Draft Final Report: Measles risk assessment, modelling, and benefit–cost analyses for New Zealand

David T S Hayman*[1], Jonathan C Marshall[1], Nigel P French[1], Tim Carpenter[2], and Mick G Roberts[3]

[1]mEpiLab, Infectious Diseases Research Centre, Massey University, Palmerston North 4442, New Zealand
[2]EpiCentre, Infectious Diseases Research Centre, Massey University, Palmerston North 4442, New Zealand
[3]Institute of Natural & Mathematical Sciences, New Zealand Institute for Advanced Study and the Infectious Disease Research Centre, Massey University, Private Bag 102 904, North Shore Mail Centre, Auckland, New Zealand

1 Abstract

New Zealand has been working towards elimination of endemic (domestic) measles virus transmission, but has suffered from small, yet significant outbreaks after measles introductions from abroad. In this draft final report we review the draft *Progress Towards Measles Elimination in New Zealand - Final* report from the New Zealand Ministry of Health to the World Health Organization (WHO) Western Pacific Region. We identify additional analyses that may help understand risk of infection in New Zealand. Here we present the results of statistical analyses of risk factors for measles cases in New Zealand during outbreaks since 2007. We provide cost analyses for the measles outbreaks in New Zealand, and include modelling of measles outbreaks, including pre- and post-vaccination scenarios, based on the numbers of naïve people at the District Health Board (DHB) and national level. We provide 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 are:

*D.T.S.Hayman@massey.ac.nz

- The *Progress Towards Measles Elimination in New Zealand - Final* report was of high quality and contained substantial information and useful analyses.

- The regression analyses suggest that age is a particularly strong risk factor for measles. People of European ethnicity, however, make up the majority of cases. However, our analyses also highlight other groups that are at greater risk of measles on a per capita basis. 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.

- Of the 11% of the population of New Zealand that are currently considered to be immunologically naïve, it was estimated that approximately 28% would require additional vaccination to ensure measles does not persist, leading to an additional 131,500 vaccinations.

- New Zealand is at risk of frequent measles importation due to travel and endemic measles elsewhere in the globe.

- Peak overall travel rates, and thus presumably risk from measles importation, is in December. However, New Zealander and immigrant or non–New Zealander travel is otherwise out of phase, with peak travel for New Zealanders during winter, and non–New Zealanders during summer.

- Analyses of outbreak data suggest that measles basic reproduction number (R_v, the number of secondary infections in a partially vaccinated population) values often include 1 and the current 2013–2014 outbreak, as analysed from data until June, is well above one. This analysis suggests improved vaccination is a requisite to prevent measles persisting in the population.

- The cost of the current 2013–2014 measles outbreak is estimated to be at least $805,000.

- The mean wage loss per measles case is estimated to be $839

- The mean cost per measles case attending hospital is estimated to be $1,877 per case, and approximately 17% of measles cases attend hospital

- The mean management cost per case is $1,765

- The benefit–cost (B/C) ratio analyses suggest additional vaccination is extremely beneficial financially (B/C >1).

- Outbreaks, with a mean size of 61 cases per year, median of 2 cases, but possibly a peak size of up to many thousands, may occur due to importation, despite R_v being below one and the epidemic predicted to die out following additional vaccinations.

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, as achieved in the Americas in 2002. The Western Pacific Region is expected to be the second WHO region to achieve measles elimination and it was announced in March 2014 that Australia, Macao, Mongolia and the Republic of Korea have achieved measles elimination.

The last widespread measles outbreaks in New Zealand occurred in 1991 and in 1997. Since then, smaller but significant outbreaks have occurred in 2009 (mainly in Canterbury) and in 2011–2012 (mainly in the Auckland region) and another significant outbreak is currently ongoing in the Auckland and Waikato regions. The outbreak in 2011–2012 lasted for more than 12 months and the current 2013–2014 outbreak started at the end of December 2013 and is ongoing (as of 3 July 2014). In 2013, but prior to the current 2013–2014 outbreak, New Zealand was advised by the Western Pacific Regional Verification Commission for Measles Elimination (RVC) that it can request verification of non-endemic status three years after the last case of the 2011–12 outbreak in June 2012.

Previous measles analyses, including two in New Zealand by Prof. Roberts, estimated the interruption of measles virus transmission can be achieved by herd immunity when approximately 95 percent of the population is homogeneously immune to 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 (as described above). Current estimates suggest that approximately 85 to 90 percent of the population is immune to measles (see subsection 4.2), 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. Since 2009, all the outbreaks in New Zealand have been linked to infections acquired (imported) from overseas, though previous work suggests these outbreaks still largely affect school-aged children and children under two years of age. Those under two year olds are thought be be consistently among the most affected age groups because the first of two doses of measles, mumps and rubella vaccine (MMR) is not due until fifteen months.

3 Risk analysis review

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 this section we review 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*.

Overall, the review is very thorough. The report includes substantial background information on measles immunisation in New Zealand (*Section 1.3*), the epidemiology of measles in New Zealand (*Section 2*), the quality of epidemiological surveillance and laboratory testing for measles (*Section 3*), and the levels of population immunity against the virus (*Section 4*). Additional details are included for many aspects of measles epidemiology and control, not least regarding the recent MMR coverage rates by birth cohort in New Zealand (*Section 4.2*) and the sustainability of the national immunisation programme (*Section 5*).

Within the report there are many tables and figures which give considerable detail on the measles situation in New Zealand. Overall these are of high quality, reporting both absolute measles case numbers and rates per 100,000 population in New Zealand.

Specific epidemiological details are provided for the 2011–2012 outbreak including *Figure 4*, the number and classification of measles notifications in New Zealand by month and year (2011 and 2012), with additional breakdown by age group in both years (*Figure 5*) and per 100,000 population (*Figures 6–8*). Similar presentation of the case data are provided for ethnicity (*Figures 9–10*) and New Zealand Index of Deprivation (NZDep) (*Figures 11–13*). Three figures, *Figures 12, 13,* and *28*, show that there was spatial clustering of cases.

The report concludes that New Zealand's surveillance system has been performing well and that the Ministry is confident that measles has not been circulating since June 2012 and has not become endemic in NZ. We agree with the statement that measles did not become endemic and provide some preliminary analyses on the outbreaks since endemic measles elimination (see section 5) that give information regarding the likelihood of measles persisting within the population and becoming endemic, including analysis of the current outbreak.

We agree with the *Progress Towards Measles Elimination in New Zealand - Final* report conclusions that testing for measles is performed appropriately within the required timeframe. Clearly improving inter-laboratory communication and collaboration and timeliness of the testing and reporting is necessary for rapid responses to measles introductions following measles control. Vaccination coverage presented in the report and to ourselves confirms that immunisation levels are approaching 94% for MMR dose one (birth cohorts 2009 and 2010) and 89% for MMR dose two (birth cohorts 2006 and 2007). However, only Asian and Pacific ethnicities have consistently had MMR dose one coverage approaching or exceeding 95% for cohorts from 2007 onwards, and thus we agree with the report's conclusions that timeliness and coverage of vaccination need improving. This is particularly in light of our modelling and risk analyses results (section 4 and section 5).

Thus in this report we include regression analyses that help understand risk factors for being measles cases in New Zealand (section 4), descriptions of the New Zealand population in terms of vaccination coverage and immunity (subsection 4.2), and we use those data to model the likely measles outbreak sizes

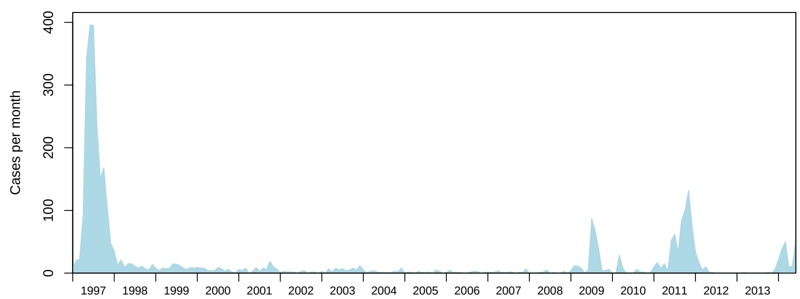

Figure 1: Measles incidence in New Zealand from 1997 to 2014

in each District Health Board (DHB) and the country (section 5). We estimate the costs of previous and the current measles outbreaks (subsection 6.1) and use these estimates, the modelling results and the population data to estimate the benefit–cost ratio for catch-up vaccination programmes (subsection 6.3). This report includes further developments of the analyses provided in previous interim reports.

4 Risk analyses

In this section we provide work that we believe will help inform the Ministry of Health regarding the understanding of risk from measles. These analyses are intended to build on the analyses already included in the *Progress Towards Measles Elimination in New Zealand - Final* report reviewed above.

We include multivariate modelling to account for confounding within the univariate analyses for measles cases in New Zealand (subsection 4.1), descriptive analyses of risk of infection due to previous vaccination history (subsection 4.2), and current rates of immunity within the population (subsection 4.2). In light of the apparent increasing trend in measles incidence in the last few years (Figure 1), we reviewed the information on measles importation and the origins of the introductions of measles into New Zealand. To help understand the risk of measles importation, with a particular goal of enabling the Ministry to better inform travellers and understand high risk periods, we sought to quantitatively evaluate the risk of measles importation from travel (subsection 4.3).

4.1 Risk of measles infection in New Zealand 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 ESR data (not shown) suggested that denominator data were required to perform multivariate analyses to adjust for confounding due to a lack of independence among risk factors. Specifically Age $\times$ Prioritised Ethnicity $\times$ NZDep data for New Zealand were required to adjust for confounding and test whether interactions among covariates provide additional information on risk in demographically–defined subgroups 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 NZDep that might exist among cases allowing better understanding of measles infection risk.

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 of 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, the numerous combinations of variables led us to have 250 categories. Because for measles cases the very young appear to be disproportionately affected (Figure 2), we split the 0–5 age category into two classes, 0–2 and 3–5 years old for each of the University of Otago denominator data, 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]).

This large number of categories, some with small population sizes, leads to both overdispersion and zeroinflation, as there are 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 ten to two: NZDep 1–5 (least deprived) and NZDep 6–10 (most deprived) (www.otago.ac.nz). 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; Asian; Middle Eastern/Latin American/African (MLA); Other Ethnicity; Residual Categories. 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 and population sizes for the complete data set from 2007-2014 can be seen in Table 2. Subsequent regression analyses (not shown) also suggested that the MLA category was over– or underrepre-

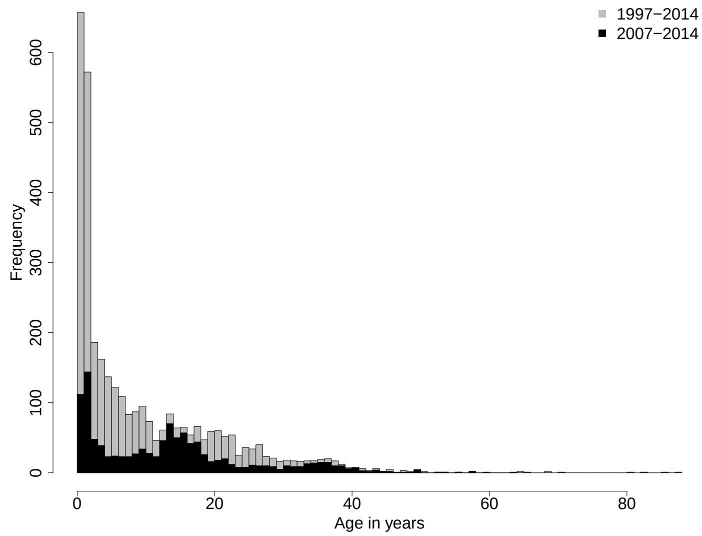

Figure 2: Numbers and age of measles cases in years in New Zealand for two periods, 1997–2014 and 2007–2014

NZDep	Age	Ethnicity	Cases
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

Table 1: Absolute number of measles cases with no ethnicity recorded for specific age and socio-economic deprivation (NZDep) categories from 2007-2014.

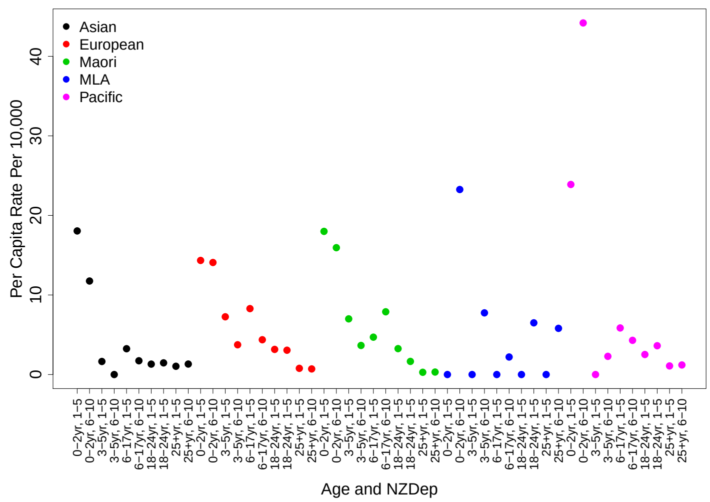

Figure 3: Per capita rates of measles infections for specific age categories (0–2, 3–5, 6–17, 18–24, and 24+ years) and New Zealand deprivation indices (NZDep, 1–5 and 6–10) for 2007–2014, broken down by ethnicity (Table 2 for details)

sented in per capita rates given the very small sample sizes for this classification (Figure 3, Table 2), leading to very large standard error in regression analyses. However, there are numerous issues with the data for MLA ethnicity category above and beyond the small population sizes (see Table 2), thus creating issues for estimating the denominator data 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 (Table 2).

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 then 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:

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

Table 2: Numbers of measles cases (Cases), population sizes (Ppulation) and per capita rates per 10,000 (Per capita) of measles in specific age (Age), ethnicity (Ethnicity) and socio-economic deprivation (NZDep) categories from 2007-2014

NZDep	Age	Ethnicity	Population	Cases 1	Per capita
1-5	0-2	Asian	6094	11	18.0505
6-10	0-2	Asian	6806	8	11.7543
1-5	3-5	Asian	6094	1	1.6410
6-10	3-5	Asian	6806	0	0.0000
1-5	6-17	Asian	33918	11	3.2431
6-10	6-17	Asian	28905	5	1.7298
1-5	18-24	Asian	22917	3	1.3091
6-10	18-24	Asian	34107	5	1.4660
1-5	25+	Asian	96357	10	1.0378
6-10	25+	Asian	98715	13	1.3169
1-5	0-2	European	57872	83	14.3420
6-10	0-2	European	45445	64	14.0830
1-5	3-5	European	57872	42	7.2574
6-10	3-5	European	45445	17	3.7408
1-5	6-17	European	264330	219	8.2851
6-10	6-17	European	182937	80	4.3731
1-5	18-24	European	107649	34	3.1584
6-10	18-24	European	117840	36	3.0550
1-5	25+	European	1001916	78	0.7785
6-10	25+	European	724317	51	0.7041
1-5	0-2	Maori	10003	18	17.9946
6-10	0-2	Maori	30104	48	15.9447
1-5	3-5	Maori	10003	7	6.9979
6-10	3-5	Maori	30104	11	3.6540
1-5	6-17	Maori	40461	19	4.6959
6-10	6-17	Maori	116640	92	7.8875
1-5	18-24	Maori	15360	5	3.2552
6-10	18-24	Maori	48495	8	1.6497
1-5	25+	Maori	71217	2	0.2808
6-10	25+	Maori	192729	6	0.3113
1-5	0-2	MLA	728	0	0.0000
6-10	0-2	MLA	1290	3	23.2558
1-5	3-5	MLA	728	0	0.0000
6-10	3-5	MLA	1290	1	7.7519
1-5	6-17	MLA	2991	0	0.0000
6-10	6-17	MLA	4539	1	2.2031
1-5	18-24	MLA	1710	0	0.0000
6-10	18-24	MLA	3078	2	6.4977
1-5	25+	MLA	8028	0	0.0000
6-10	25+	MLA	10335	6	5.8055
1-5	0-2	Pacific	2093	5	23.8892
6-10	0-2	Pacific	13124	58	44.1938
1-5	3-5	Pacific	2093	0	0.0000
6-10	3-5	Pacific	13124	3	2.2859
1-5	6-17	Pacific	8541	5	5.8541
6-10	6-17	Pacific	51183	22	4.2983
1-5	18-24	Pacific	3972	1	2.5176
6-10	18-24	Pacific	22098	8	3.6202
1-5	25+	Pacific	18492	2	1.0815
6-10	25+	Pacific	91533	11	1.2018

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

4.2 Vaccination history of measles infection and population immunity estimation methods

In this section we describe the vaccination history of the measles cases from 2007–2014 outbreaks using the data provided by ESR. We describe the population immunity levels at both a national level and for each DHB in New Zealand. To do this we use the census data from NZ statistics (Statistics New Zealand, 2013) and the vaccination and serosurvey data provided by the Ministry of Health at the commencement of this work. Specifically, we use the data in Table Table 3, derived from the serosurvey results and the National Immunisation Register (NIR) for under 6 year olds.

Age	Proportion immune
0	0
1	0.89
2	0.92
3	0.93
4	0.93
5	0.92
6-13	0.8
14-18	0.83
19-23	0.77
24-32	0.85
33-52	0.92
>52	0.99

Table 3: Vaccination coverage (0–5 years) and serosurvey estimates of immunity ($>$ 5 years) among different age classes used in these analyses

4.3 Measles importation risk methods

For our measles importation risk analyses, we use arrivals data from New Zealand immigration and New Zealander travel destination data by country and year (www.immigration.govt.nz), to measure human movement to and from New Zealand. We collated country population size, measles incidence and measles vaccination cover from the WHO (www.who.int/research/en/). Note the immigration figures use all immigration of foreign nationals, coming for whatever purpose, and includes non-New Zealanders resident in New Zealand, but not yet holders of New Zealand passports. We use the WHO data to determine per capita measles cases for each year and use these data and the number of immigrants to New Zealand to begin to understand where measles is likely to

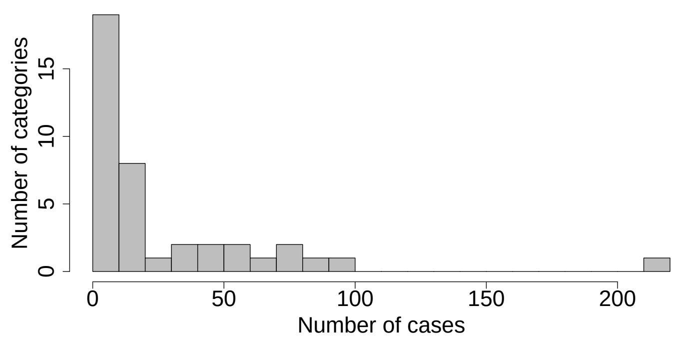

Figure 4: Distribution of measles cases per category (Table 2) used in the final regression model (Equation 1)

	Df	Deviance	Resid. Df	Resid. Dev	F	Pr(>F)
NULL			39	1453.62		
Age	4	1304.20	35	149.43	183.58	0.0000
Ethnicity	3	20.00	32	129.43	3.75	0.0285
NZDep	1	10.70	31	118.74	6.02	0.0239
Age:Ethnicity	12	81.91	19	36.83	3.84	0.0045

Table 4: Significance of different predictor variables for measles risk factors from 2007-2014, estimated using Equation 1 and a quasipoisson error structure

be imported from. We use simple per capita rates for measles and the number of travellers to each country to score and map the risk of mealses importation. We present the data from 2012 because this year had the most complete WHO measles data and yet is most recent, thus accounts for improved measles vaccination coverage following the United Nations Millenium Development Goals' improvements in measles vaccination coverage.

4.4 Regression analyses results

The distribution of the meases cases per category used in the regression analyses are in Figure 4.

The predicted values from the regression model plotted against the reported cases are shown in Figure 5, and the residuals are shown in Figure 6.

The significance of the different predictor variables can be seen in the ANOVA results (Table 4).

A summary of the regression model (Equation 1) with the individual effects

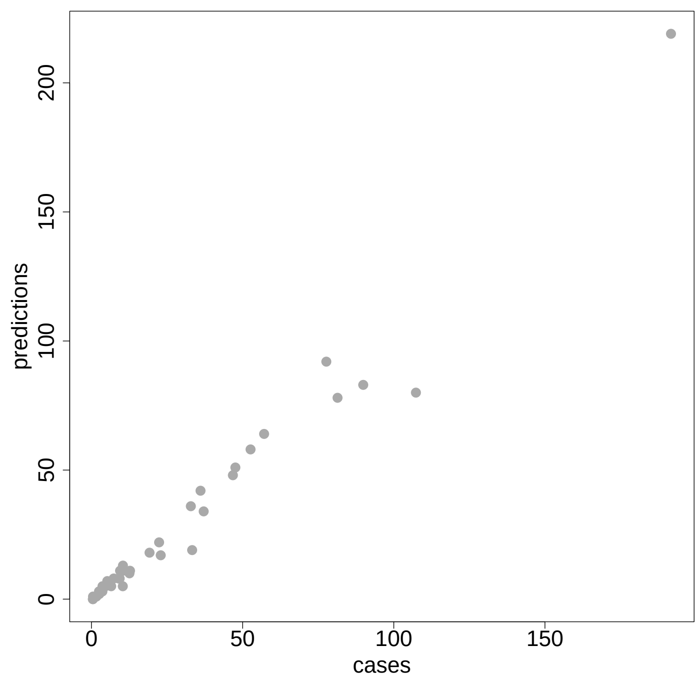

Figure 5: Regression model (Equation 1) predictions plotted against the case data (Table 2)

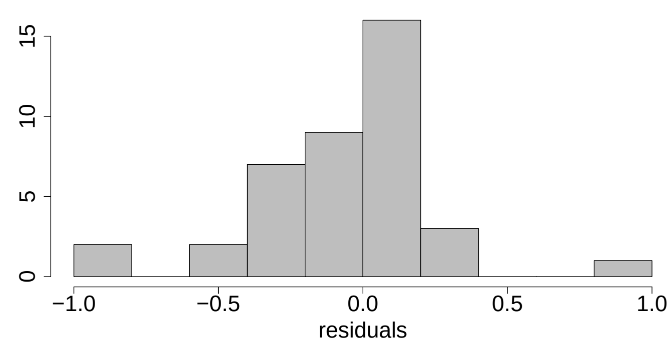

Figure 6: Histogram of residuals from the regression model (Equation 1)

	Estimate	Std. Error	t value	Pr(>|t|)
(Intercept)	-6.4674	0.1148	-56.32	0.0000
Age3-5	-0.9129	0.2054	-4.44	0.0003
Age6-17	-0.7618	0.1343	-5.67	0.0000
Age18-24	-1.5050	0.1937	-7.77	0.0000
Age25+	-2.9507	0.1608	-18.35	0.0000
EthnicityAsian	0.0530	0.3250	0.16	0.8721
EthnicityMaori	0.2124	0.1994	1.07	0.2999
EthnicityPacific	1.1603	0.2043	5.68	0.0000
NZDep6-10	-0.2119	0.0855	-2.48	0.0227
Age3-5:EthnicityAsian	-2.0315	1.3827	-1.47	0.1581
Age6-17:EthnicityAsian	-1.0074	0.4717	-2.14	0.0459
Age18-24:EthnicityAsian	-0.8311	0.5941	-1.40	0.1779
Age25+:EthnicityAsian	0.4211	0.4433	0.95	0.3541
Age3-5:EthnicityMaori	-0.3864	0.4096	-0.94	0.3573
Age6-17:EthnicityMaori	-0.0855	0.2469	-0.35	0.7328
Age18-24:EthnicityMaori	-0.5828	0.4484	-1.30	0.2092
Age25+:EthnicityMaori	-1.0482	0.5242	-2.00	0.0600
Age3-5:EthnicityPacific	-2.1316	0.8139	-2.62	0.0169
Age6-17:EthnicityPacific	-1.4541	0.3347	-4.35	0.0003
Age18-24:EthnicityPacific	-0.9827	0.5129	-1.92	0.0705
Age25+:EthnicityPacific	-0.6127	0.4367	-1.40	0.1767

Table 5: Summary of the regression model results for measles risk factors for cases from 2007-2014

and the statistical support for the estimated coefficients can be seen in Table 5.

Apart from over-representation of some MLA categories discussed above and not included here, the results of the regression model suggest that 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 generally decreases with age (see also Figure 2).

The majority of measles cases are among people of European ancestry (Table 2 and Figure 2), however, people of Pacific origin are also over-represented as measles cases on a per capita basis (β = 1.16, standard error (SE) = 0.2, p–value < 0.0001). Those people in NZDep levels 6-10 are 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 measles outbreaks (since 2007) there has been a shift in the distribution of ages infected. The very young (<2 years old) are still most likely to be infected, but school aged children and older teenagers are more likely to be represented then the under tens (Figure 2 and Figure 7, Table 3, and subsection 4.6). This pattern

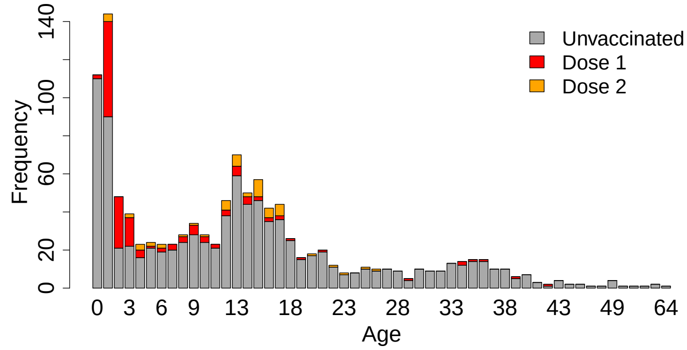

Figure 7: Age and vaccination status of measles cases, 2007–2014

suggests that improving vaccination coverage in the young is reducing the burden of measles in those age categories (Table 2). Interestingly the regression results suggest risk of measles in the 6–17 year age category was greater for Europeans and Maori.

4.5 Vaccination history and measles infection results

The majority of the measles cases (82.8%, 955/1154) from 2007–2014 were in unvaccinated people (Figure 7). However, 12.6% (154/1154) cases had received their first dose of vaccine and 4.7% had received their second. A further breakdown of those data suggest that majority of those 'vaccine failures' were vaccinated around the first year of age (Figure 8).

4.6 Population immunity results

The majority of the naïve among the general New Zealand population are in their first years of life (Figure 9). However, the distribution of naïve at a national level shows that the recent MMR vaccination schemes are reducing the proportions of naïve population in the 3–5 year old age group to greater levels than in older young people (Figure 9). Plotting the breakdown of these figures by DHB clearly shows that the greatest numbers of naïve people are in DHBs with larger urban areas (Figure 10). The distribution of the numbers of naïve and the total naïve populations per DHB, assuming national immunisation and immunity rates are representative, are given in the following figures:

- Northland: Figure 11
- Waitemata: Figure 12
- Auckland: Figure 13
- Counties Manukau: Figure 14
- Waikato: Figure 15

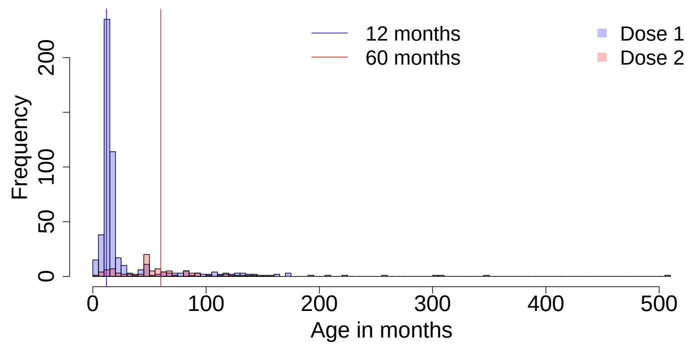

Figure 8: Age of vaccination of vaccinated measles cases, 2007–2014

- Lakes: Figure 16
- Bay of Plenty: Figure 17
- Tairawhiti: Figure 18
- Taranaki: Figure 19
- Hawke's Bay: Figure 20
- Whanganui: Figure 21
- Mid-Central: Figure 22
- Hutt: Figure 23
- Capital and Coast: Figure 24
- Wairarapa: Figure 25
- Nelson Marlborough: Figure 26
- West Coast: Figure 27
- Canterbury: Figure 28
- South Canterbury: Figure 29
- Southern: Figure 30

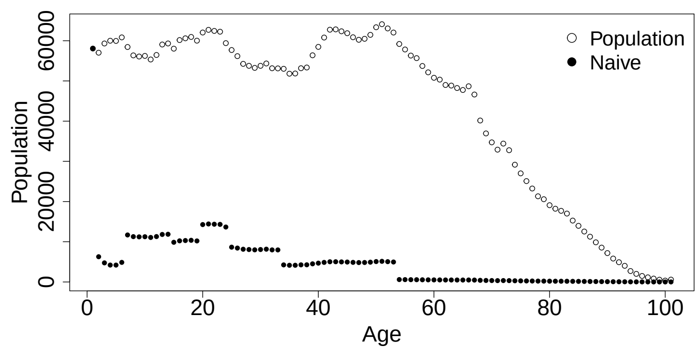

Figure 9: New Zealand population by age and estimated numbers of naïve people in each age class using national immunity data (Table 3)

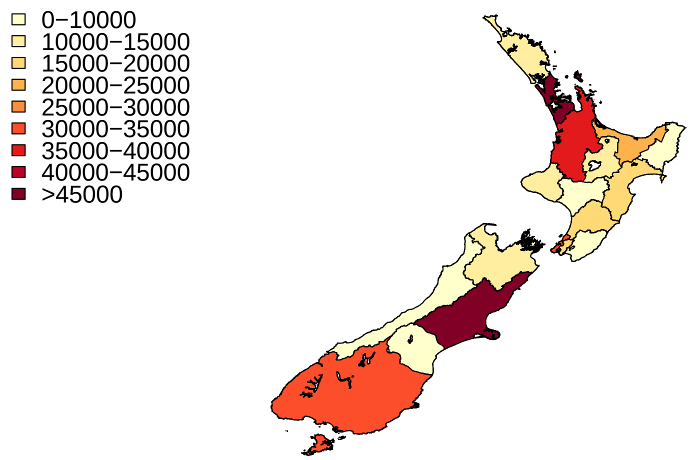

Figure 10: Numbers of naïve individuals per District Health Board, using national immunity data (Table 3)

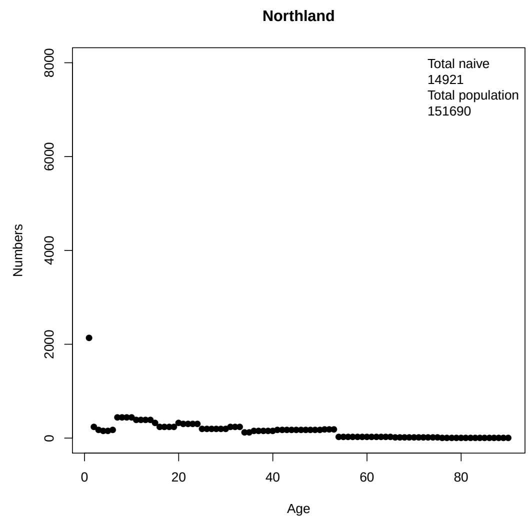

Figure 11: Numbers of naïve individuals per age class, Northland District Health Board, using national immunity data (Table 3)

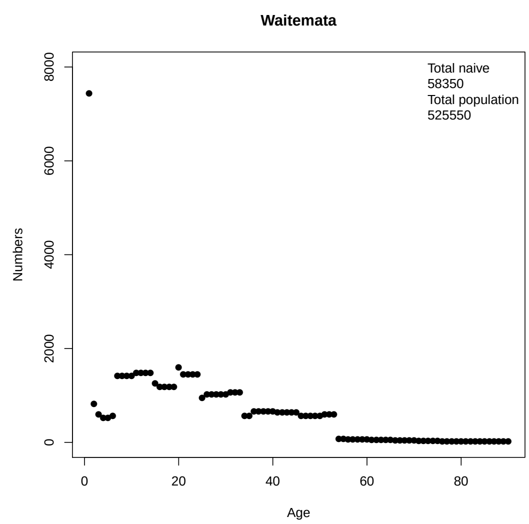

Figure 12: Numbers of naïve individuals per age class, Waitemata District Health Board, using national immunity data (Table 3)

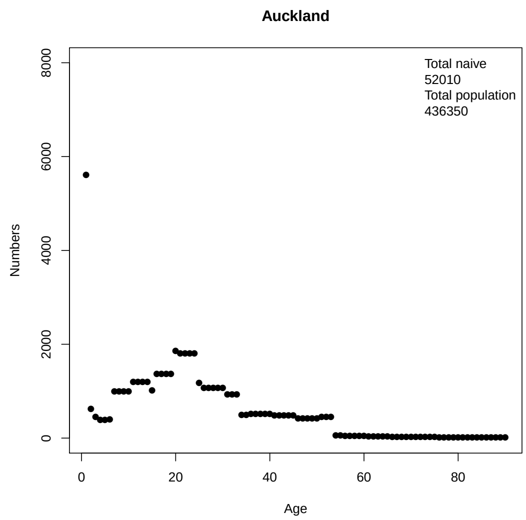

Figure 13: Numbers of naïve individuals per age class, Auckland District Health Board, using national immunity data (Table 3)

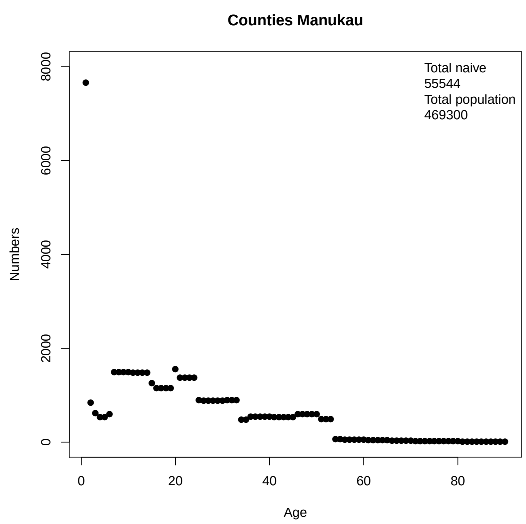

Figure 14: Numbers of naïve individuals per age class, Counties Manukau District Health Board, using national immunity data (Table 3)

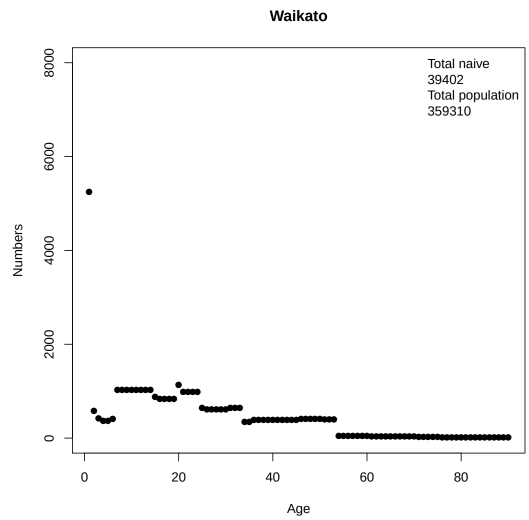

Figure 15: Numbers of naïve individuals per age class, Waikato District Health Board, using national immunity data (Table 3)

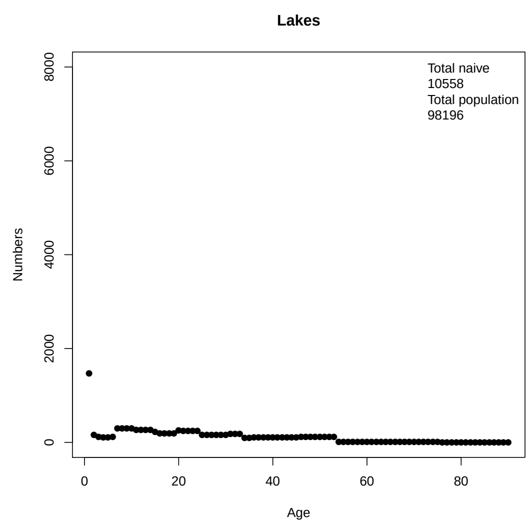

Figure 16: Numbers of naïve individuals per age class, Lakes District Health Board, using national immunity data (Table 3)

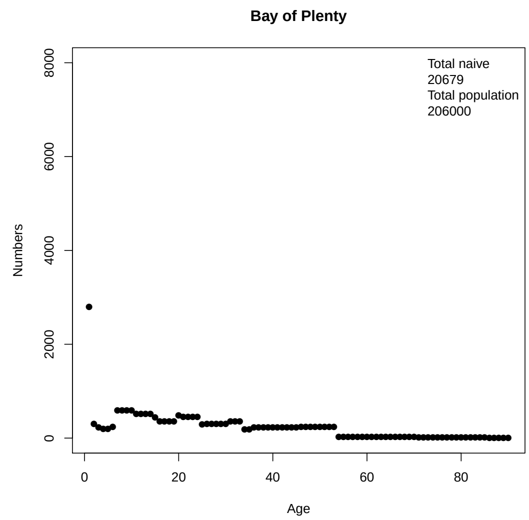

Figure 17: Numbers of naïve individuals per age class, Bay of Plenty District Health Board, using national immunity data (Table 3)

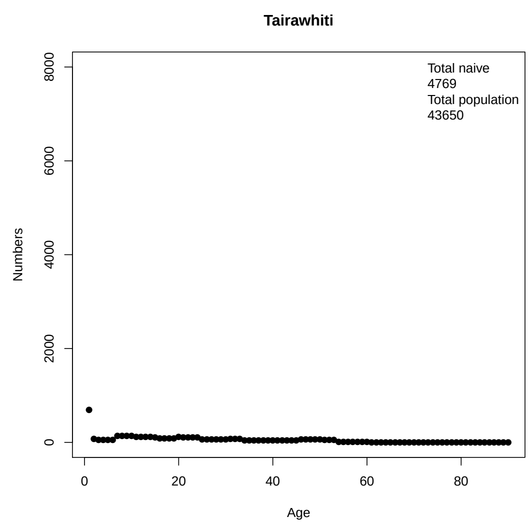

Figure 18: Numbers of naïve individuals per age class, Tairawhiti District Health Board, using national immunity data (Table 3)

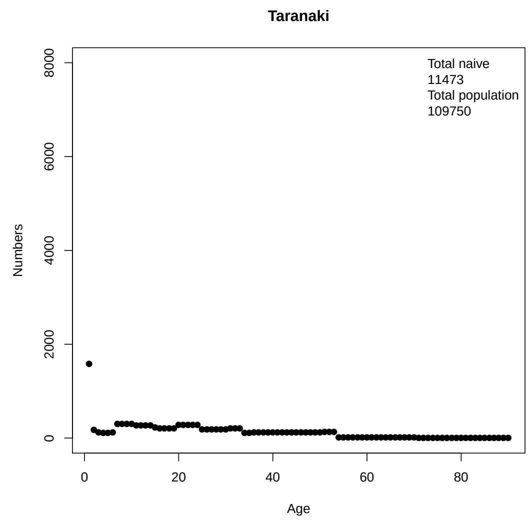

Figure 19: Numbers of naïve individuals per age class, Taranaki District Health Board, using national immunity data (Table 3)

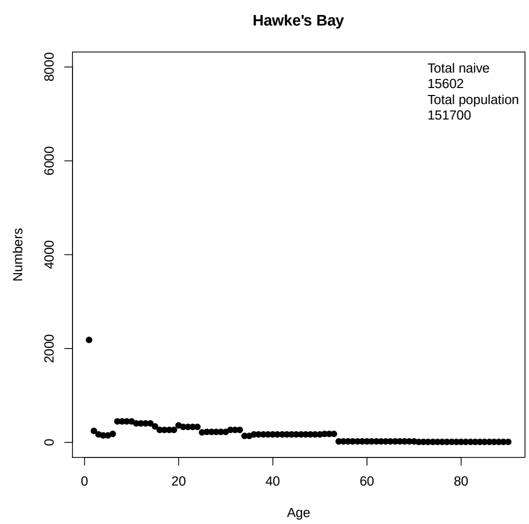

Figure 20: Numbers of naïve individuals per age class, Hawke's Bay District Health Board, using national immunity data (Table 3)

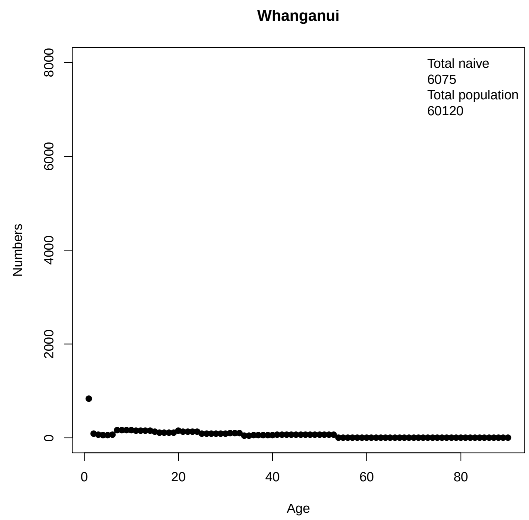

Figure 21: Numbers of naïve individuals per age class, Whanganui District Health Board, using national immunity data (Table 3)

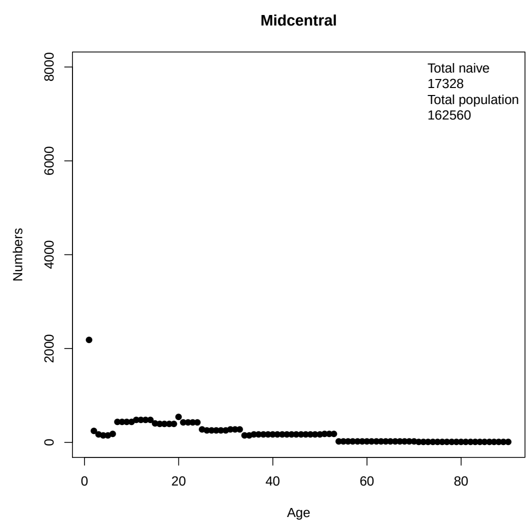

Figure 22: Numbers of naïve individuals per age class, Midcentral District Health Board, using national immunity data (Table 3)

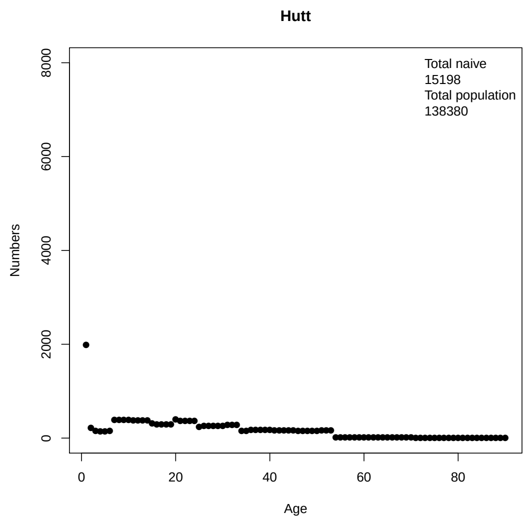

Figure 23: Numbers of naïve individuals per age class, Hutt District Health Board, using national immunity data (Table 3)

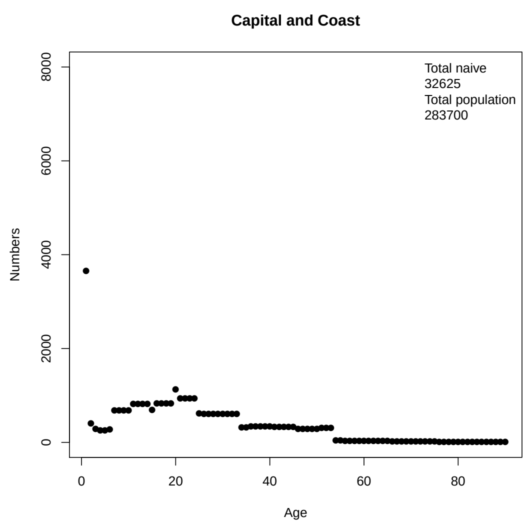

Figure 24: Numbers of naïve individuals per age class, Capital and Coast District Health Board, using national immunity data (Table 3)

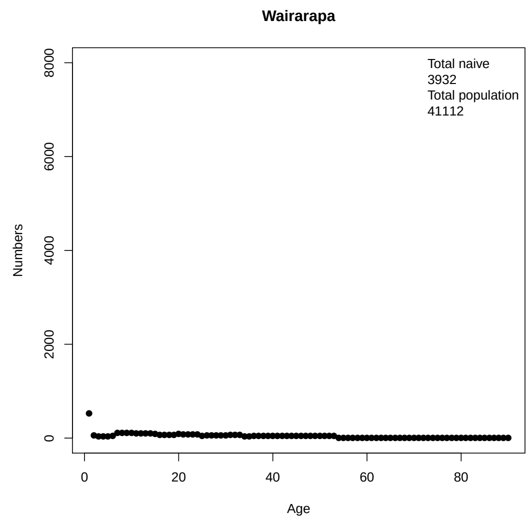

Figure 25: Numbers of naïve individuals per age class, Wairarapa District Health Board, using national immunity data (Table 3)

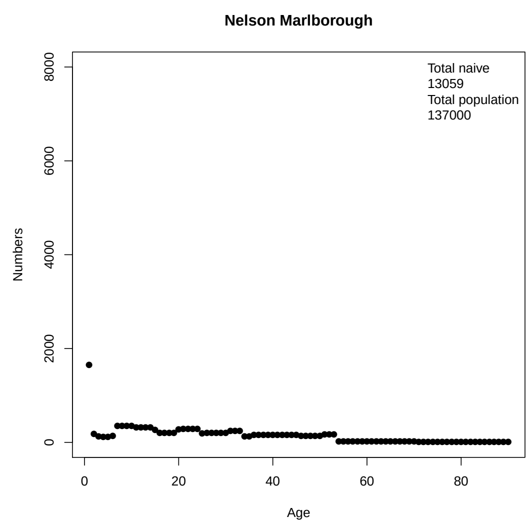

Figure 26: Numbers of naïve individuals per age class, Nelson Marlborough District Health Board, using national immunity data (Table 3)

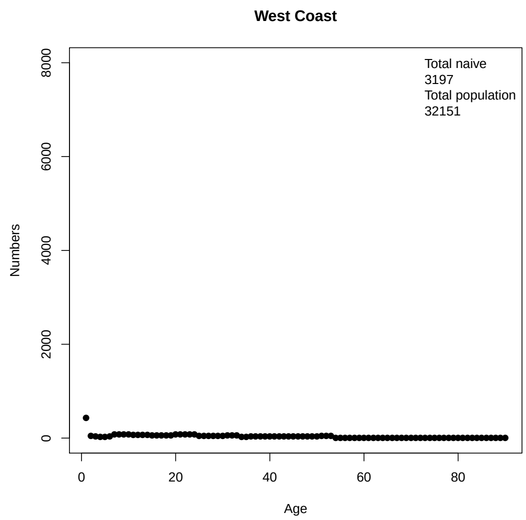

Figure 27: Numbers of naïve individuals per age class, West Coast District Health Board, using national immunity data (Table 3)

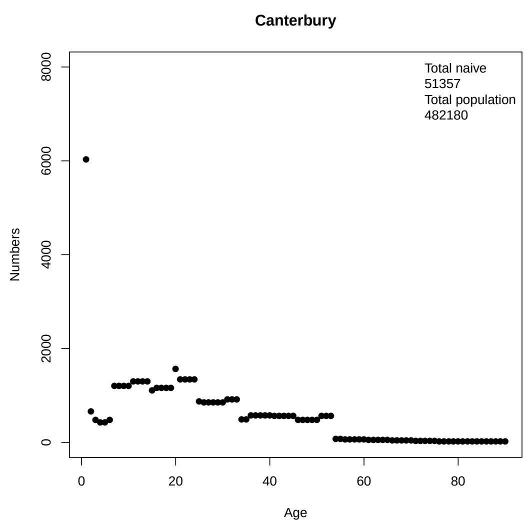

Figure 28: Numbers of naïve individuals per age class, Canterbury District Health Board, using national immunity data (Table 3)

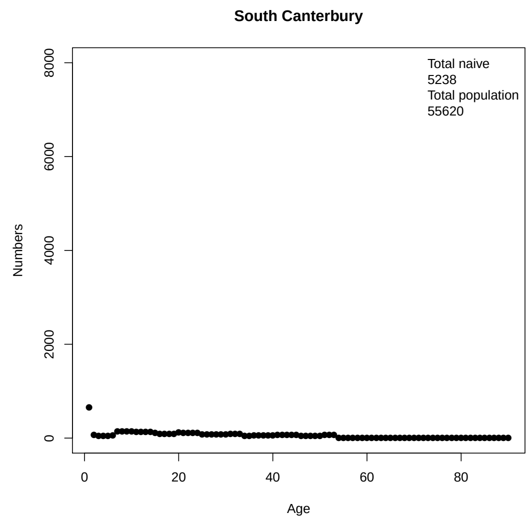

Figure 29: Numbers of naïve individuals per age class, South Canterbury District Health Board, using national immunity data (Table 3)

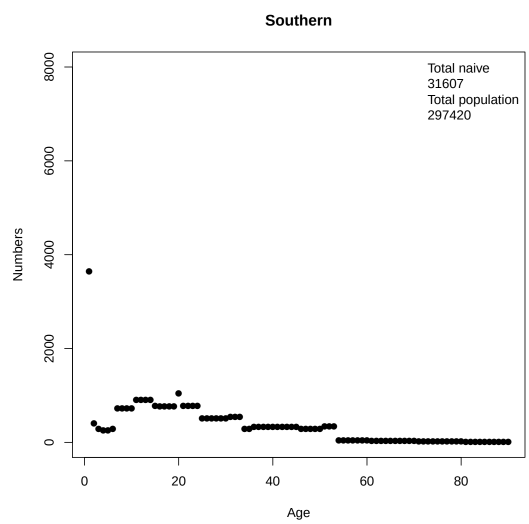

Figure 30: Numbers of naïve individuals per age class, Southern District Health Board, using national immunity data (Table 3)

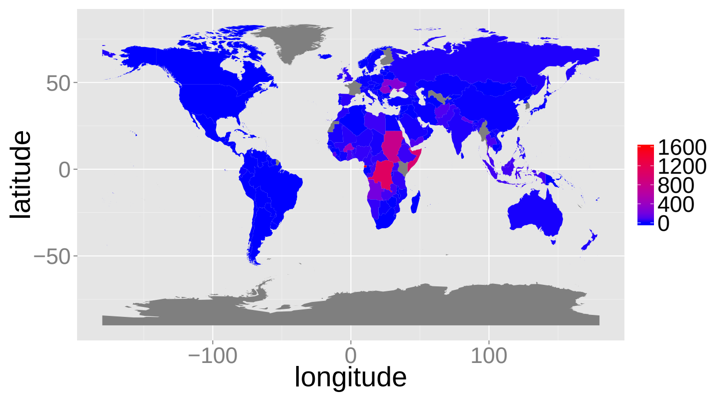

Figure 31: Measles incidence per million, 2012. Data: WHO (www.who.int/research/en/). Grey indicates not reported.

4.7 Measles importation risk results

Globally, analyses of the most complete and recent year of data available, 2012, suggest measles incidence highest and vaccination coverage is lowest in less developed nations (Table 6 and Table 7, and Figure 31 and Figure 32). Immigration by non-New Zealanders (whether for work, pleasure, etc.) is dominated by people from Australia, United Kingdom, China, and the United States, as shown in Table Table 8 and Figure 33. However, travel by New Zealanders is dominated by that to Australia (Table 9 and Figure 34). Together, these mean that the greatest travel location for New Zealanders and immigration origin is from Australia (Table 10 and Figure 33. Though the precise interactions between these different risk factors are unknown, the most simple, a product of measles incidence in 2012 and immigration numbers in 2012, suggest that those countries with greatest international travel, Australia and New Zealand, pose the greatest risk to New Zealand for measles importation. Though immigration from and travel to some Asian countries is lower, some Asian countries also poses a high risk of measles importation to New Zealand. These data are shown in Table 11. The breakdown of risk of measles importation by New Zealander and non-New Zealander travellers is in Table 12 and Table 13 and Figure 37 and Figure 38.

The measles incidence and vaccination coverage for those countries identified as posing the greatest risk for measles importation to New Zealand are in Table 14.

Table 6: Highest measles incidence per million (2012)

country	incidence
Equatorial Guinea	1617
Nauru	1100
Democratic Republic of the Congo	1096
Somalia	979
Djibouti	824
Sudan	786
Burkina Faso	447
Romania	342
Ukraine	280
Sudan	229
Angola	214
Monaco	132
Nepal	122
Sierra Leone	113
Afghanistan	93
Yemen	91
Lesotho	87
Qatar	78
Thailand	78
Malaysia	64
Zambia	64
Ghana	64
Indonesia	63
Congo	60
Uganda	56
Libyan Arab Jamahiriya	52
Ethiopia	47
Pakistan	45
Myanmar	41
Nigeria	38

Table 7: Lowest national measles vaccine cover (%), 2012

country	cover
Equatorial Guinea	34
Somalia	49
Lesotho	60
Central African Republic	65
Papua New Guinea	67
Chad	69
Haiti	69
South Sudan	70
Gabon	71
Yemen	71
Benin	72
Lao People's Democratic Republic	72
Togo	72
Suriname	73
Timor-Leste	73
Paraguay	74
Mauritania	75
Namibia	76
Eritrea	77
Marshall Islands	78
Nigeria	78
Syrian Arab Republic	78
Ukraine	79
Congo	80
Ethiopia	80
Liberia	80
Afghanistan	81
Cameroon	82
Mozambique	82
Senegal	82

Table 8: Non-New Zealander travel and immigration numbers (2012)

country	immigration
Australia	809775
United Kingdom	306177
China	256036
United States	194438
Japan	86676
Germany	83608
Korea, Republic of	73459
France	71448
India	69038
Canada	54981
Malaysia	50506
Fiji	46723
Netherlands	33431
South Africa	30600
Tonga	26717
Singapore	25460
Ireland	25036
Samoa	24547
Philippines	24527
Taiwan	23815
Thailand	20258
Hong Kong	19103
Indonesia	15692
Switzerland	14851
Brazil	14778
Sweden	13719
Italy	13388
Spain	10104
Denmark	10056
Russia	8103

Table 9: New Zealander travel numbers by destination (2012)

country	immigration
Australia	989880
United States	121620
Fiji	104720
United Kingdom	95560
Cook Islands	71960
China	66040
Samoa	46020
Thailand	41100
India	38580
Canada	20400
Japan	20040
Malaysia	19860
Indonesia	19660
Hong Kong	18220
Tonga	17760
Singapore	17120
South Africa	15380
Philippines	15220
France	14500
Korea, Republic of	13960
Viet Nam	12920
Germany	12700
Vanuatu	12520
Italy	11820
Taiwan	10460
New Caledonia	7340
Ireland	6360
French Polynesia	6360
Papua New Guinea	6140
Netherlands	5720

Table 10: Total New Zealand traveller numbers by country (New Zealand nationals and immigrants, 2012)

country	immigration
Australia	1799655
United Kingdom	401737
China	322076
United States	316058
Fiji	151443
India	107618
Japan	106716
Germany	96308
Korea, Republic of	87419
France	85948
Canada	75381
Samoa	70567
Malaysia	70366
Thailand	61358
South Africa	45980
Tonga	44477
Singapore	42580
Philippines	39747
Netherlands	39151
Hong Kong	37323
Indonesia	35352
Taiwan	34275
Ireland	31396
Italy	25208
Viet Nam	18574
Switzerland	18431
Brazil	17878
Vanuatu	16261
Spain	15604
Sweden	15479

Table 11: Risk of measles importation to New Zealand in 2012, all travellers, estimated by traveller numbers multiplied by measles incidence in the source or destination location, see also Table 12 and Table 13

country	risk
Australia	15537152
United Kingdom	13386328
Thailand	4774688
Malaysia	4495338
Indonesia	2216871
India	1620172
China	1432659
Ukraine	765096
Ireland	734128
Romania	655107
Philippines	631303
Spain	401823
Samoa	373370
Singapore	337236
Nepal	324526
Germany	193081
Japan	191585
Israel	174177
Italy	155674
Russia	155632
Pakistan	148514
Sudan	141552
Switzerland	140589
Nauru	126500
Viet Nam	118241
Afghanistan	111854
Somalia	104775
Saudi Arabia	82584
United Arab Emirates	67606
Belgium	63784

Table 12: Risk of measles importation to New Zealand due to New Zealander travel in 2012, estimated by traveller numbers multiplied by measles incidence in the source or destination location, see also Table 13 and Table 11

country	risk
Australia	8546036
Thailand	3198274
United Kingdom	3184166
Malaysia	1268758
Indonesia	1232849
India	580816
China	293759
Samoa	243492
Philippines	241740
Nepal	188450
Romania	164376
Ireland	148715
Spain	141632
Singapore	135591
Ukraine	100781
Viet Nam	82248
Sudan	78640
Afghanistan	74756
Italy	72995
United Arab Emirates	60508
Pakistan	58435
Nauru	44000
Democratic Republic of the Congo	43850
Qatar	43686
Israel	40301
Japan	35977
Russia	35334
Angola	34258
Switzerland	27308
Saudi Arabia	25775

Table 13: Risk of measles importation to New Zealand due to non-New Zealander travel and immigration in 2012, estimated by traveller numbers multiplied by measles incidence in the source or destination location, see also Table 12 and Table 11

country	risk
United Kingdom	10202161
Australia	6991116
Malaysia	3226580
Thailand	1576414
China	1138900
India	1039356
Indonesia	984022
Ukraine	664315
Ireland	585413
Romania	490731
Philippines	389563
Spain	260191
Singapore	201644
Germany	167620
Japan	155607
Nepal	136076
Israel	133876
Samoa	129878
Russia	120298
Switzerland	113281
Pakistan	90079
Somalia	85191
Italy	82679
Nauru	82500
Sudan	62912
Saudi Arabia	56809
Belgium	53337
Sweden	43273
Afghanistan	37098
Viet Nam	35993

Table 14: Measles and travel data from 2012 for the top 10 countries identified as high risk for measles importation. incidence: measles incidence per million; cover: percent vaccination cover (%); immigration: the number of travellers entering New Zealand from the country

country	incidence	cover	immigration
Australia	9	94	1799655
United Kingdom	33	93	401737
Thailand	78	98	61358
Malaysia	64	95	70366
Indonesia	63	84	35352
India	15	85	107618
China	4	99	322076
Ukraine	280	79	2733
Ireland	23	92	31396
Romania	342	94	1913

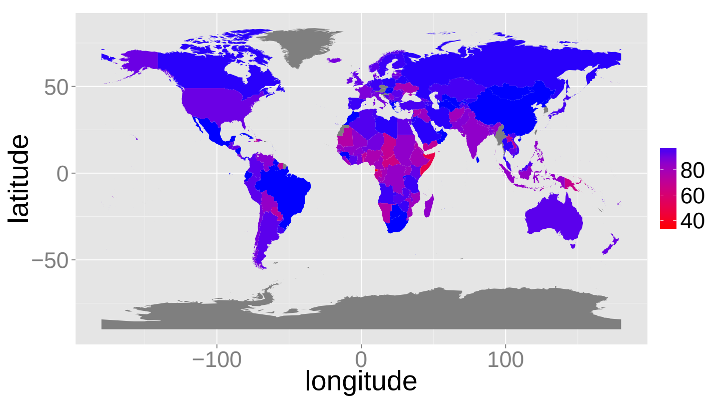

Figure 32: Measles vaccination cover (%), 2012. Data: WHO (www.who.int/research/en/). Grey indicates not reported.

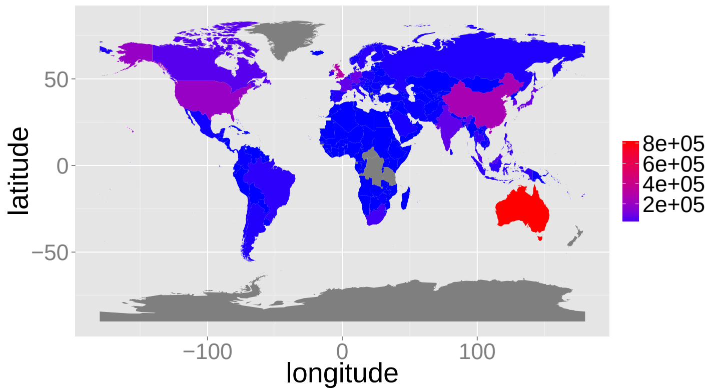

Figure 33: Non-New Zealander international travel and immigration, 2012

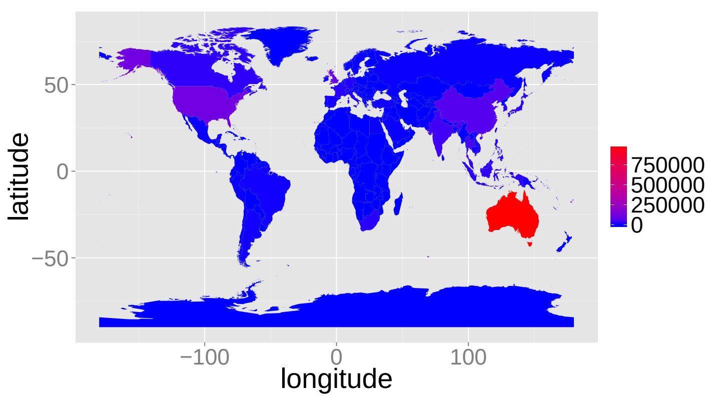

Figure 34: New Zealander international travel, 2012

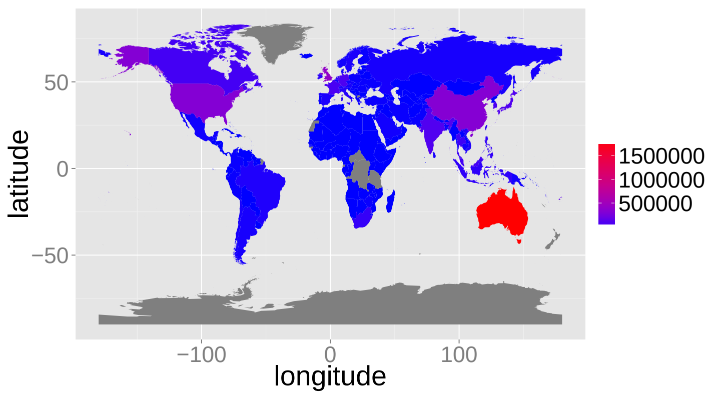

Figure 35: Total international travel, 2012

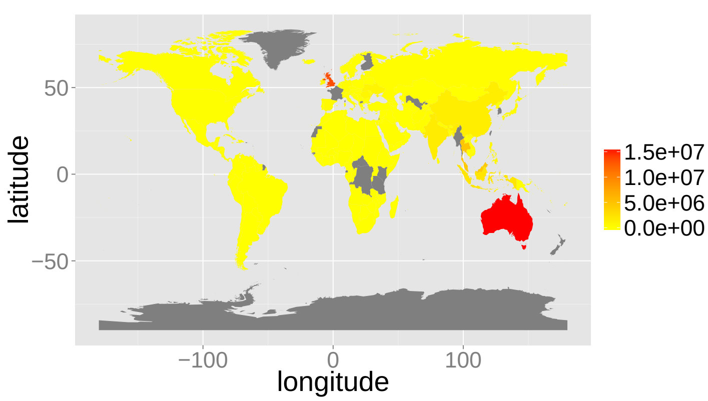

Figure 36: Risk map for measles importation, 2012

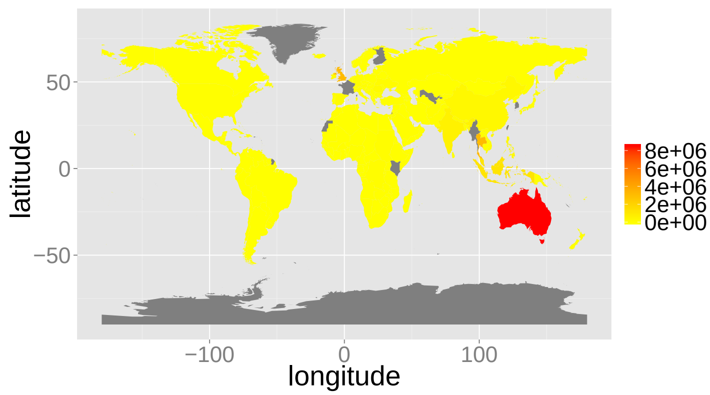

Figure 37: Risk map for measles importation from New Zealander international travel, 2012

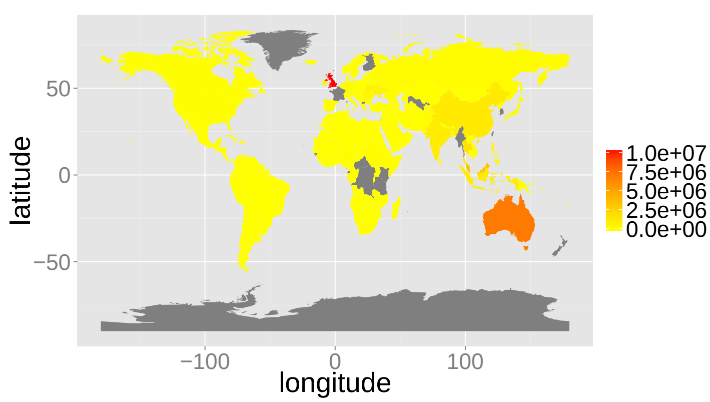

Figure 38: Risk map for measles importation from non-New Zealander international travel and immigration, 2012

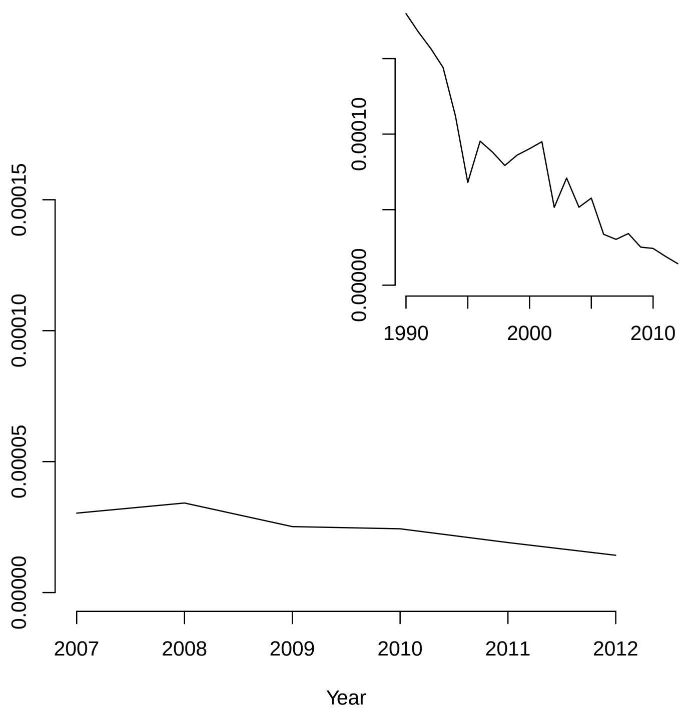

Figure 39: Trend in global per capita measles incidence

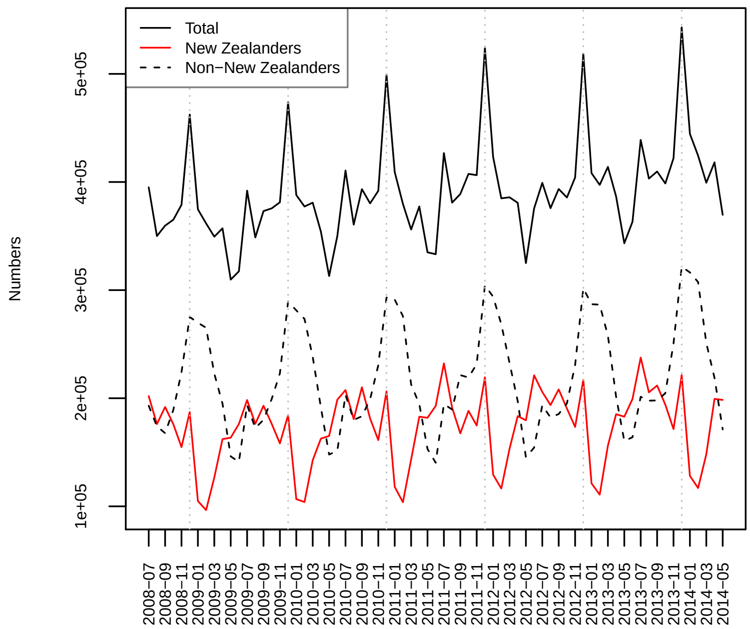

Figure 40: Trends in international travel, determined by immigration arrival data and New Zealander travel departure destinations

Though the global incidence of measles is declining, in recent years that decline has slowed (Figure 39) and immigration rates to New Zealand have risen (Figure 40). This suggests that the risk of measles importation could increase, though further analyses are require to understand the interaction between these variables. Of note, however, is the clear seasonality in immigration and travel (Figure 40). This seasonality suggests that there may be period of increased risk of measles importation, though again the interactions with seasonal measles transmission from the nations of origin will be an important factor in determining the risk of measles importation. Of interest is the asynchrony, or lack of phase, between peak non-New Zealander immigration and New Zealanders travelling. The Christmas summer period being an exception to this, when there is substantial New Zealander travel and combined these lead to a very sharp peak in travel rates in December (Figure 40).

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 greater risk of measles. In particular, Pacific people are at greater risk per capita, as are the less deprived (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 NIR. A key issue with incorporating the spatial immunisation data has been the denominator data and the NIR data. The data suggest that census data and NIR data are recording children living in different DHBs to that in which they are vaccinated, or subsequent to the census or NIR data moving. This leads to some area census units having more than 100% children vaccinated, with some many times more, and some with very low levels reportedly vaccinated. Another issue was how to deal with people of greater age than those recorded in the NIR. Thus, these analyses are possible future directions for this work and a focus of future data collection could be to better understand the link between denominator data and NIR data.

The distribution of the measles cases (Figure 7) appears to reflect the distribution of naïve individuals in the population (Figure 9). The vaccination history of the cases suggests that lack of vaccination cover is the main contributor to the outbreak, though it is noticable that a number ($> 16\%$) of cases had been vaccinated at least once. However, the majority of these received only one vaccination, and were vaccinated when they were young (Figure 8). The majority of naïve among the New Zealand population is clearly focused in the DHB with large urban areas (Figure 10).

Unfortunately, additional data we received from the Ministry that we hoped would allow us to provide finer scale results (lower than DHB) immunisation coverage data are not able to provide reliable results, as discussed above. Frequently the numbers of vaccinated children in a census area provided in the NIR was greater than the number reported in the census area unit population census. Given these data gaps we are unable to provide finer scale risk maps.

The distribution of naïve among the DHBs also varies (subsection 4.6, Figure 11, Figure 12, Figure 13, Figure 14, Figure 15, Figure 16, Figure 17, Figure 18, Figure 19, Figure 20, Figure 21, Figure 22, Figure 23, Figure 24, Figure 25, Figure 26, Figure 27, Figure 28, Figure 29, Figure 30). We hope that the Ministry will find these informative, as they indicate which age classes may be the focus of vaccination efforts for each DHB. However, it is worth bearing in mind that the data here assume that the national NIR vaccination coverage and serosurvey results are appropriate for all DHB.

Further analyses are required to see if the seasonal patterns in travel match seasonality in measles incidence in the countries from which most individuals come from when travelling to, or back to, New Zealand. However, the strong seasonality in travel around the summer vacation in December suggests this may be a time where extra effort and vigilence is required for measles vaccination and control efforts. The area identified as greatest risk for measles importation, Australia, simply reflects the enormous amount of travel between Australia and New Zealand (Table 10 and Figure 33). However, recently Australia was declared free of endemic measles and so the 2012 data must reflect imported measles there. However, other areas of high risk include the United Kingdom, where measles persists, and South, Southeast and East Asia, where measles is endemic (Table 11 and Figure 36).

4.8 Risk analysis summary

- Risk of measles infection decreases significantly with age.
- European ethnicity comprise the largest number of measles cases.
- Pacific people are statistically more at risk per capita of measles infection.
- 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 per capita than European or Maori children.
- The majority of cases are unvaccinated.
- The majority of vaccine failures occur in those people which recieved single vaccinations around 1 year old.
- Distribution of numbers of naïve among New Zealand is uneven, with the majority predictably in DHBs with larger urban areas.
- There is a continued, and perhaps increasing, risk of measles importation due to travel and endemic measles elsewhere in the world.
- There may be seasonal changes in risk of measles importation, with travel numbers peaking in December.

5 Modelling measles epidemics

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.

The original mathematical model for the dynamics of measles in New Zealand prepared in 1996 [33] successfully predicted the 1997 epidemic, which was curtailed by a mass vaccination campaign [22, 28]. Subsequent extension of this work in 1998 showed that the then current schedule of MMR1 at 15 months and MMR2 at 11 years was insufficient to prevent further epidemics [28]. The model supported the change in the immunisation schedule that took effect in January 2001, at which time MMR2 was changed from delivery at 11 years to delivery before the age of five. The schedule was changed in 2000 with MMR2 now being administered before 5 years [3]. Later analyses suggested high levels of vaccination coverage (but less than 95%) could eliminate measles, but emphasised that it is necessary to maintain high coverage rates in order to prevent future epidemics [27].

These results were comparable to others, for example: a two-dose schedule for England and Wales, with the second vaccination given at age four [5]; and a second vaccination at either 18 months or five years were recommended to complement the first vaccination at 12 months in Canada [16]. In addition, vaccinating 85% of susceptible children aged one to seven years at five-yearly intervals was found to predict the prevention of measles epidemics in Israel [1]. All modelling studies agree that two vaccinations at no less than five years apart are necessary to prevent measles epidemics. Existing policies in eight European countries were analysed and researchers estimated the coverage rates required to reduce R_v below one and eliminate endemic measles [34]. They found that results depended on the age at delivery, but no strategy succeeded if coverage rates were below approximately 87%.

Numerous models for measles vaccination strategies for various regions [1, 5, 13, 16, 34] based on sets of nonlinear ordinary differential equation (ODE) models have reached similar conclusions. The differences in the models have been in the details of the representation of the infectious period, and in the ways in which the age and contact structures of the population have been specified. While analyses suggest that 85% coverage at MMR1 and MMR2 could be sufficient to prevent future measles epidemics, in the Netherlands analyses showed that high overall levels of measles vaccination can obscure pockets of poor coverage, resulting in localised regions with increased risk of infection and effective immunisation difficult to evaluate [17].

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 $R_0 = 12.8$ [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 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.

5.1 Modelling methods

To understand 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 [24, 35]. We are 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 41). The outbreaks we used in our analyses are shown in Figure 42.

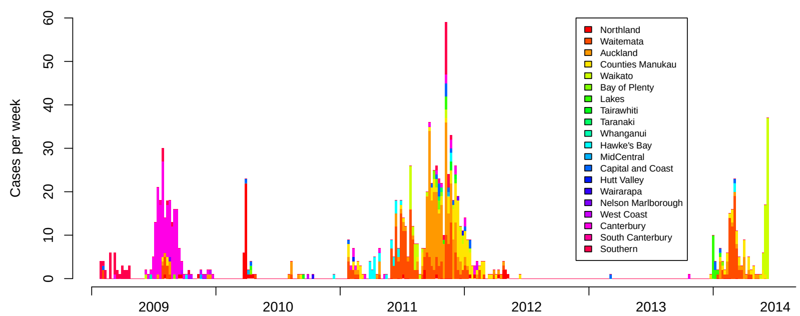

Figure 41: Measles cases by District Health Board (DHB) from 2009 to 2014

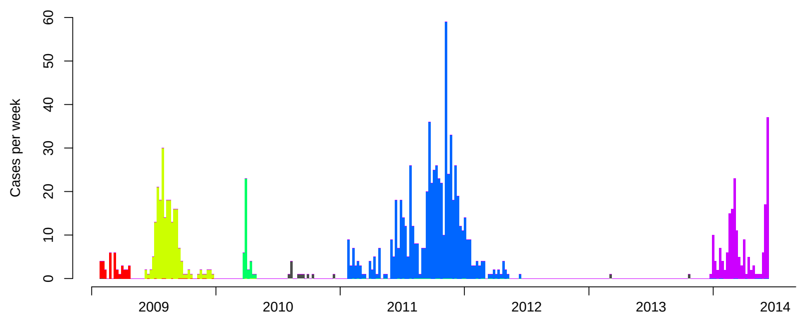

Figure 42: Measles data classified as outbreaks for reproduction number of the infection (R_v) estimation from 2009 to 2014

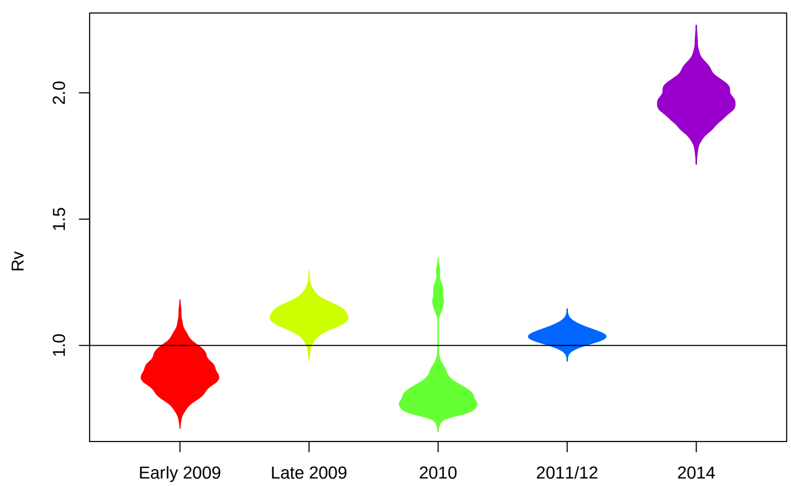

Figure 43: Estimates of R_v for the outbreaks each year, as classified by outbreaks in Figure 42. Sporadic cases are excluded.

To estimate the proportion of the population requiring vaccination utilising our estimates of R_v, we use the well-known equation for the final size of an epidemic in a homogeneously mixing susceptible population [12]:

$$\log(1-\mathcal{P}) + \mathcal{R}_0\mathcal{P} = 0 \tag{2}$$

where $\mathcal{R}_0$ is the basic reproduction number and $\mathcal{P}$ is the proportion of the population infected over the course of the outbreak.

If a proportion x_0 of the population is susceptible following vaccination, then the reproduction number under vaccination is $\mathcal{R}_V = x_0\mathcal{R}_0$, and the final size equation becomes

$$\log\left(1 - \frac{\mathcal{P}}{x_0}\right) + \mathcal{R}_0\mathcal{P} = 0 \tag{3}$$

Hence the relationship between the proportion initially susceptible and the proportion infected in an epidemic is

$$x_0 = \frac{\mathcal{P}}{1 - e^{-\mathcal{R}_0\mathcal{P}}} \tag{4}$$

In order to prevent future epidemics, it is necessary that $\mathcal{R}_V < 1$. Hence, the proportion of the population that must be vaccinated to prevent future outbreaks, $\mathcal{P}_v$ is

$$\mathcal{P}_v = x_0 - 1/\mathcal{R}_0 \tag{5}$$

These formulae are applied at a District Health Board (DHB) level, assuming no mixing between DHBs.

5.2 Modelling results and discussion

The estimated R_v for each outbreak is shown in Figure 43. The 95% confidence intervals for our analyses suggest the R_v for the 2009–2014 outbreaks is 0.92–1.19, and for the current 2013–2014 outbreak 1.82–2.13. The probability density of the R_v estimates for each outbreak all include one. Of particular note is the ongoing outbreak (as of 12 June 2014), which has an R_v well above one and thus we may expect this outbreak to persist if conditions remain the same. An 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.

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 subsection 4.3 is likely to continue, these analyses suggest substantial efforts are required to maintain immunisation to high enough levels that measles does not become endemic. 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 its 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 reproduction 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.

If fewer cases occur during each outbreak, then this suggests that R_v is lower, but that measles is introduced to New Zealand more frequently. The regularity of these outbreaks, however, implies that the approximately yearly importation of measles is an ongoing process. Given the risk of importation of measles as highlighted in subsection 4.3 is likely to continue, we include the effects of this in the benefit–cost section (subsection 6.3).

To use the results from our modelling exercise to help inform the appropriate measles vaccination coverage, we use Equation 5. The proportion of the population requiring additional vaccination to make $R_v < 1$ ranged from 17% to 34% at the DHB level, with a national average of approximately 28% (Table 15). These additional vaccination numbers can be calculated in a number of different ways, as discussed in the benefit–cost section (subsection 6.3). However, they require differing numbers of vaccinations per DHB. Estimates for West Coast, Wairarapa, and South Canterbury, for example, are fewer than 1000 (Table 15). The estimated numbers to vaccinate in the Auckland area, however, are higher for each DHB, with those estimated for Waitemata, Auckland, and Counties Manukau DHBs all over 17,000 (Table 15).

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 43). However, the naïve population (Figure 9 and Figure 10) and the higher R_v for the 2013–2014 outbreak (Figure 43) suggests that catch up vaccination may be necessary (Table 15). The results of these analyses support other studies that suggest very high rates of vaccination are required to eliminate measles and prevent epidemics. Vaccinating 85% of susceptible children aged one to seven years at five-yearly intervals was suggested to be sufficient to 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, with approximately 11% currently naïve. Analysis of measles vaccination in various regions suggest that 85% coverage at MMR1 and MMR2 could be sufficient to prevent future measles epidemics [1, 5, 13, 16, 34], whereas [17] showed that high overall levels of measles vaccination can obscure pockets of poor coverage, resulting in localised regions with increased risk of infection making effective immunisation difficult. Future analyses at a smaller, more local level would be useful, but the lack of appropriate data matching between the NIR data and the census unit area data currently prevent these.

5.3 Summary of modelling

- Regular introductions of measles pose an ongoing threat to New Zealand's efforts to eliminate measles (also see section 4).
- The reproduction number for measles in the partially immune New Zealand population is often close to one, suggesting increased population level immunity is required to ensure prevention of measles persistence following importation.

DHB	Size	Naïve	Attack	Vacc
Auckland	436350	52010	31159	17920
Bay of Plenty	206000	20679	8437	4585
Canterbury	482180	51357	24695	13687
Capital and Coast	283700	32625	18403	10461
Counties Manukau	469300	55544	32903	18880
Hawke's Bay	151700	15602	6846	3751
Hutt Valley	138380	15198	7836	4388
Lakes	98196	10558	5192	2886
MidCentral	162560	17328	8348	4628
Nelson Marlborough	137000	13059	4411	2356
Northland	151690	14921	5688	3071
South Canterbury	55620	5238	1678	893
Southern	297420	31607	15115	8371
Tairawhiti	43650	4769	2431	1359
Taranaki	109750	11473	5262	2899
Waikato	359310	39402	20248	11331
Wairarapa	41112	3932	1346	720
Waitemata	525550	58350	30774	17291
West Coast	32151	3197	1265	685
Whanganui	60120	6075	2530	1378
TOTAL	4241739	462924	234567	131539

Table 15: Size: DHB Population, Statistics NZ 2013; Naïve: DHB naïve population ($x_0 \times$ Size); Attack: Number infected in DHB in an outbreak of measles ($\mathcal{P}$); Vacc: Number to be vaccinated in DHB to reduce $\mathcal{R}_V$ below one ($(x_0 - 1/\mathcal{R}_0) \times$ Size).

- The reproduction number, R_v, for measles in the current outbreak is over one, suggesting that this outbreak has the potential to persist for prolonged periods, with the caveat that this estimate was made during the ongoing outbreak.

- Additional vaccination levels to push R_v below one among the currently naïve population in New Zealand range from 17% to 34% among DHBs, and 28% at the national level (approximately 131,500 vaccinations).

6 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 2013–2014 measles outbreak.

About 50 years ago, approximately 135 million cases of measles causing 7–8 million deaths were believed to occur in the world [9]. Thirty years later, it was estimated there were still approximately 45 million cases of measles occurring annually, including 6 million measles-related fatalities. It was estimated that in 1999 measles was responsible for more than 30 million disability adjusted life years (DALYs) lost and 12 million in 2005 [37]. The incidence of cases was reduced by more than 50% from 43 million in 1999 to approximately 20 million in 2005. Approximately 7.5 million deaths from measles were avoided from 2000–05 due vaccination [37]. 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 be 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, has been evaluated. The costs associated with 5,154 hospitalisations where measles was the main discharge diagnosis was calculated. 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, 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 economic 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. 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 its endemic nature 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 cases. The economic impact to public health departments in the US as the result of 16 outbreaks in 2011 has been estimated [23]. 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 overheads. 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 labour, 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 $= 1.27$), and B/C values $10.8 - 54.2$ have been estimated for MMR vaccination in the USA [39].

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.

6.1 Cost analyses methods

Costs are 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 will tend to reduce the present value of the future earnings (saved by avoiding a case).

Data to estimate the costs relating to the current measles outbreak were obtained from the New Zealand Ministry of Health, for the period 2008 through June 2014. Data include 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, 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 are reported as direct, additional (above normal budgeting) costs required to enable the management of measles. The data 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 is calculated as $1.2 \times \mathsf{full\ time\ equivalent\ (FTE)} \times \mathsf{number\ of\ days\ worked}$. Overtime is calculated as $1.6 \times \mathsf{FTE}$ (M-F) and $2.0 \times \mathsf{FTE}$ (weekend). A full day is considered as 8 hours worked. Salary (hourly) rates are 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 have 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 are calculated at a daily rate of $600 and operations partners and IMT controller partners at $729.

Wages lost due to measles are calculated for the period January 2008 - August 2014. Calculations are based on the assumptions that 5 days of work are lost for each case; however, individuals between 0-14 years of age are not assumed to be employed and therefore did not suffer an income loss and the employment rate of teenagers 15-19 years of age was 41.9% (Statistics New Zealand, 2013). If the case is < 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 $207,155. This consisted of $104,539 for the cases and $102,616 for the care giver, but did not include wage losses for cases <15 years of age. Overall, the cost per case from 2008 - 2014 was estimated to be $2,513 ($839 in forgone wages and $1,710 in hospital costs).

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.

Table 16: Estimated costs (NZ$) for measles management in New Zealand, January 1 – March 9, 2014. PHN: public health nurse; PHA: public health assistant; IMT: incident management team; SSO: safety/security officer (SSO)

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

6.2 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 16. The reported direct medical costs do not appear to include hospital medical costs, which are reported separately in Table 17.

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 17). 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 18. 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 44).

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 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

Table 17: Reported direct costs in NZ$, with the number of cases, length of hospital day, total cost (NZ$), cost per case (NZ$) and cost per day (NZ$) for patients with measles as the primary diagnosis, 2000–2014

Year	Cases	Days	Cost	Cost per case	Cost 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 18: 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 – 19 years	132	12	0.09
>19 years	33	11	0.33
Total	201	34	0.17

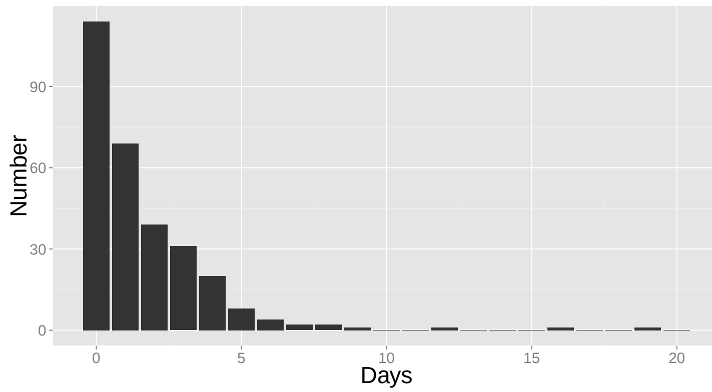

Figure 44: Number of measles cases attending hospital and stay duration from 2000–2014

year and gender for 2000–2014 appear in Table 19.

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 20). 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 was 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 are calculated for the period January 2008 – August 2014. Calculations are based on the assumption that 5 days of work are lost for each case; however, individuals under 15 years of age are not assumed to be employed and therefore did not suffer an income loss. If the case are 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 \$4,327 (\$839 in forgone wages, \$1,765 in management costs, and \$1,710 in hospital costs).

This final figure brings an approximate estimate of \$809,149 for 187 cases for the current outbreak in 2014 alone, which is comprised of earnings lost, case management and hospitalisation costs.

6.3 Benefit–cost analyses methods

To estimate the benefits from additional vaccinations, as estimated from the above modelling section (section 5), we carried out a number of analyses.

Table 19: Number of cases, length of hospital stay, cost (NZ$), cost per case (NZ$) and cost per day (NZ$) for patients with measles as the primary diagnosis, by year and gender, 2000–2014. Note "Length of stay" is number of complete days spent in hospital, thus 0 is no nights spent in hospital (see Table 20)

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	21	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 20: Regression results ($R^2_{\mathsf{adj}} = 0.43$, 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

Primarily, we used Equation 5 to estimate the proportion of the naïve populations in each DHB (Figure 10 and Table 15) and the national level requiring vaccination to reduce the R_v to <1 (section 5).

We assume that the number of cases prevented by this is proportional to the outbreak size. However, there is a continued risk of introduction and despite R_v being <1, smaller outbreaks may occur. Thus, we simulated expected outbreak sizes with $R_v < 1$. We use these values of numbers of predicted cases prevented and numbers expected despite additional vaccination to calculate the savings.

The cost figures above are used to estimate the savings for vaccinating additional populations, using estimated per case costs saved. The costs of the catch up vaccination schemes are estimated to be two different values, to determine how sensitive the benefit–cost ratio ((B/C) was to differing vaccination costs. Values of $20 and $50 per vaccine are used. Thus the expected measles-related costs due to constant introduction of measles despite increased population immunity and the costs of the vaccination schemes are used to estimate the costs of additional vaccine programs for the B/C analysis. The financial savings from reduced measles cases are used to work out the benefits for the additional vaccination programs. The costs for the catch up vaccination programs are presumed to be over a single year. The benefits for the cases saved are presumed to be over a ten year period. Because benefits are assessed over a 10–year time period, a discounting rate of 3% discount per year for the costs saved was used, as is common for healthcare discounting [18]. Measles introductions are expected to be annually occurring events, though the costs per year for each event was also discounted. Thus, the B/C ration was:

$$B/C = \frac{\sum\limits_{n=0}^{9} \frac{B_n}{(1+r)^n}}{\sum\limits_{n=0}^{9} \frac{C_n}{(1+r)^n}} \tag{6}$$

Where B is the benefit in saved funds from cases prevented and C is the cost of vaccination, discounted over time, where n is the year and r the annual discount rate of 0.03 (3%). 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.

6.4 Benefit–cost analyses results

The estimated vaccinaton rates, with percentages are shown in Table 21.

The numbers of susceptible people to vaccinate in New Zealand, assuming a homogeneously mixed population to achieve the 28% currently naïve catch up in vaccination numbers and using Equation 5 are shown in Figure 45.

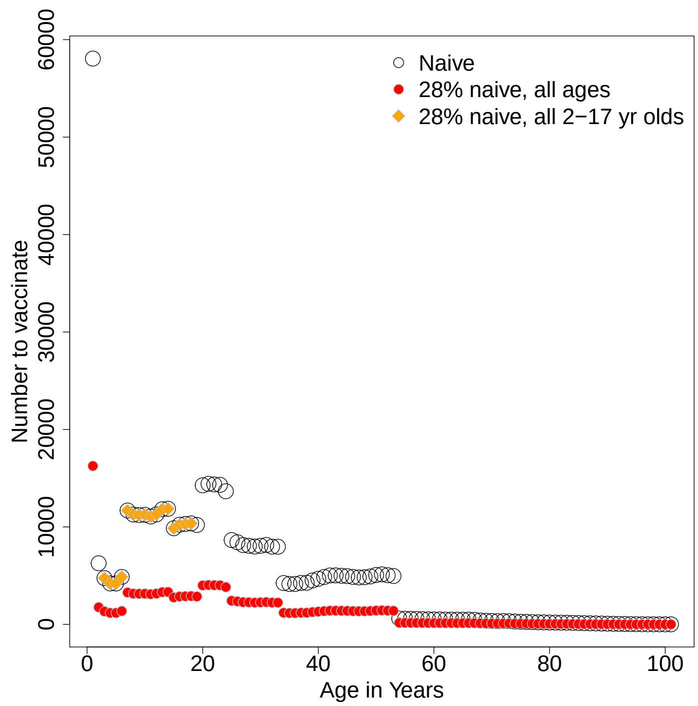

Figure 45: The estimated numbers of the currently naïve New Zealand population requiring additional vaccination to reduce the R_v to less than one (section 5, Table 22 and Table 23)

The expected number of cases in New Zealand, assuming homogenous mixing, in a naïve population of subsequently lower (8%) numbers of naïve of the population and assuming measles R_v is <1 is shown in Figure 46 and Figure 47. These simulations show that even in scenarios when R_v is lower than one, and thus deterministically should fail to persist (i.e. become endemic), outbreaks can occur due to stochastic processes following measles importation. The most likely scenario is that very few cases occur, with the median value from 1000 simulations low (2 cases). Thus most measles introductions will be single cases

Table 21: DHB and national level catch up vaccination rates and estimated outbreak sizes post catch-up vaccination. Size: DHB Population, Statistics NZ 2013; Naïve: DHB naïve population ($x_0 \times$ Size); Attack: Number infected in DHB in an outbreak of measles ($\mathcal{P}$); Vacc: Number to be vaccinated in DHB to reduce $\mathcal{R}_V$ below one ($(x_0 - 1/\mathcal{R}_0) \times$ Size); Proportion: the proportion of the currently naïve population requiring vaccination; Naïve.post.vaccination: the naïve population following catch up vaccination; with Median.outbreak and Mean.outbreak: the expected median and mean outbreak size post–vaccination catch up from 1000 simulations of a stochastic model

DHB	Size	Naïve	Attack	Vacc	Proportion	Naïve.post.vaccination	Median.outbreak	Mean.outbreak
Auckland	436350	52010	31159	17920	0.34	34090	2	82
Bay of Plenty	206000	20679	8437	4585	0.22	16094	2	71
Canterbury	482180	51357	24695	13687	0.27	37670	2	62
Capital and Coast	283700	32625	18403	10461	0.32	22164	3	96
Counties Manukau	469300	55544	32903	18880	0.34	36664	3	50
Hawke's Bay	151700	15602	6846	3751	0.24	11851	2	56
Hutt Valley	138380	15198	7836	4388	0.29	10810	2	86
Lakes	98196	10558	5192	2886	0.27	7672	2	62
MidCentral	162560	17328	8348	4628	0.27	12700	2	75
Nelson Marlborough	137000	13059	4411	2356	0.18	10703	3	90
Northland	151690	14921	5688	3071	0.21	11850	3	70
South Canterbury	55620	5238	1678	893	0.17	4345	3	72
Southern	297420	31607	15115	8371	0.26	23236	2	102
Tairawhiti	43650	4769	2431	1359	0.28	3410	2	47
Taranaki	109750	11473	5262	2899	0.25	8574	3	68
Waikato	359310	39402	20248	11331	0.29	28071	2	95
Wairarapa	41112	3932	1346	720	0.18	3212	3	59
Waitemata	525550	58350	30774	17291	0.30	41059	2	70
West Coast	32151	3197	1265	685	0.21	2512	2	50
Whanganui	60120	6075	2530	1378	0.23	4697	2	58
Total	4241739	462924	234567	131540	0.28	331384	2	106

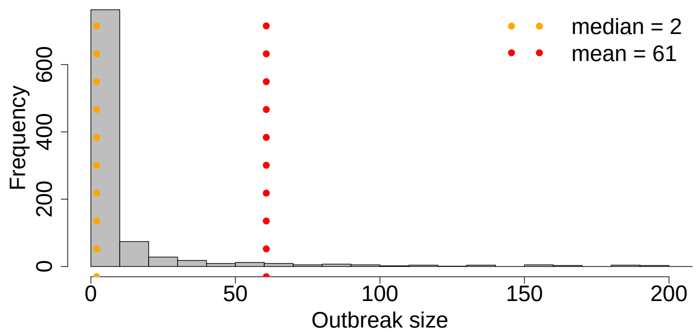

Figure 46: A subset of the expected number of measles cases from 1000 simulations of a model (section 5) in a homogeneously mixed population in New Zealand with 28% of the currently 11% susceptible to measles infection vaccinated, using an R_v <1. The full distribution of results can be seen in Figure 47

or lead to minor outbreaks. In this modelling exercise the mean value was 61 cases, suggesting this is likely to be an outbreak size to be expected. The maximum predicted number of cases was nearly 8,000 cases. Note, however, that larger values are very rarely predicted and this does not take into account spatial variation or heterogeneous contact rates.

For the cost analyses we used the values from the above cost section (subsection 6.3). Specifically, we used the average cost of a case for the analyses to be \$839 lost in wages and \$1877 in hospitalisation costs for those attending hospital, with 17% of cases predicted to be hospitalised (Table 17). We estimated there would be approximately one introduction of measles per year (section 4). We provide two costs for measles vaccinations for our cost analyses, \$20 and \$50, based on US literature.

The model estimates for each DHB, with the vaccination percentages and the expected outbreak size following additional vaccination is shown in Table 21. The benefit–cost results are in Table 22 and Table 23, for two different vaccine prices. The results in the two tables show the benefits of vaccination are always substantially greater than the costs of the increased supplementary vaccination (Table 22 and Table 23).

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 7) were vaccinated with a single vaccine at a very young age (Figure 8). Furthermore, it may be unnecessary to vaccinate very young, as it appears possible to reach the appropriate figure (28% of currently naïve) by vaccinating all the currently naïve 2–17 year olds, so pre-school and school age children.

Table 22: Benefit–cost analyses with 20 dollars per vaccine. *Vacc* is numbers to vaccinate (see Table 15); *Vacc costs* is cost for the catch up vaccination programme; *Wages saved* is wages of care givers and cases saved ($839 per case); *Manage saved* is management costs saved ($1,765 per case); *Hospitalised* is number of hospitalisations saved, given the proportion of cases hospitalised 0.17; *Hosp saved* is the hospitalisation costs saved ($1,877 per case); *Costs save* is the discounted costs saved; *Outbreak* is the predicted outbreak size despite $R_v < 1$ due to measles importation from 1000 simulations; *OB costs* is costs expected due to continued measles importations based on 10 introdcutions of measles, one per year, but costs discounted on the same discounted rate; B/C is the benefit–cost ratio.

DHB	Vacc	Vacc costs	Wages saved	Manage saved	Hospitalised	Hosp saved	Costs saved	Outbreak	OB costs	B/C
Auckland	17920	358400	26547468	55010965	5297	9942525	80393738	82	2115693	32.5
Bay of Plenty	4585	91700	7188324	14895456	1434	2692162	21768413	71	1831880	11.3
Canterbury	13687	273740	21040140	43598824	4198	7879928	63715888	62	1599670	34.0
Capital and Coast	10461	209220	15679356	32490349	3129	5872213	47481818	96	2476908	17.7
Counties Manukau	18880	377600	28033356	58089983	5594	10499018	84893455	50	1290056	50.9
Hawke's Bay	3751	75020	5832792	12086558	1164	2184490	17663453	56	1444863	11.6
Hutt Valley	4388	87760	6676272	13834395	1332	2500389	20217765	86	2218897	8.8
Lakes	2886	57720	4423584	9166434	883	1656715	13395946	62	1599670	8.1
MidCentral	4628	92560	7112496	14738327	1419	2663763	21538783	75	1935085	10.6
Nelson Marlborough	2356	47120	3758172	7787585	750	1407506	11380878	90	2322102	4.8
Northland	3071	61420	4846176	10042118	967	1814984	14675682	70	1806079	7.9
South Canterbury	893	17860	1429656	2962496	285	535433	4329429	72	1857681	2.3
Southern	8371	167420	12877980	26685411	2570	4823045	38998407	102	2631715	13.9
Tairawhiti	1359	27180	2071212	4291911	413	775708	6272254	47	1212653	5.1
Taranaki	2899	57980	4483224	9290019	895	1679052	13576554	68	1754477	7.5
Waikato	11331	226620	17251296	35747682	3442	6460934	52242126	95	2451107	19.5
Wairarapa	720	14400	1146792	2376352	229	429495	3472832	59	1522267	2.3
Waitemata	17291	345820	26219448	54331250	5232	9819676	79400395	70	1806079	36.9
West Coast	685	13700	1077780	2233347	215	403649	3263843	50	1290056	2.5
Whanganui	1378	27560	2155560	4466695	430	807298	6527686	58	1496465	4.3

Table 23: Benefit–cost analyses with 50 dollars per vaccine. *Vacc* is numbers to vaccinate (see Table 15); *Vacc costs* is cost for the catch up vaccination programme; *Wages saved* is wages of care givers and cases saved ($839 per case); *Manage saved* is management costs saved ($1,765 per case); *Hospitalised* is number of hospitalisations saved, given the proportion of cases hospitalised 0.17; *Hosp saved* is the hospitalisation costs saved ($1,877 per case); *Costs save* is the discounted costs saved; *Outbreak* is the predicted outbreak size despite $R_v < 1$ due to measles importation from 1000 simulations; *OB costs* is costs expected due to continued measles importations based on 10 introdcutions of measles, one per year, but costs discounted on the same discounted rate; B/C is the benefit–cost ratio.

DHB	Vacc	Vacc costs	Wages saved	Manage saved	Hospitalised	Hosp saved	Costs saved	Outbreak	OB costs	B/C
Auckland	17920	896000	26547468	55010965	5297	9942525	80393738	82	2115693	26.69
Bay of Plenty	4585	229250	7188324	14895456	1434	2692162	21768413	71	1831880	10.56
Canterbury	13687	684350	21040140	43598824	4198	7879928	63715888	62	1599670	27.90
Capital and Coast	10461	523050	15679356	32490349	3129	5872213	47481818	96	2476908	15.83
Counties Manukau	18880	944000	28033356	58089983	5594	10499018	84893455	50	1290056	38.00
Hawke's Bay	3751	187550	5832792	12086558	1164	2184490	17663453	56	1444863	10.82
Hutt Valley	4388	219400	6676272	13834395	1332	2500389	20217765	86	2218897	8.29
Lakes	2886	144300	4423584	9166434	883	1656715	13395946	62	1599670	7.68
MidCentral	4628	231400	7112496	14738327	1419	2663763	21538783	75	1935085	9.94
Nelson Marlborough	2356	117800	3758172	7787585	750	1407506	11380878	90	2322102	4.66
Northland	3071	153550	4846176	10042118	967	1814984	14675682	70	1806079	7.49
South Canterbury	893	44650	1429656	2962496	285	535433	4329429	72	1857681	2.28
Southern	8371	418550	12877980	26685411	2570	4823045	38998407	102	2631715	12.79
Tairawhiti	1359	67950	2071212	4291911	413	775708	6272254	47	1212653	4.90
Taranaki	2899	144950	4483224	9290019	895	1679052	13576554	68	1754477	7.15
Waikato	11331	566550	17251296	35747682	3442	6460934	52242126	95	2451107	17.31
Wairarapa	720	36000	1146792	2376352	229	429495	3472832	59	1522267	2.23
Waitemata	17291	864550	26219448	54331250	5232	9819676	79400395	70	1806079	29.73
West Coast	685	34250	1077780	2233347	215	403649	3263843	50	1290056	2.46
Whanganui	1378	68900	2155560	4466695	430	807298	6527686	58	1496465	4.17

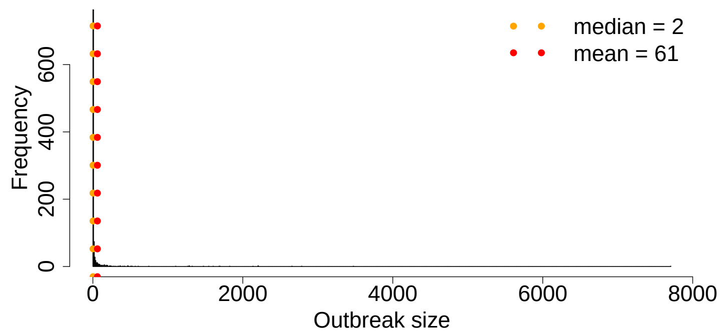

Figure 47: The distribution of the expected number of measles cases from 1000 simulations of a model (section 5) in a homogeneously mixed population in New Zealand with 28% of the currently 11% susceptible to measles infection vaccinated, using an R_v <1, showing the rare but possible large epidemic sizes possible. A subset of the distribution of results can be seen in Figure 46

6.5 Benefit–cost analyses discussion

Our estimates of the costs of the measles outbreaks in New Zealand suggest that measles management costs per case in New Zealand is high. We used the mean values per case in the absence of alternative data and used as much data as possible. The exact costs will vary, however, our benefit–cost analyses suggest that in all cases catch up vaccination schemes will be financially beneficial for New Zealand (see Table 22 and Table 23).

The results presented here are based on available data. While some of the data are complete and detailed, this is not true of all the data. In order to perform an accurate analysis of the current measles outbreak in New Zealand, more complete data would be better. For instance, age, gender, ethnicity, year of discharge, length of stay and estimated cost data are available for cases reported by publicly funded hospitals. Similar data would be needed for cases occurring outside the period 2011–2013 at publicly funded hospitals, non-publicly funded hospitals, and private clinics. Other factors that would be useful to investigate in the future include the relationship between the costs over time. For these analyses we use the mean cost per case. However, as stated previously, it is uncertain as to whether that is a valid measure or not and whether there may be other relationships. Furthermore, a linear term for case age may not be appropriate, and we have not accounted for alternative interactions there might be between age and length of stay in hospital.

Detailed measles outbreak management costs were provided for the period of January 1 – March 9, 2014. Similar data are needed for the period preceding 2014. In the abscence of these data we have used mean case data from aggregated data available. It may 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, but we have done so for these purposes.

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]. These values are substantially lower than our estimates, however, it is noticable that these estimates are also from more than a decade ago. The containment of a single case (also 2 secondary cases) of measles in 2004 in Iowa, USA was estimated to cost US$142,542. In this outbreak, more than 2500 hours of personnel time were needed to investigate and respond to the outbreak [11]. They estimated direct costs per case to be less than US$500. However, the combined direct costs of €520 per case in Germany [30] suggests costs may be higher. Thus, our estimates of the additional costs, including indirect costs and wages lost may be appropriate.

The annual cost for long-term care of people with moderate of severe mental retardation over a period of 50 years is estimated at US$31,059 and US$78,448, respectively in Minnesota [26]. In 2000 expenditures for care in large state mental retardation/developmental disabilities (MR/DD) facilities continued to increase and reached a national annual average of US$113,864 per person. In 2000 the average annual expenditures for care in large state MR/DD facilities were $113,864. The cost of a case of measles was estimated to range from $71 (no complications and no hospitalisation) to $29,556 (encephalitis and hospitalisation for 8.7 days). They estimated the annual cost of measles vaccination in the US with its vaccination program to be $1,234,083 (52.5% direct cost and 47.5% indirect cost) [39]. Work by others also finds that measles vaccination is extremely cost effective, however, in their analyses they also include the costs of mumps and rubella (see Table 24) [39]. However, the cost of measles in their analyses was substantially higher than mumps and rubella (Table 24) [39].

Our estimates for the benefit–cost ratio of catch up vaccination are also higher than those in some studies. If we presume the R_0 estimated for measles in New Zealand is representative and following 28% vaccination of the naïve population, measles will be unable to persist ($R_v < 1$), our B/C ratio is substantially greater than 1. Estimates in Korea suggest catch up vaccination schemes have a benefit–cost ratio of just over one [6]. However, the estimated B/C ratio for MMR has been estimated to be between 10.2 and 54.2, much greater than one (see Table 25) [39]. As stated above, these authors also consider the costs and benefits of mumps and rubella, so making direct comparison difficult without reanalysis.

Our results for the benefits of MMR vaccination may be conservative. We presume that in a totally naïve population R_0 for measles was around 12. However, R_0 for measles has been estimated to be more than 18 (i.e. 1 case infects 18 others on average, [2]) in other countries. It is unlikely R_0 was so high as 18 in New Zealand, as measles would still be endemic given current vaccination rates. However, the benefits of catch up vaccination are clear if R_v is greater than one (Table 22 and reftable:cost20) and our analyses do not include the additional benefits of mumps and rubella immunity. As noted in our previous report, if

Parameter, disease	Direct costs	Indirect costs	Total costs
Cost of disease without vaccination program			
Measles	\$2,645,779,861	\$3,228,846,601	\$5,874,626,462
Mumps	\$936,032,273	\$522,974,252	\$1,459,006,525
Rubella	\$88,352,366	\$292,537,083	\$380,889,449
Congenital rubella syndrome	\$114,726,378	\$57,975,659	\$172,702,037
Subtotal	\$3,784,890,878	\$4,102,333,595	\$7,887,224,473
Cost of disease with vaccination program			
Measles	\$647,488	\$586,595	\$1,234,083
Mumps	\$1,960,182	\$1,124,249	\$3,084,431
Rubella	\$260,982	\$258,240	\$519,222
Congenital rubella syndrome	\$2,662,760	\$1,345,595	\$4,008,355
Subtotal	\$5,531,412	\$3,314,679	\$8,846,091
Costs averted by MMR vaccination program	\$3,779,359,466	\$4,099,018,916	\$7,878,378,382
MMR vaccination program costs			
Vaccine	\$147,802,803		\$147,802,803
Administration	\$94,756,438		\$94,756,438
Transportation	\$7,164,227		\$7,164,227
Parental productivity		\$34,787,438	\$34,787,438
Adverse events	\$16,413,145	\$2,154,826	\$18,567,971
Subtotal	\$266,136,613	\$36,942,264	\$303,078,877
Net present value (net saving)	\$3,513,222,853	\$4,062,076,652	\$7,575,299,505

Table 24: Summary of all measles, mumps, and rubella diseases and measles-mumps-rubella vaccination costs, USA, from [39]

measles R_v in the currently naïve population is less than one, the benefits will not be so clear, 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 remains 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 naïve population. The spatial effects of measles transmission may have affected both our multivariate regression analyses (section 4) and will affect the predictions from modelling exercises (section 5). 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 may produce some larger and costly outbreaks, even if vaccination cover is high and R_v is less than one (Figure 46 and Figure 47). Given that, the greater the vaccination coverage, the smaller the outbreaks will be.

6.6 Benefit–cost analysis summary

- The mean wage losses per measles case is estimated to be $839
- The mean cost per measles case attending hospital is estimated to be $1,877
- Approximately 17% of measles cases attend hospital
- The mean management cost per measles case for the current outbreak, estimated from three months of data is estimated to be $1,765
- Using R_0 values estimated for measles in New Zealand prior to vaccination and the current naïve population sizes, the benefits of catch up vaccination strategies are clear (>1 B/C ratio).
- Outbreaks with a mean size of approximately 61 cases per year, but median of 2 cases per year may occur regularly due to importation, despite R_v being below one and the epidemic predicted to die out without additional interventions. There is, however, a small chance for some of these outbreaks to reach several thousand in number.

7 Acknowledgments

The authors wish to thank Tomasz Kiedrzynski, Lisa Oakley and Nic Aagaard from the Ministry of Health, Ruth Pirie and colleagues from ESR, and June Atkinson from University of Otago for help in obtaining the appropriate materials for analyses.

Parameter	B/C direct costs	B/C societal perspective	Costs per disc. yrs life saved
Base case	14.2	26.0	$4195
Discount rate 0%	21.7	54.2	$1628
Discount rate 5%	12.3	19.6	$6569
Discount rate 8%	10.8	15.5	$10,615

Table 25: Benefit–cost ratios for Measles-Mumps-Rubella (MMR) vaccination, USA, from [39]

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., J. A. P. Heesterbeek, and T. Britton (2013). *Mathematical tools for understanding infectious disease dynamics*. Princeton: Princeton University Press.

[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] Filia, 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] Honeycutt, A. A., L. Clayton, O. Khavjou, E. A. Finkelstein, M. Prabhu, J. L. Blitstein, W. Dougles Evans, and J. M. Renaud (2006). Guide to Analyzing the Cost-Effectiveness of Community Public Health Prevention Approaches. http://aspe.hhs.gov/health/reports/06/cphpa/report.pdf

[19] 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

[20] Koopmanschap, M. A. (1998). Cost-of-illness studies: useful for health policy? *Pharmacoeonomics*, 14, 143–148.

[21] Larg, A. and J. R. Moss (2011). Cost-of-illness studies: a guide to critical evaluation. *Pharmacoeconomics*, 29,653–671.

[22] 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.

[23] 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.

[24] 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.

[25] 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.

[26] 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.

[27] Roberts, M. (2004). A mathematical model for measles vaccination. Wellington: Ministry of Health.

[28] 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.

[29] 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.

[30] 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.

[31] 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.

[32] *Statistics New Zealand* (2014). http://nzdotstat.stats.govt.nz/, accessed 17 June 2014.

[33] 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.

[34] 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.

[35] 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.

[36] 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.

[37] 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.

[38] World Health Organisation measles media centre, January (2013) Geneva: World Health Organization. www.who.int, accessed July 1, 2014.

[39] 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.