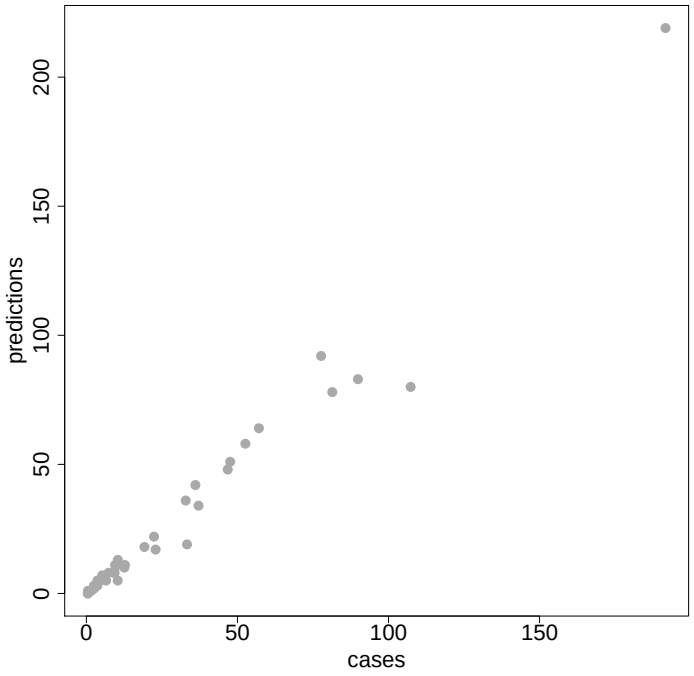

Figure 4: Regression model predictions plotted against the cases (Equation 1)

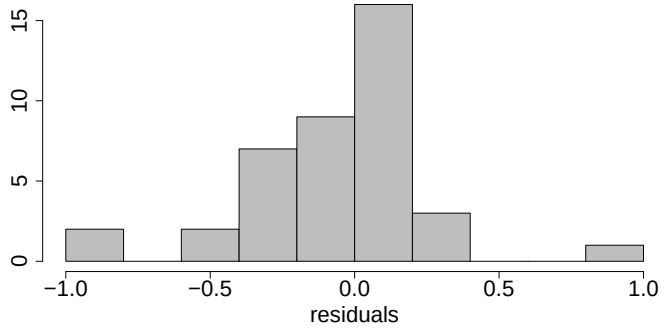

Figure 5: Histogram of residuals from the regression model (Equation 1)

```
> 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 MLA 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 (β = 1.16, standard error (SE) = 0.2, p–value < 0.0001), NZDep levels 6-10 under-represented (β = -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 infected, but of school aged children older teenagers are more likely to be represented then 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. 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 regression analyses suggest that age is a particularly strong risk factor for measles. This comes as no surpise 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 and Maori 6–17 year old children compared to Asian and Pacific ethnicity children of the same age. Interpretation of these results must still be viewed with some caution, however, as there is very likely a spatial effect that might not be accounted for in these analyses. 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.

The results of these regression analyses are also discussed in the benefit–cost section below (Section 5.2)

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 caterories 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 [28, 27, 33]. 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 interupt measles [28, 27]. 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 etimated using the NZ census data [32] and the proportion of each age class immune, based on data provided to us by the Ministry of Health on commencing this project. The figure shown (Figure 6) and for all subsequent analyses assume a currently susceptible population in New Zealand of approximately 11% of the total population.

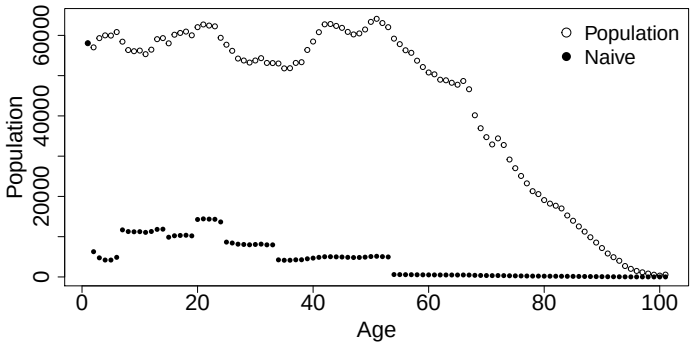

Figure 6: New Zealand population by age and estimates numbers of naive people in each age class

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

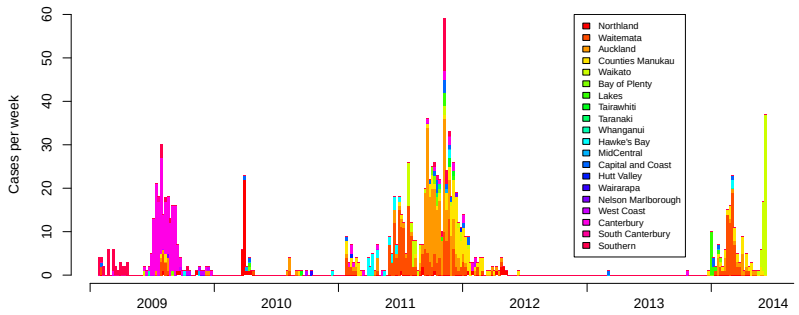

Figure 7: Measles cases by district health board (DHB) from 2009 to 2014

occur following an introduction of infection. The best estimate for measles in New Zealand was $R_0 = 12.8$ [27]. 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 predicted to be prevented (but see below) and infection persistence is 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 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 previously 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 [24, 35]. 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 [19]. 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,

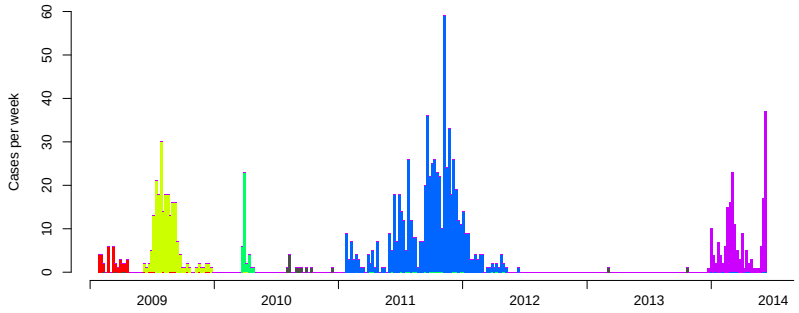

Figure 8: Measles data classified as outbreaks for reproductive number of the infection (R_v) estimation

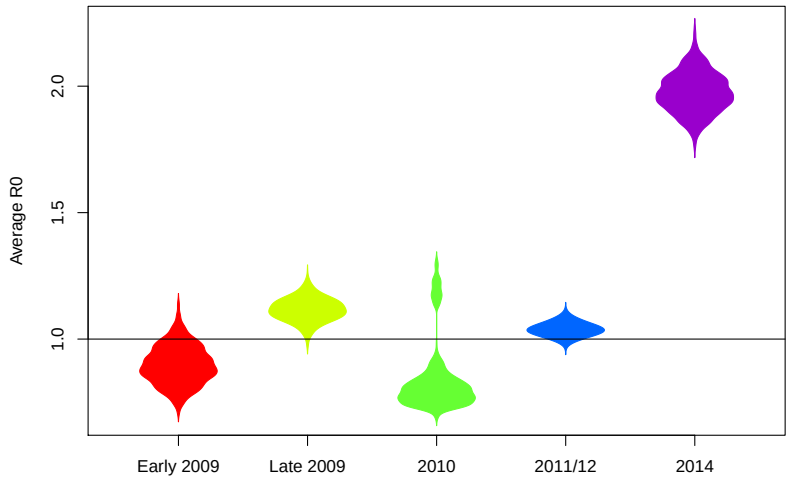

Figure 9: Estimates of R_v (R_0) for the outbreaks each year, as classified in Figure 8

we use the simple relationship:

$$p_c = 1 - (1/R_0) \tag{2}$$

We then assume that the measles epidemics are occuring in a naive population that is the size of the naive population remaining in New Zealand and thus R_0 is equivalent to R_v. We estimated the susceptible population in NewZealand 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 (Equation 2), 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).

finally, we used the same model structure and generation times to estimate the epidemic sizes once vaccination catch up protocols had been implemented assuming $R_v < 1$ and the population of suscpetible people in New Zealand was now reduced by the numbers vaccinated. Because the model is stochastic, we ran 1000 simulations and report the mean values, though the distribution of these is shown in the benefit–cost section (Section 5.2).

4.2 Modelling results and discussion

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_v is necessarily over one, and so the comparison with others must be cautious. However, the results of these differences are presented and discussed 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, we explore the effects of this in the benefit–cost section (Section 5.2).

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, we use Equation 2. 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).

The results of these modelling exercises 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. 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 succeded 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, 34] 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.

4.3 Summary of modelling

- 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 2013–2014 outbreak is well over one, suggesting that this outbreak has the potential to persist for prolonged periods within the population is it 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. [37] 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 vaccination. The World Health Organization (WHO) estimated 158,000 deaths from approximately 355,000 measles cases in 2011 [38]. 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]. [31] 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 ≈ 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 [36]. 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 [30]. An eco-

nomic analysis was performed of the 614 measles cases reported in an 8-month period in Duisburg in the state of North Rhine-Wesphalia (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 [25]. Several studies have been conducted in the United States to assess the economic impact of recent measles outbreaks due to imported measles. [23] 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 [25], 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 medical and non-medical [29]. 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 $1.2 \times$ full time equivalent (FTE) $\times$ number of days worked. Overtime was calculated as $1.6 \times$ FTE (M-F) and $2.0 \times$ 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 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

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

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

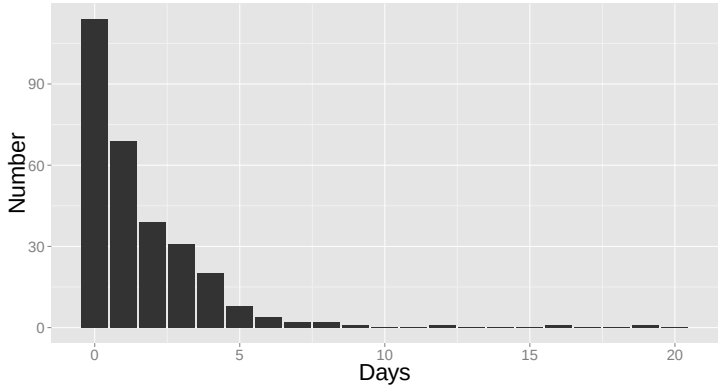

Figure 10: Number of cases attending hospital and stay duration

(222/293) spent less than three nights in the hospital. Only eight cases spent a 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 –

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

As of 7 August, 2014.

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

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).

5.3 Benefit–cost analyses methods

To estimate the benefits from additional vaccinations, as estimated from the above modelling section (Section 4), we did several things. Primarily, we simulated 1000 measles outbreaks using the estimated R_v from (Section 4) in the estimated susceptible population of naive New Zealanders (Figure 6), assuming recovery from infection led 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 what the cost of not vaccinating additional populations would be. 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 prevented, and the savings made from the additional vaccinations. We then use the costs of the catch up vaccination schemes, the costs of the expected measles-related costs due to constant introduction of measles despite increased population immunity, and the savings from reduced measles cases to work out the benefit–cost ratio ((B/C), where a B/C ratio > 1 means that the program benefits exceed their costs. A B/C value less than one suggests the costs are higher than the economic benefits. Lastly, benefits were assessed over a 10–year time period, using a discounting rate of 3% discount per year for the costs, as is common for

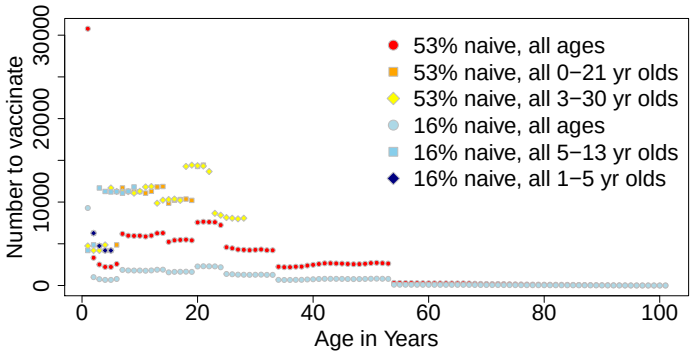

Figure 11: The estimated proportion of the currently naive New Zealand population requiring additional vaccination given alternative R_v values to reduce the R_v to one (Section 4)

healthcare discounting [18]:

$$present\ value = \sum future\ value_{yr} * (1/(1 + discount\ rate)^{yr} \quad (3)$$

Where $_{yr}$ is the year 0 (current) through to 9 (ten years into the future).

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 susceptible New Zealand population would become infected during the outbreak, or the epidemic it would stutter after a few infects and fail to cause a large epidemic 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 once the epidemic gets beyond the initial stuttering infection chains and this assumption is discussed below. However, to address this, we not only use R_v values of 1, but we 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.

The numbers of susceptible people to vaccinate in New Zealand, assuming a homogeneously mixed population and using the upper limits of our R_v estimates (Section 4) are shown in Figure **??**.

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 12 and Figure 13. 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 due to stochastic processes. Though the median value from 1000 simulations is low (2 cases), and thus most measles introductions will be single cases or lead to minor outbreaks, in this modelling exercise the mean value was 151 cases and the maximum nearly 25,000 cases.

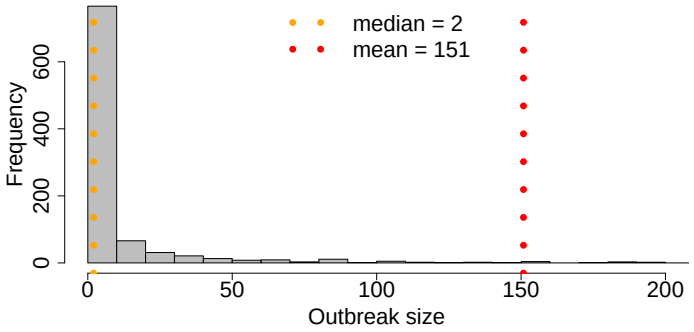

Figure 12: A subset of the expected number of measles cases from 1000 simulations of a model (Section 4) in a homogeneously mixed population in New Zealand with 11% susceptible to measles infection using an R_v =1. The full distribution of results can be seen in Figure 13

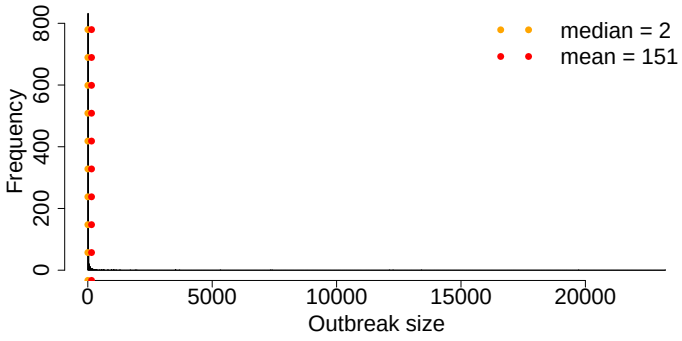

Figure 13: The distribution of the expected number of measles cases from 1000 simulations of a model (Section 4) in a homogeneously mixed population in New Zealand with 11% susceptible to measles infection using an R_v =1, showing the rare but possible large epidemic sizes possible. A subset of the distribution of results can be seen in Figure 12

For the cost analyses we used the values from the above cost section (Section 5.2). Specifically, we 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.

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 currently 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 14) were vaccinated with a single vaccine at a very young age (Figure 15).

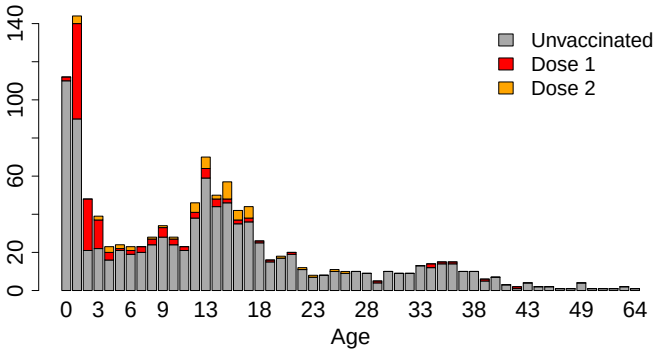

Figure 14: Age and vaccination status of cases

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,

Table 8: Cost benefit analyses using simulated epidemic sizes

Years R_v estimated from	R_v range	R_v for simulations	Additional vaccines required to reduce R_v to 1	Costs per vaccine ($)	Present value of discounted vaccination costs ($)	Mean total cases in over 10 years without additional vaccination	Total hospitalised cases*	Total undiscounted case costs without additional vaccination ($)**	Present value of discounted case costs of baseline program ($)(Equation 2)	Mean epidemic size in immune pop over 10 years with R_v = 1 †	Total cases over 10 years following additional vaccination***	Total hospitalised cases following adtional vaccination	Total costs for cases assuming supplemental vaccination ($)	Total cases reduce by vaccination alternative vs baseline	Present value of discounted benefits from reducing cases with supplemental vaccination program	Discounted net benefit of supplemental vaccination program	Benefit–cost ratio
2009-2014	0.92-1.19	0.92	0	na	0	130	22	148551	130519	13	130	22	148551	0	0	0	na
2009-2014	0.92-1.19	1.19	80000	20	1600000	128901	21913	147295173	129415143	145	1450	247	1656915	127451	127959360	126359360	79.97
2009-2014	0.92-1.19	1.19	80000	50	4000000	128901	21913	147295173	129415143	145	1450	247	1656915	127451	127959360	123959360	31.99
2013-2014	1.82-2.13	1.82	208153	20	4163060	340032	57805	388554566	341388274	116	1160	197	1325532	338872	340223647	336060587	81.72
2013-2014	1.82-2.13	1.82	208153	50	10407650	340032	57805	388554566	341388274	116	1160	197	1325532	338872	340223647	329815997	32.69
2013-2014	1.82-2.13	2.13	252561	20	5051220	382074	64953	436595960	383597966	116	1160	197	1325532	380914	382433339	377382119	75.71
2013-2014	1.82-2.13	2.13	252561	50	12628050	382074	64953	436595960	383597966	116	1160	197	1325532	380914	382433339	369805289	30.28

† 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 historic epidemic sizes since 1997

Years R_v estimated from	R_v range	R_v for simulations	Additional vaccines required to reduce R_v to 1	Costs per vaccine ($)	Present value of discounted vaccination costs ($)	Mean total cases in over 10 years without additional vaccination	Total hospitalised cases*	Total undiscounted case costs without additional vaccination ($)**	Present value of discounted case costs of baseline program ($)(Equation 2)	Mean epidemic size in immune pop over 10 years with R_v = 1 †	Total cases over 10 years following additional vaccination***	Total hospitalised cases following adtional vaccination	Total costs for cases assuming supplemental vaccination ($)	Total cases reduce by vaccination alternative vs baseline	Present value of discounted benefits from reducing cases with supplemental vaccination program	Discounted net benefit of supplemental vaccination program	Benefit–cost ratio
2009-2014	0.92-1.19	0.92	0	na	0	130	22	148551	130519	13	130	22	148551	0	0	0	na
2009-2014	0.92-1.19	1.19	80000	20	1600000	2200	374	2513940	2208775	145	1450	247	1656915	750	752991	-847009	0.47
2009-2014	0.92-1.19	1.19	80000	50	4000000	2200	374	2513940	2208775	145	1450	247	1656915	750	752991	-3247009	0.19
2013-2014	1.82-2.13	1.82	208153	20	4163060	2200	374	2513940	2208775	116	1160	197	1325532	1040	1044148	-3118912	0.25
2013-2014	1.82-2.13	1.82	208153	50	10407650	2200	374	2513940	2208775	116	1160	197	1325532	1040	1044148	-9363502	0.10
2013-2014	1.82-2.13	2.13	252561	20	5051220	2200	374	2513940	2208775	116	1160	197	1325532	1040	1044148	-4007072	0.21
2013-2014	1.82-2.13	2.13	252561	50	12628050	2200	374	2513940	2208775	116	1160	197	1325532	1040	1044148	-11583902	0.08

† 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

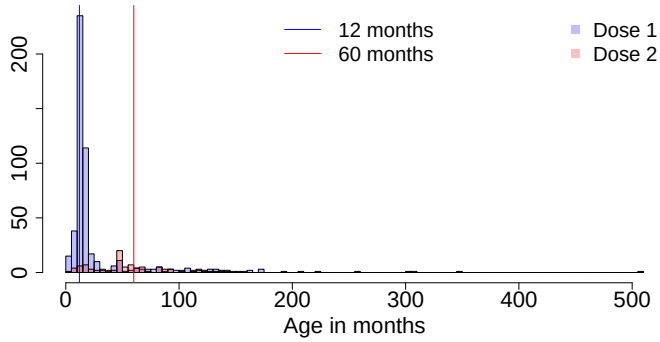

Figure 15: Age of vaccination of vaccinated measles cases

we will focus here on the benefit–cost analyses. However, for all analyses more detailed costs of all aspects of hopsitalisation would be beneficial. So too would information of the cost of measles vaccination in New Zealand.

We have used standard discounting from healthcare of 3% per annum [18], 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. Including these could be done, but we would like some further data of these before including them in our benefit–cost analsyes. It is likely to be unrealistic 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 * 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 amont the presently naive and susceptible New Zealand population until overyone has been 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 estimated 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). The benefits of catch up vaccination are clear once R_v is greater than one (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 outreaks depending on contact structure and other scenarios, such as the size of the local naive population. The spatial effects of measles transmission may have affected both our multivariate regression analyses (3) and will affect the predictions from modelling exercises. Whatever happens, however, it is clear that there will be ongoing costs to maintain New Zealand free of endemic measles and introductions occuring 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 12 and Figure 13).

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 hopsital
- 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 caterories have been at lower risk of measles 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 hopsital
- 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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