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

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1 Abstract

New Zealand has been working towards elimination of endemic (domestic) measles virus transmission, but has suffered from small, yet significant outbreaks of measles 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 identified 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 were:

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

- Age is the best predictor of risk of measles infection in multivariate regression analyses, though some groups, such as people of Pacific ethnicity, the less socially deprived, and European and Maori school age children have been more likely to be measles cases in outbreaks since 2007.

- Estimates of the proportion of the currently naïve New Zealand population (11%) requiring additional vaccination to ensure measles does not persist is approximately 28%, 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 the winter, and non–New Zealanders summer.

- Analyses of outbreak data suggest that measles basic reproductive number (R_v, the number of secondary infections) values often include 1 and this 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 losses per measles case is estimated to be $839

- The mean cost per measles case attending hospital is estimated to be $1710, and approximately 17% of measles cases attend hospital

- The mean management cost per case was $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 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 with 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 that 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, prior to the 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 [29, 28]. 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 overall population immunity estimates suggest that approximately 85 to 90 percent of the population is immune to measles (see Section **??**), 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 were 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. 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 was very thorough. The report included 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 were of high quality, reporting both absolute measles case numbers and rates per 100,000 population in New Zealand.

Specific epidemiological details were 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 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).

4 Additional 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 (section 4), descriptive analyses of risk of infection due to previous vaccination history (section 4), and current rates of immunity within the population (section 4). In light of the ap-

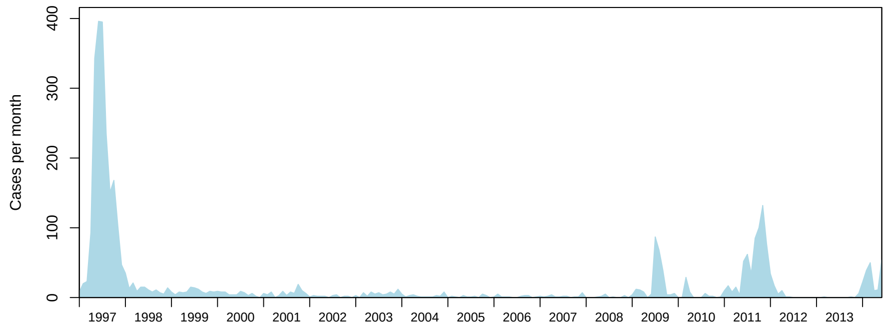

Figure 1: Measles incidence from 1997 to 2014

parent 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 (section 4).

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 avoid confounding results due to a lack of independence among risk factors. Specifically Age × Prioritised Ethnicity × NZDep data for New Zealand were required to test whether interactions among case covariates provide additional information on risk over the univariate analyses performed in the *Progress Towards Measles Elimination in New Zealand - Final* report. These Age × Prioritised Ethnicity × 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 risk of measles infection.

The University of Otago denominator data provided were not to the same detail as the ESR case data. Notably, the denominator age data were categorised into several classes: 0–5, 6–17, 18–24, 25–64, and 65+ year categories. The ethnicity denominator data were not Prioritized Ethnicity at the Level 1 Ethnic Group Codes, but at the Level 2 Ethnic Group Codes, though with some

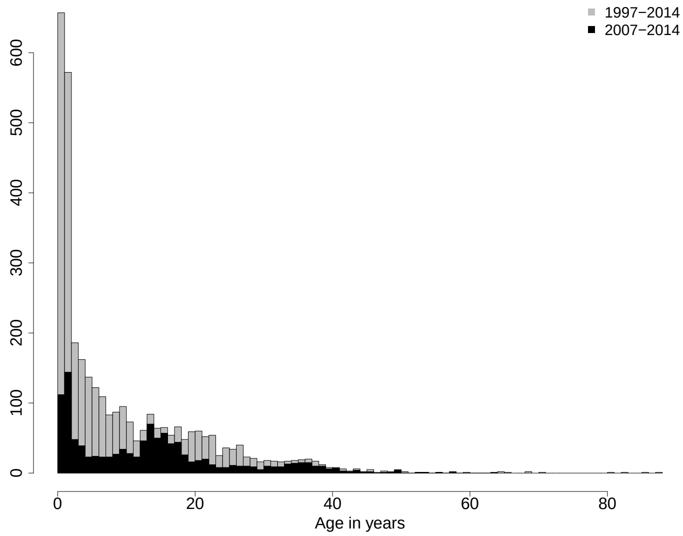

Figure 2: Age of measles cases in years in New Zealand for two periods, 1997–2014 and 2007–2014

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 [33]).

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

The Prioritized Ethnicities for cases are: European; Maori; Pacific Peoples; Asian; Middle Eastern/Latin American/African (MLA); Other Ethnicity;

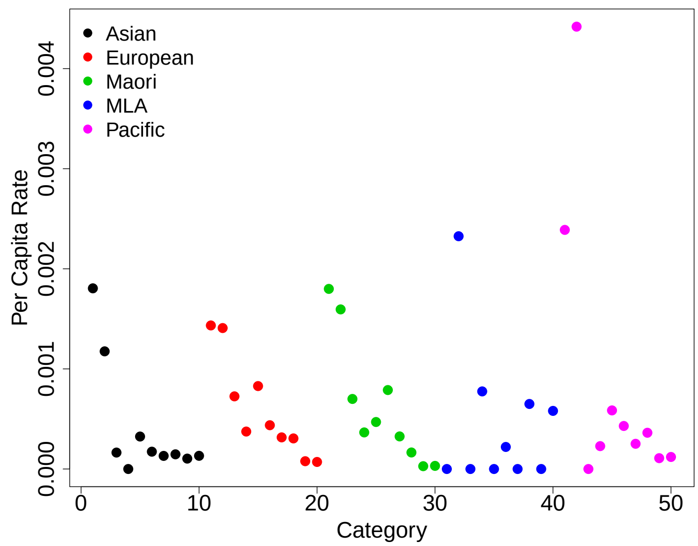

Figure 3: Per capita rates of measles infections for 2007–2014 broken down by ethnicity (Table 2 for details)

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 Middle Eastern/Latin American/African category was over– or underrepresented 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 Middle Eastern, Latin American and African ethnicities category, and along with small population sizes (Table 2), and there several issues with 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

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

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

Table 2: Numbers of measles cases, population sizes and per capita rates of measles in specific age, ethnicity and socio-economic deprivation categories from 2007-2014

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

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:

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

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

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 that 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 3, that uses the serosurvey results and the National Immunisation Register 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 (> 5 years) of immunity 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 data by country and year to mea-

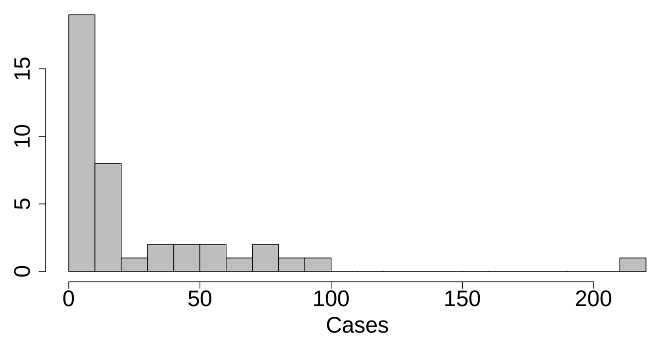

Figure 4: Distribution of measles cases per category used in the final regression model

sure human movement to and from New Zealand (www.immigration.govt.nz). 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 used the WHO data to determine per capita measles cases for each year and used these data and the number of immigrants to New Zealand to begin to understand where measles was likely to be imported from. We used simple per capita rates for measles and the number of travellers to each country to score and map the risk of mealses importation. We use the data from 2012 because this year had the most complete WHO measles data and yet was 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 and the statistical support for the estimated coefficients can be seen in Table 18.

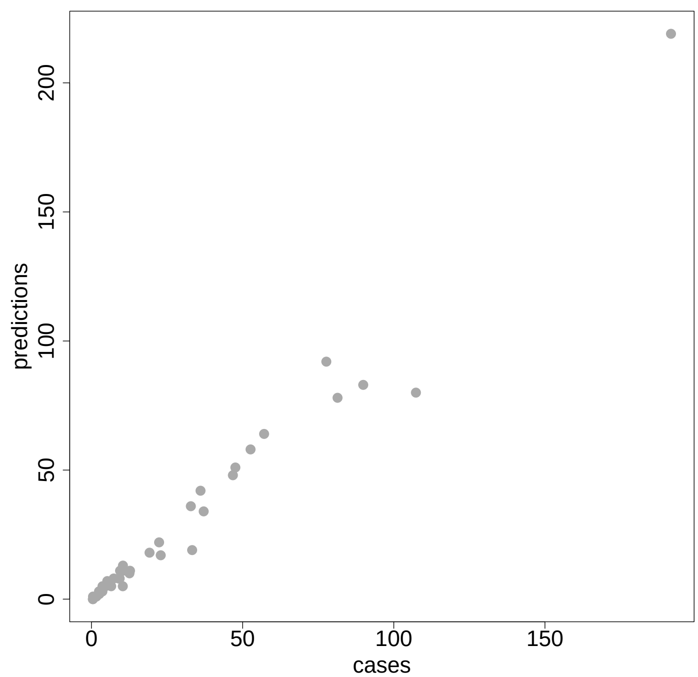

Figure 5: Regression model (Equation 1) predictions plotted against the cases (Table 2)

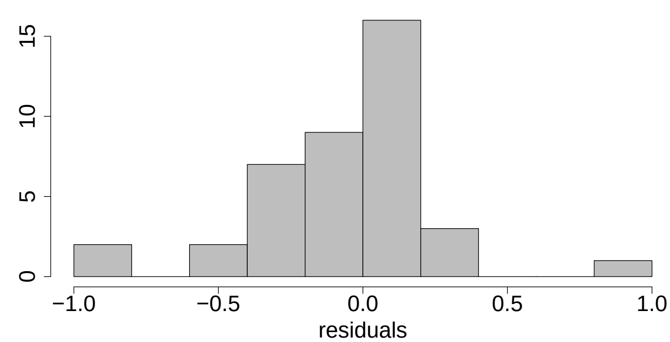

Figure 6: Histogram of residuals from the regression model (Equation 1)

	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

	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

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 (Figure 2).

People of Pacific origin are also over-represented as measles cases (β = 1.16, standard error (SE) = 0.2, p–value < 0.0001), NZDep levels 6-10 under-represented (β = -0.21, SE = 0.085, p–value = 0.02), and there are some other age:ethnicity classes that are significantly less represented in the data compared to Europeans in those ages classes, particularly in the 6–17 age classes. In later measles outbreaks (since 2007) there has been a shift in the distribution of ages infected. The very young are still most likely to be infected, but of school aged

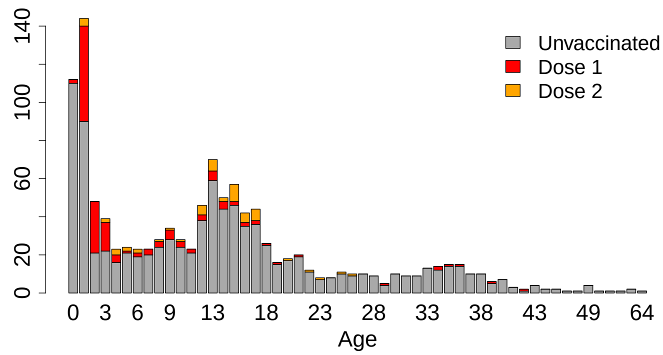

Figure 7: Age and vaccination status of measles cases, 2007–2014

children older teenagers are more likely to be represented then the under tens (Figures 2 and 7). This pattern suggests that improving vaccination coverage in the young is reducing the burden of measles in those age categories (Table **??**). Interestingly the regression results suggest risk of measles cases 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 in the very young 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:

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

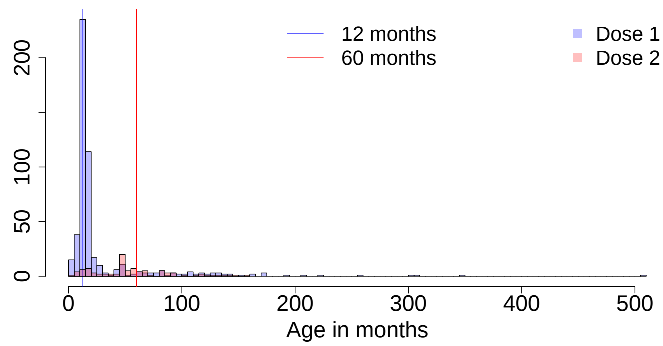

Figure 8: Age of vaccination of vaccinated measles cases, 2007–2014

- Waikato: Figure 15
- 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

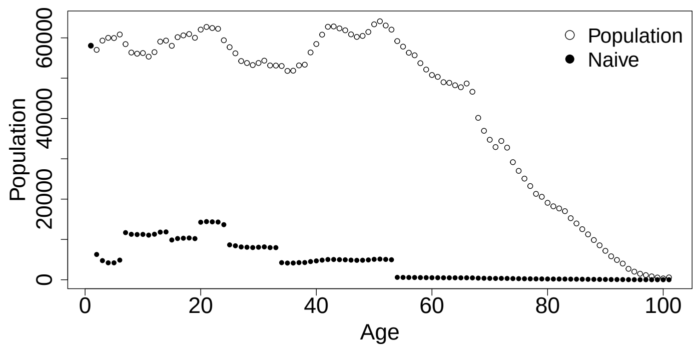

Figure 9: New Zealand population by age and estimated numbers of naïve people in each age class using national immunity data (Table 3)

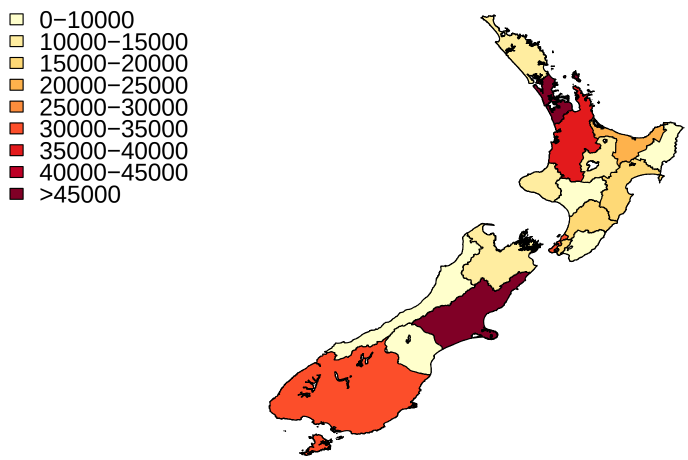

Figure 10: Numbers of naïve individuals per District Health Board, using national immunity data (Table 3)

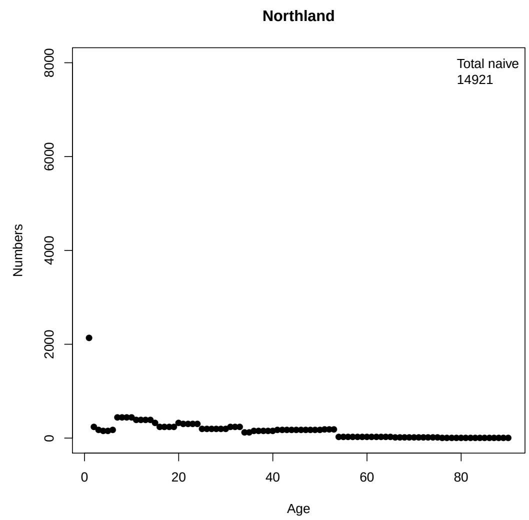

Figure 11: Numbers of naïve individuals per age class, Northland District Health Board, using national immunity data (Table 3)

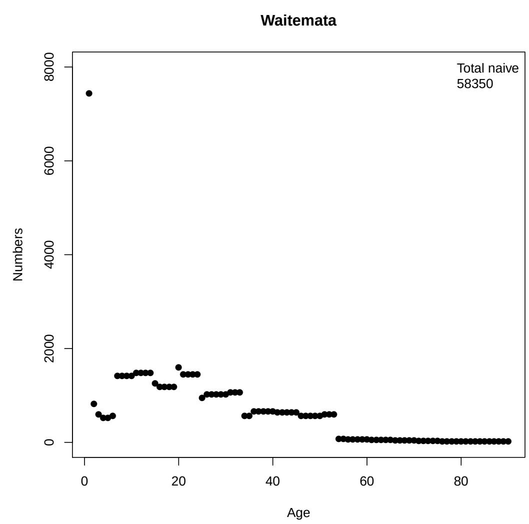

Figure 12: Numbers of naïve individuals per age class, Waitemata District Health Board, using national immunity data (Table 3)

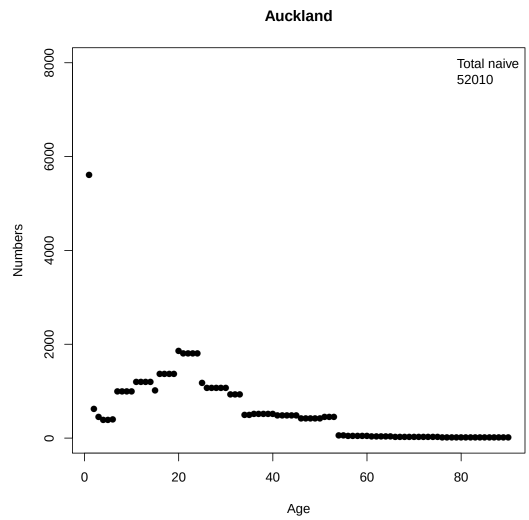

Figure 13: Numbers of naïve individuals per age class, Auckland District Health Board, using national immunity data (Table 3)

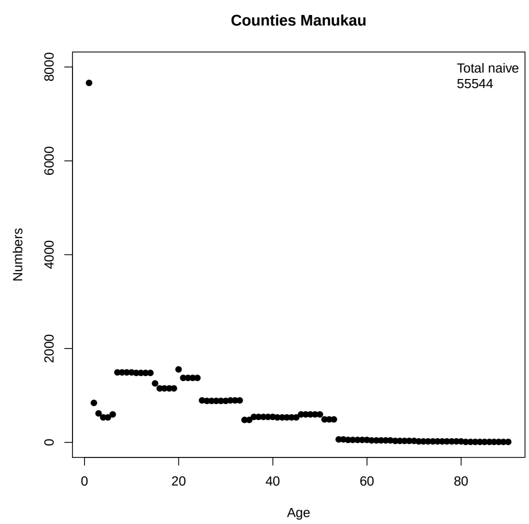

Figure 14: Numbers of naïve individuals per age class, Counties Manukau District Health Board, using national immunity data (Table 3)

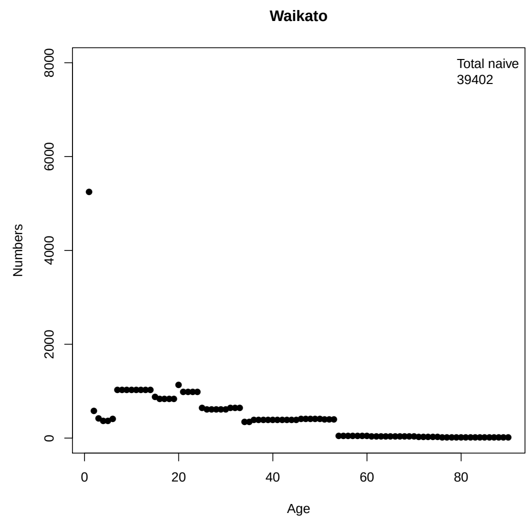

Figure 15: Numbers of naïve individuals per age class, Waikato District Health Board, using national immunity data (Table 3)

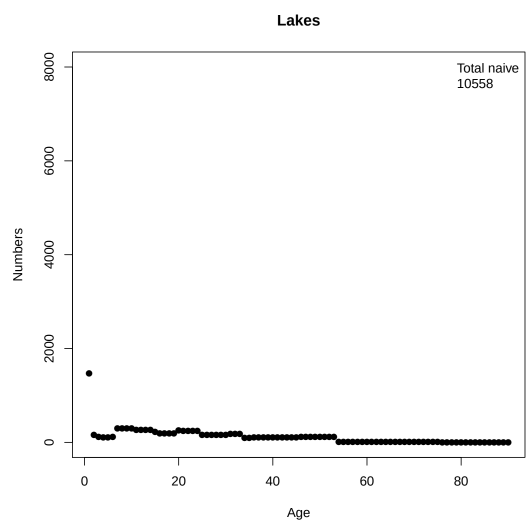

Figure 16: Numbers of naïve individuals per age class, Lakes District Health Board, using national immunity data (Table 3)

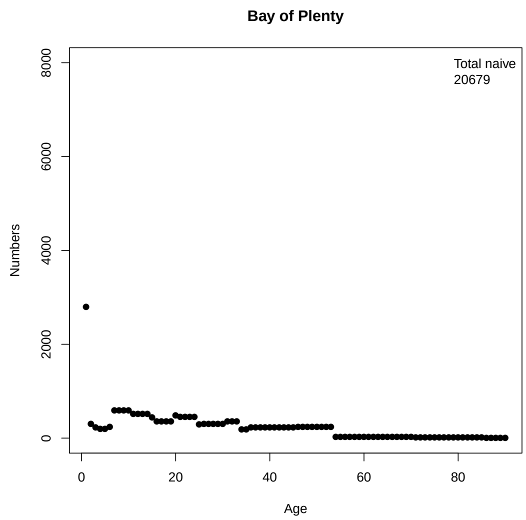

Figure 17: Numbers of naïve individuals per age class, Bay of Plenty District Health Board, using national immunity data (Table 3)

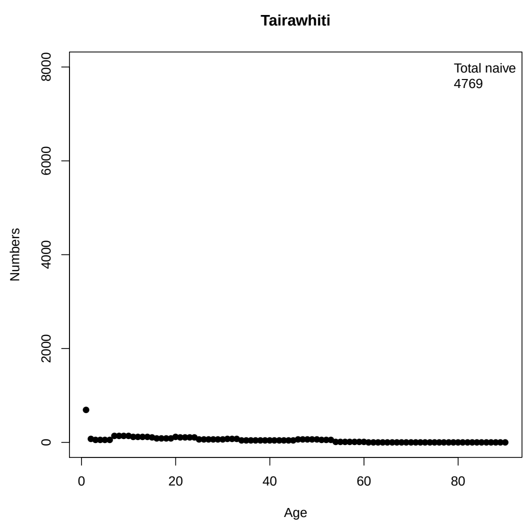

Figure 18: Numbers of naïve individuals per age class, Tairawhiti District Health Board, using national immunity data (Table 3)

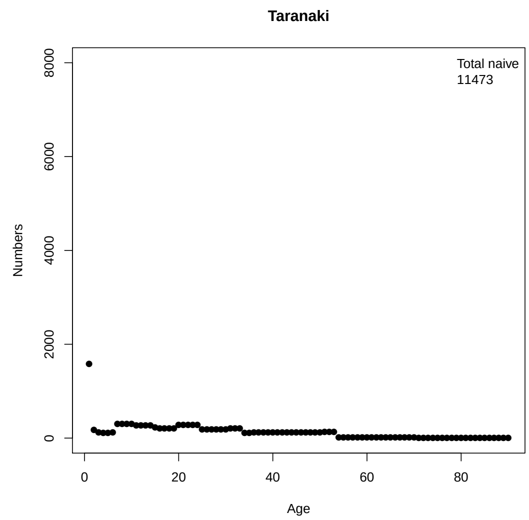

Figure 19: Numbers of naïve individuals per age class, Taranaki District Health Board, using national immunity data (Table 3)

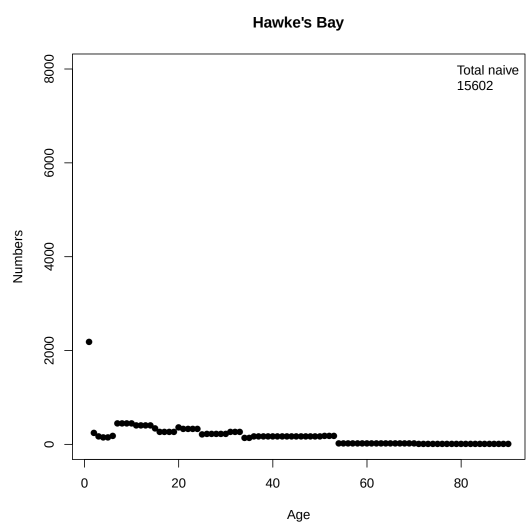

Figure 20: Numbers of naïve individuals per age class, Hawke's Bay District Health Board, using national immunity data (Table 3)

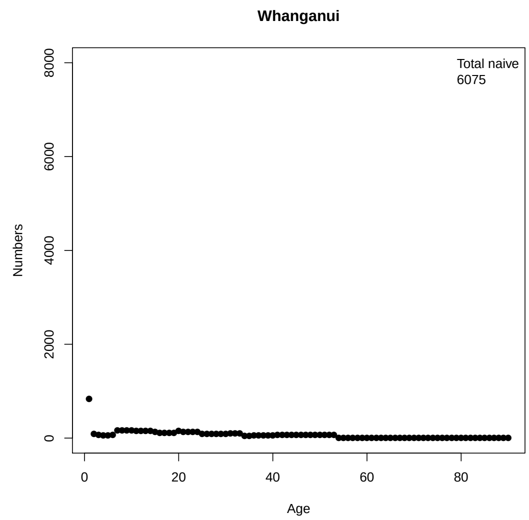

Figure 21: Numbers of naïve individuals per age class, Whanganui District Health Board, using national immunity data (Table 3)

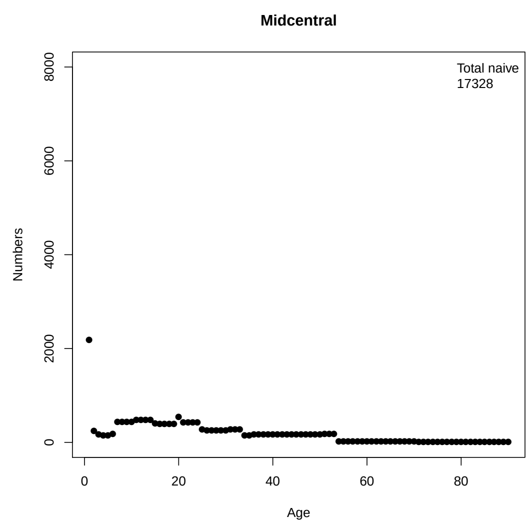

Figure 22: Numbers of naïve individuals per age class, Midcentral District Health Board, using national immunity data (Table 3)

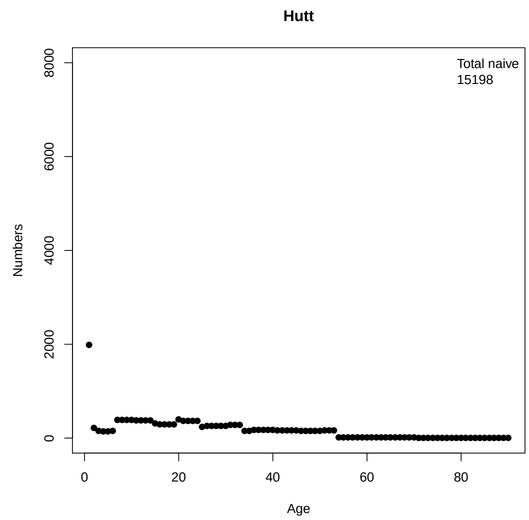

Figure 23: Numbers of naïve individuals per age class, Hutt District Health Board, using national immunity data (Table 3)

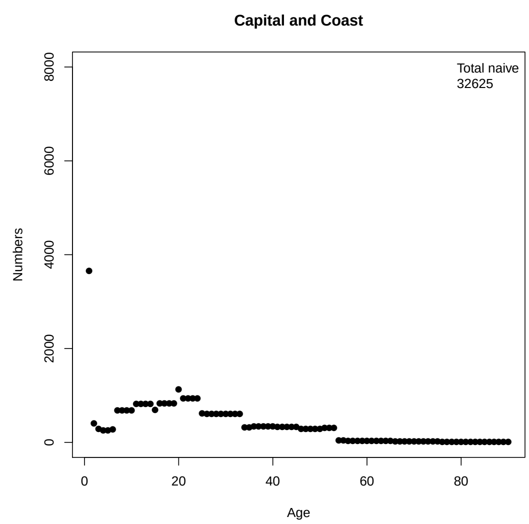

Figure 24: Numbers of naïve individuals per age class, Capital and Coast District Health Board, using national immunity data (Table 3)

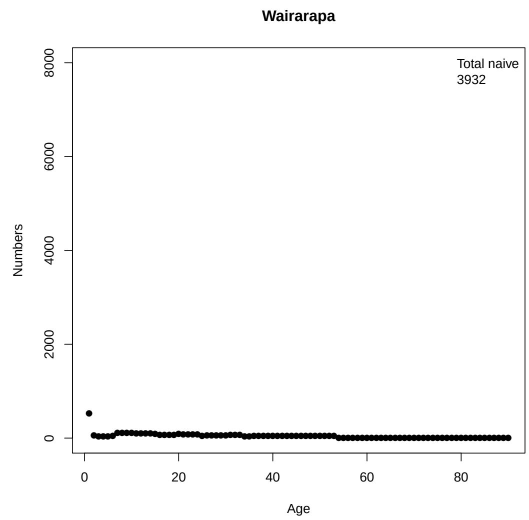

Figure 25: Numbers of naïve individuals per age class, Wairarapa District Health Board, using national immunity data (Table 3)

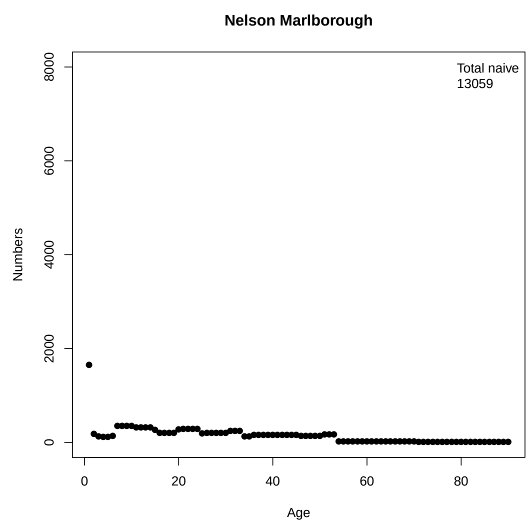

Figure 26: Numbers of naïve individuals per age class, Nelson Marlborough District Health Board, using national immunity data (Table 3)

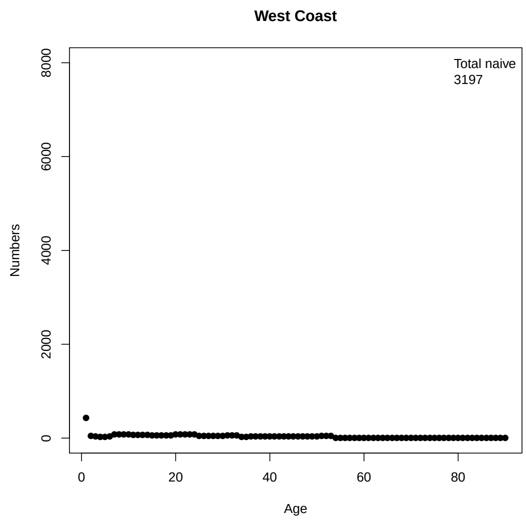

Figure 27: Numbers of naïve individuals per age class, West Coast District Health Board, using national immunity data (Table 3)

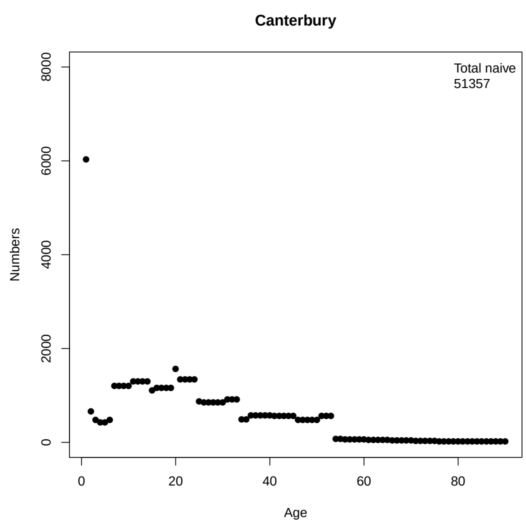

Figure 28: Numbers of naïve individuals per age class, Canterbury District Health Board, using national immunity data (Table 3)

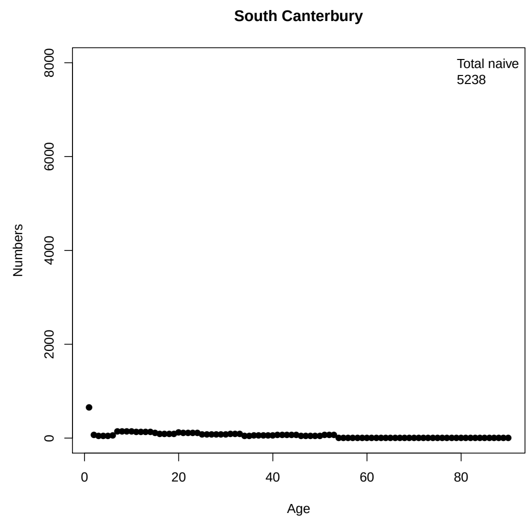

Figure 29: Numbers of naïve individuals per age class, South Canterbury District Health Board, using national immunity data (Table 3)

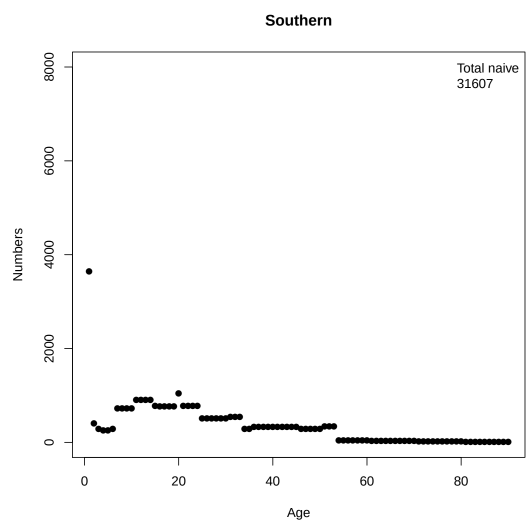

Figure 30: Numbers of naïve individuals per age class, Southern District Health Board, using national immunity data (Table 3)

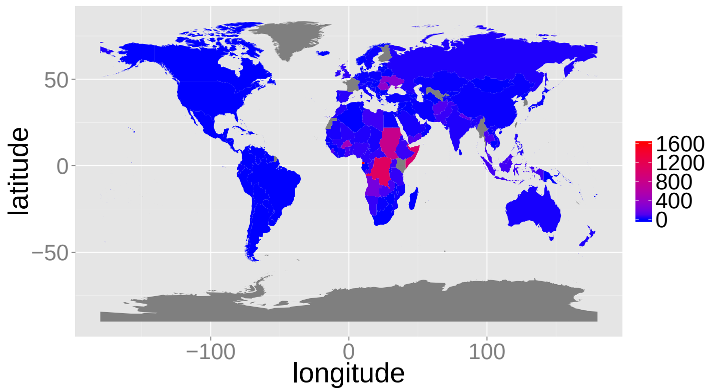

Figure 31: Measles incidence per million 2012

4.7 Measles importation risk results

Globally, vaccination coverage is lowest and measles incidence highest in less developed nations (Table 5 and Table 6, and Figures 32 and 31. Analyses of 2012 data, the most complete and recent year of data, suggest immigration (whether for work, pleasure, etc.) is dominated by people from Australia, United Kingdom, China, and the United States, as shown in Table 9 and Figure **??**. However, travel by New Zealanders is dominated by that to Australia (Table 8 and Figure 34). Together, these mean that the greatest travel location for New Zealanders and immigration travel is from Australia (7 and 35. 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 though immigration is lower from some Asian countries, travel from (and thus we presume to) some Asian countries also poses a high risk of measles importation to New Zealand. These data are shown in Table 12. The data for all the variables for each nation state and territories for 2012 are plotted in Figure 35, Figure 31, and Figure 32 and the risk map for measles incidence and immigration in Figure 36. The breakdown by New Zealander and non-New Zealander travellers is in Tables 10 and 11 and Figures 37 and 38

Though global incidence of measles in 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 trav-

Table 5: 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 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: 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 8: 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 9: 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 10: Risk of measles importation to New Zealand due to New Zealander travel in 2012, estimated by travellers numbers$*$measles incidence

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 11: Risk of measles importation to New Zealand due to non-New Zealander travel and immigration in 2012, estimated by travellers numbers∗measles incidence

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 12: Risk of measles importation to New Zealand in 2012, all travellers

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

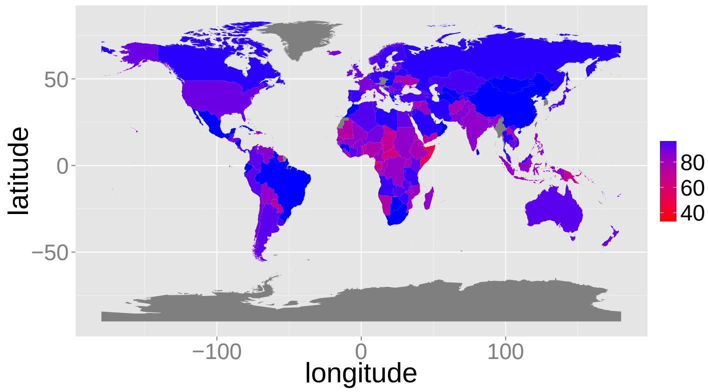

Figure 32: Measles vaccination cover (%) 2012

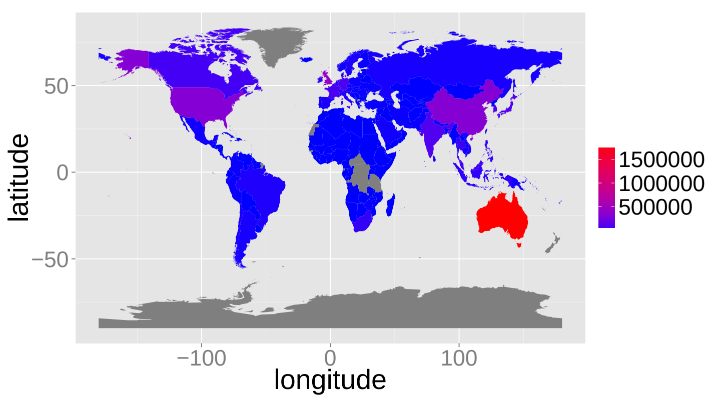

Figure 33: Total international travel, 2012

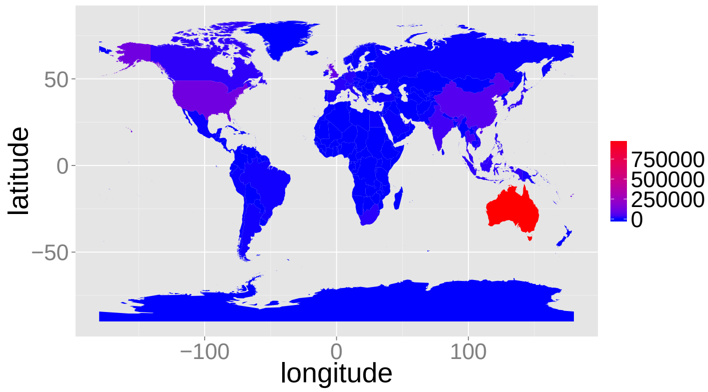

Figure 34: New Zealander international travel, 2012

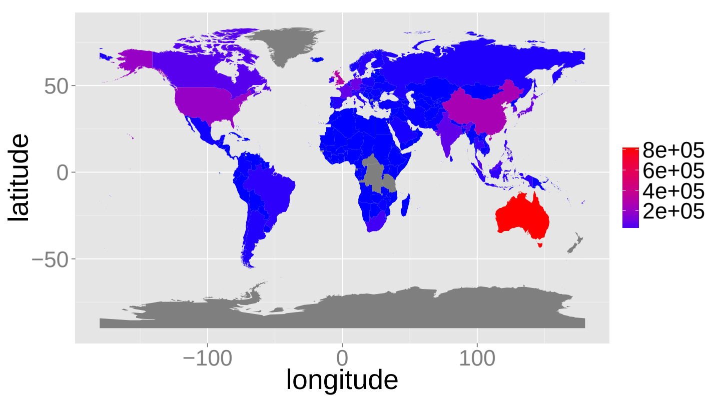

Figure 35: Non-New Zealander international travel and immigration, 2012

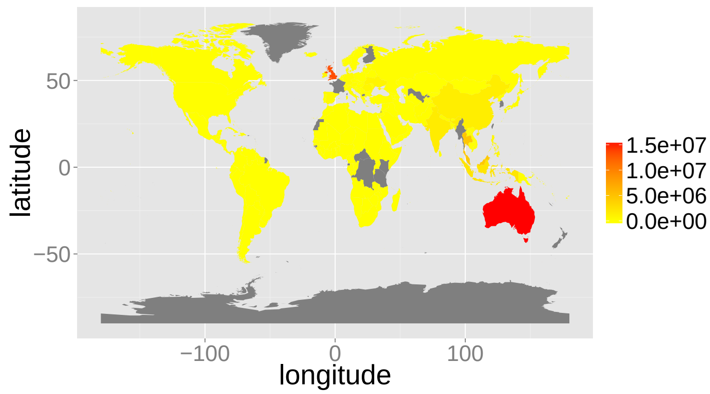

Figure 36: Risk map for measles importation, 2012

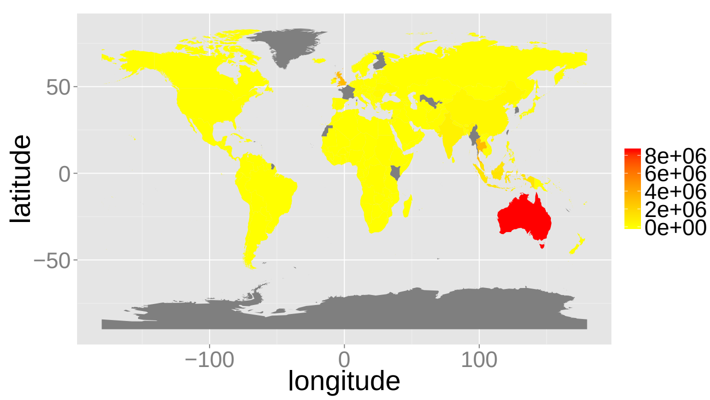

Figure 37: Risk map for measles importation from New Zealander international travel, 2012

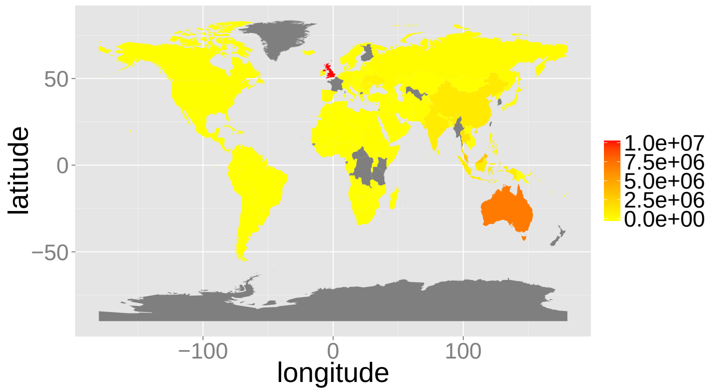

Figure 38: Risk map for measles importation from non-New Zealander international travel and immigration, 2012

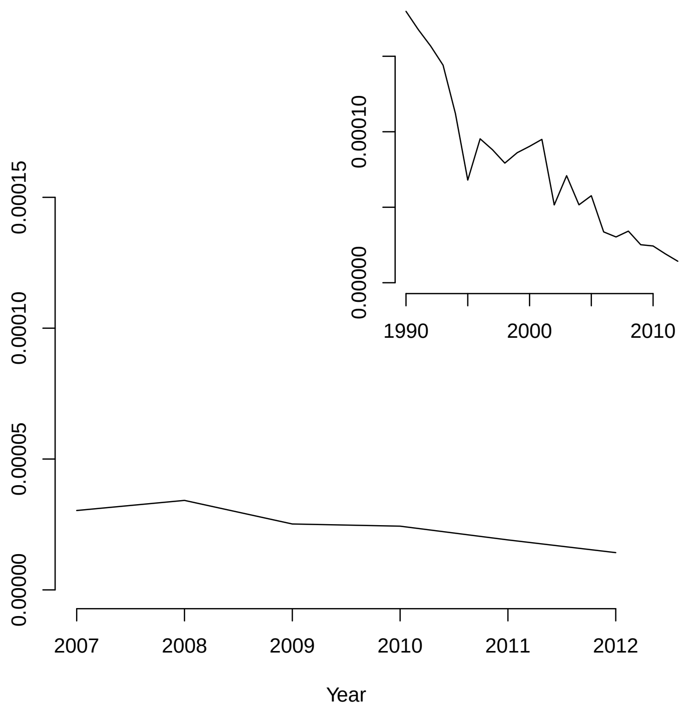

Figure 39: Trend in global per capita measles incidence

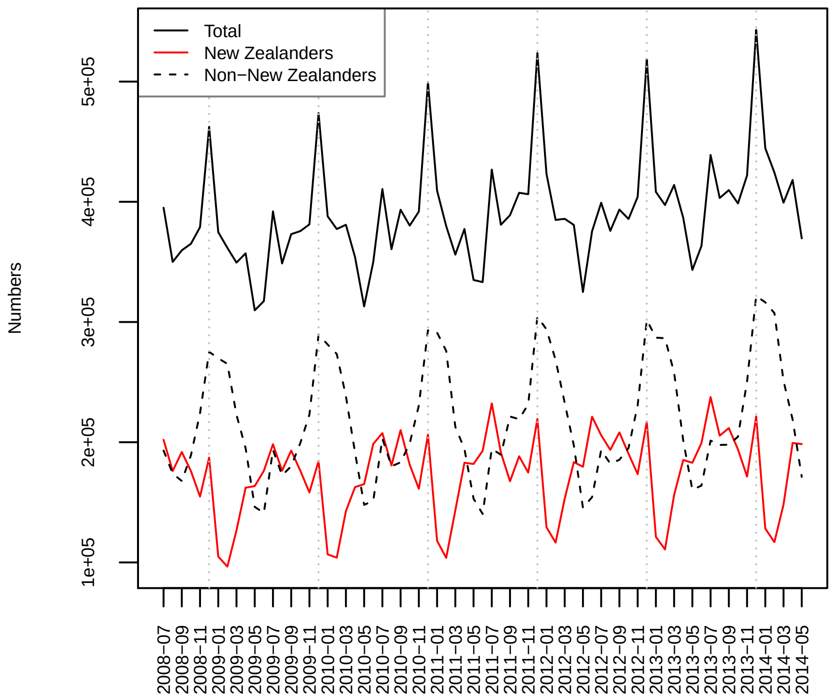

Figure 40: Trends in international travel

elling. 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).

4.8 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, as are the more wealthy (NZDep 1–5), and European and Maori 6–17 year old children compared to Asian and Pacific ethnicity children of the same age. Interpretation of these results must still be viewed with some caution, however, as there is very likely a spatial effect that might not be accounted for in these analyses. Additional data we have been provided by the Ministry of Health but are yet to incorporate in our risk analyses are finer scale (domicile level) immunisation coverage data from the National Immunisation Register (NIR). A key issue with incorporating the spatial immunisation data has been the denominator data and the NIR data. The data suggest that census data and NIR data re recording children living in different DHB to that which they are vaccinated in, or subsequent to the census or NIR data moving. The 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 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 of cases ($> 16\%$) had been vaccinated at least once (Figure 7). However, the majority of these vaccinated cases 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 District Health Board (DHB)) immunisation coverage data were not able to provide reliable results, as discussed above. The National Immunisation Register (NIR) data, but 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. Thus the data gap that we have hinder us providing fine scale risk maps.

The distribution of naïve among the DHB also varies. 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 most travel to New Zealand is coming from. However, the strong seasonality in travel around Christmas 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 7 and Figure 35). However, recently Australia was declare 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, South, Southeast and East Asia, where measles is endemic (Table 12 and Figure 36).

4.9 Risk analysis summary

- Risk of measles infection decreases significantly with age.
- Pacific people are statistically more at risk 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 than European or Maori children.
- The majority of cases are unvaccinated.
- The majority of vaccines failures occur in those people which revieved single vaccinations around 1 year old.
- Distribution of numbers of naïve among New Zealand is uneven, with the majority predictably in DHB 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 [29, 28, 34]. 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 [34] successfully predicted the 1997 epidemic, which was curtailed by a mass vaccination campaign [23, 29]. 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. The model developed by [29] 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] and later analyses suggested high levels of vaccination coverage (but less than 95%) could eliminate measles, but emphasised that it is necessary to maintaining high coverage rates in order to prevent future epidemics [28].

These results were comparable to others, for example: [5] suggested two-dose schedule for England and Wales, with the second vaccination given at age four; and [17] recommended a second vaccination at either 18 months or five years, to complement the first vaccination at 12 months in Canada. In addition, [1] found that vaccinating 85% of susceptible children aged one to seven years at five-yearly intervals would prevent epidemics in Israel. All modelling studies agree that two vaccinations at no less than five years apart are necessary to prevent measles epidemics. [35] took existing policies in eight European countries and estimated the coverage rates required to reduce R_v below one and eliminate endemic measles. 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, 14, 17, 35] based on sets of nonlinear 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, [18] in the Netherlands 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 is difficult to evaluate.

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 $R_0 = 12.8$ [28]. 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.

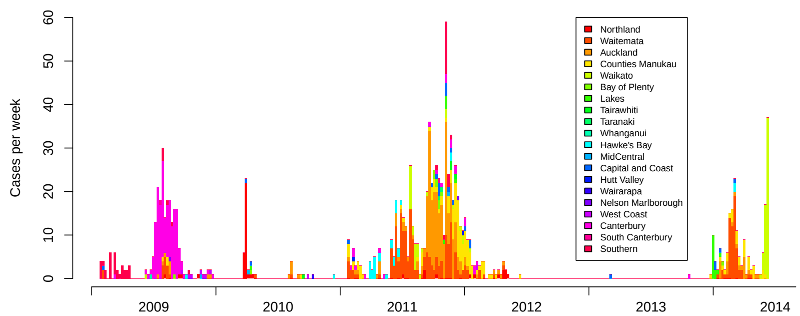

Figure 41: Measles cases by District Health Board (DHB) from 2009 to 2014

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 [25, 36]. We were required to compute the generation time for measles to do so. The generation time is the average time an index case infects others after becoming infected. We used a lognormal distribution with mean 12.0 and standard deviation (s.d.) 3.5 from [20]. 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.

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 is [13]

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

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

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

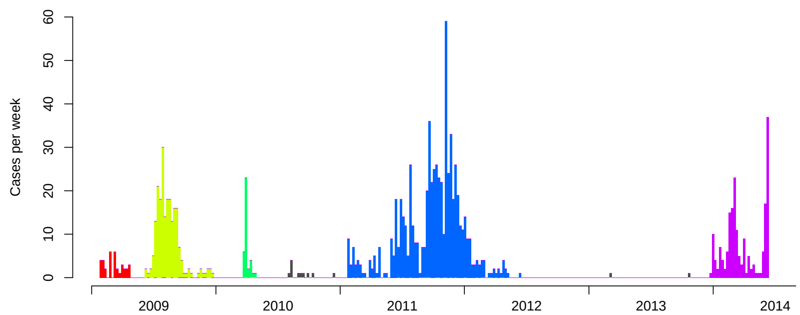

Figure 42: Measles data classified as outbreaks for reproductive number of the infection (R_v) estimation from 2009 to 2014

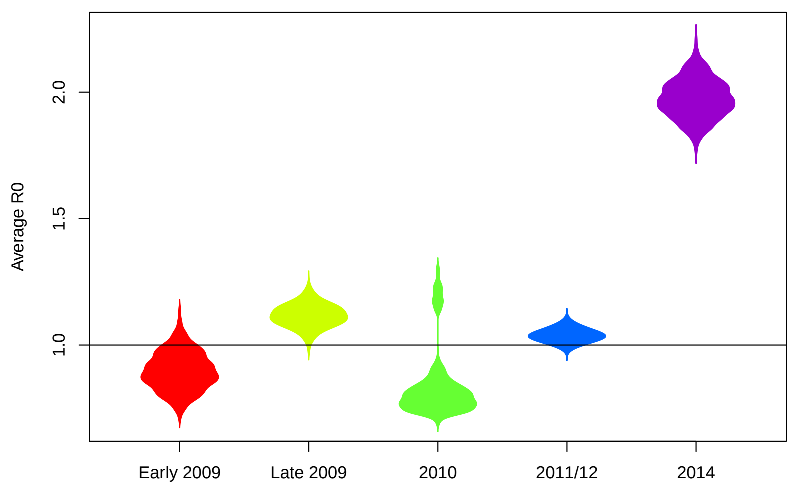

Figure 43: Estimates of R_v (Average R_0) for the outbreaks each year, as classified by outbreaks in Figure 42. Sporadic cases are excluded.

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 is

$x_0 - 1/\mathcal{R}_0$. (5)

These formulae were 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 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_0 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 section 4 is likely to continue, these analyses suggest substantial efforts are required to maintain the level of 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 it's R_v is approximately twice that of the 2011-2012 outbreak. A caveat to this and other R_v estimates is that the 2013–2014 outbreak may include some sporadic cases and thus the true basic reproductive numbers may be lower than estimated. However, sub-clinical and underreporting may lower the estimate. The relative contributions of both to our estimates are currently unknown.

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, imply that the regular (approximately yearly) importation of measles is an ongoing process. Given the risk of importation of measles as highlighted in section 4 and our previous report is likely to continue, we include the effects of this in the benefit–cost section (Section 6.2).

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 13). These additional vaccination numbers can be made up in a number of different ways, and these are discussed in the benefit–cost section (Section 6.2). However, they require differing numbers of vaccinations per DHB. Estimates for West Coast, Wairarapa, and South Canterbury, for example, are fewer than 1000 (Table 13). 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 13).

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 (Figures 9 and 10) and the higher R_v for the 2013–2014 outbreak (Figure 43) suggests that catch up vaccination may be necessary (Table 13). 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% 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, 14, 17, 35], but [18] showed that in the Netherlands high overall levels of measles vaccination can obscure pockets of poor coverage, resulting in localised regions with increased risk of infection and effective immunisation is difficult to evaluate. 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 prevented 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.
- 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).

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 13: 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).

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.

Approximately 50 years ago, approximately 135 million cases and 7–8 million deaths were believed to occur in the world due to measles [9]. Thirty years later, it was estimated there were still approximately 45 million cases of measles occurring annually, including 6 million measles-related fatalities. [38] estimated that in 1999 measles was responsible for more than 30 million disability adjusted life years (DALYs) lost and 12 million in 2005. Similarly, the number of cases was reduced by more than 50% from 43 million in 1999 to approximately 20 million in 2005. They estimated approximately 7.5 million deaths from measles were avoided from 2000–05 due vaccination. The World Health Organization (WHO) estimated 158,000 deaths from approximately 355,000 measles cases in 2011 [39]. In addition to the substantial losses occurring in measles-endemic countries, a significant impact is felt in heavily measles-vaccinated countries, which may be considered measles-free, due to contact with cases either in the country of origin or in the previously measles-free country.

The annual cost of treating and controlling measles in 11 industrialised countries was estimated to cost more than US$150 million [8]. The estimated cost for a case ranged from US$189–344 [8]; however, the average estimated cost of a typical hospital case ranges from US$967–1,755 [7]. [32] estimated the economic benefits from cases averted due to measles vaccination. They estimated that the expanded vaccination from 2005 to 2015 in 72 of the world's poorest countries could result in nearly US$10 billion of costs averted between 2011 and 2020. Ninety-nine percent of these averted costs were the result of lost productivity due to an estimated 360,000 measles-specific premature mortalities, with the remaining <1% associated with averted treatment costs and reduced caretaker productivity for the nearly 12 million measles cases avoided.

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

An outbreak of measles occurred in Sydney, Australia, lasting nearly 2 months in 2011 and resulted in 26 confirmed cases [16]. Seven (27%) of the cases required hospitalisation for more than 1 day and 10 (38%) resulted in management within a hospital emergency department. During this outbreak, a total of 1,395 contacts were identified and managed by a public health unit in western Sydney. The mean number of contacts per case was 54 (median =

28, maximum = 206). The estimated cost to the public health unit for contact management for the epidemic was in excess of AUS$48,000, with 90% of this being associated with staff time.

Germany implemented a two-dose measles vaccination program in 1991 and has seen the benefits in recent years. In 2001 more than 6,000 cases were reported in Germany but by 2004 this number fell to 122 [37]. 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 [31]. 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. In addition, to determine the total impact, it would be necessary to include the indirect losses associated with lost production of cases and care givers.

Although measles was declared eliminated from the United States in 2000, it remains a concern due to the endemic nature of it around the world [26]. Several studies have been conducted in the United States to assess the economic impact of recent measles outbreaks due to imported measles. [24] estimated the economic impact to public health departments in the US as the result of 16 outbreaks in 2011. The outbreaks lasted an average of 22 days and resulted in 107 confirmed cases; however, from these 107 cases, they estimated between approximately 8,900 and 17,500 contacts with confirmed cases, requiring between 42,600 and 83,100 personnel hours at a cost of between US$2.7 and 5.3 million. Overall, it was estimated that each contact required 4.7 personnel hours at a cost of US$298 per contact.

It was estimated that for the one week that the Iowa Department of Public Health (DPH) investigated a case in 2004, 2,525 hours were used to identify contacts, set up vaccination clinics, and institute and enforce quarantine orders for those who refused vaccination [11]. In total, it was estimated the direct costs associated with three cases of measles was US$142,452, or nearly US$50,000 per case.

The impact of a measles outbreak due to a non-autochthonous case in Indiana was also reported [26], and a total of 34 cases, 94% of which were not vaccinated against measles, were reported in the outbreak. Direct cost information was obtained from approximately 100 public health officers and infection-control officials needed to control the outbreak. Direct cost for those completing a survey showed the outbreak cost at least $167,685, 83% of which ($139,023) was for wages, salaries and overhead. This amounted to a direct cost of $4,932 per measles case. These costs did not include either patient care or indirect costs, which would have made the total and per case cost higher.

The direct medical and public health costs in response to a single case of refugee-imported measles has been reported [10]. Costs included 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 $= 1.27$).

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 were evaluated as either direct or indirect. Direct costs included physician consultations, hospitalisations, drugs, vaccination, long-term care for chronic sequelae, special education costs. Direct costs can be divided into medical and non-medical [30]. Direct medical costs include costs for diagnosis, treatment, continuing care, rehabilitation and terminal care. Personnel time (investigation and emergency response), materials (phone calls, vaccine), personnel (cost, wages and fringe benefits), overhead costs, public information, and mileage are estimated when calculating direct medical costs. Direct non-medical costs include transportation to and from health care providers.

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

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

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

Wages lost due to measles were calculated for the period January 2008 - August 2014. Calculations were based on the assumptions that 5 days of work were lost for each case; however, individuals between 0-14 years of age were 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 were $<$ 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.

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 14. The reported direct medical costs do not appear to include hospital medical costs, which are reported separately in Table 15.

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 15). The mean cost per case was \$1,877. The mean cost per day of stay in the

Table 14: Estimated costs (NZ$) for measles management in New Zealand, January 1 – March 9, 2014 (see text for abbreviations)

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

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 16. 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 year and gender for 2000–2014 appear in Table 17.

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 18). Results showed the expected hospitalisation costs in 2000 of a female measles patient who did not stay overnight in the hospital was $582. The cost was $256 less if the case were a male. It increased of approximately $406 per night of hospitalisation and $64 per year over the time period of 2000–2014. The cost of a case decreased with the age of the patient by approximately $8 per year of case age.

Wages lost due to measles were calculated for the period January 2008 –

Table 15: Reported direct costs, with the number of cases, length of hospital day, cost, cost per case and cost per day for patients with measles as the primary diagnosis, 2000–2014

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

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

Table 16: 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

Table 17: Number of cases, length of hospital stay, cost, cost per case and cost per day for patients with measles as the primary diagnosis, by year and gender, 2000–2014

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

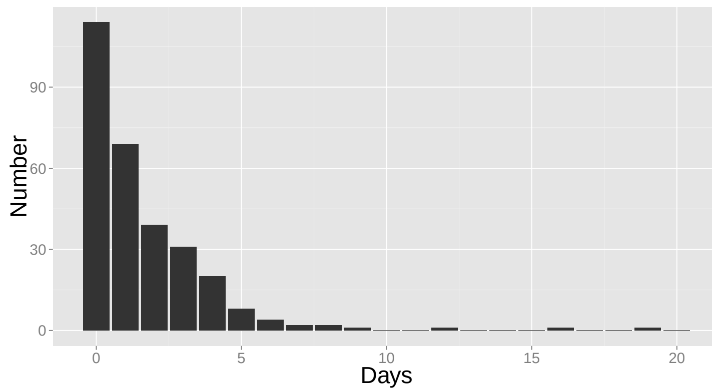

Figure 44: Number of measles cases attending hospital and stay duration from 2000–2014

Table 18: 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

August 2014. Calculations were based on the assumption that 5 days of work were lost for each case; however, individuals under 15 years of age were not assumed to be employed and therefore did not suffer an income loss. If the case were less than 20 years of age, it was assumed there was an income loss of 5 days for the care giver, in addition to the wage loss of the case if 15–19 years of age. Total wage lost for the 247 cases and care givers was estimated to be $210,436. This consisted of $107,820 for the cases and $102,616 for the care giver, but did not include wage losses for cases under 15 years of age. Overall, the cost per case from 2008–2014 was estimated to be $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 did several things. Primarily, we used Equation **??** to estimate the proportion of the naïve populations in each DHB (Figure 10 and Table 13) and the national level requiring vaccination to reduce the R_v to <1 (Section 5). We assumed that the cases prevented by this was 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 used these values of numbers of predicted cases prevented and numbers expected despite additional vaccination to calculate the savings. The cost figures above were used to estimate what the savings for vaccinating additional populations was, using estimated per case costs saved. The costs of the catch up vaccination schemes were estimated to be two differnt values, to determine how sensitive the benefit–cost ratio ((B/C) was to differing vaccination costs. Values of $20 and $50 per vaccine were used. Thus the costs of the expected measles-related costs due to constant introduction of measles despite increased population immunity and the vaccination schemes were used to estimate the costs of additional vaccine programs and costs from continued measles introductions. The financial savings from reduced measles cases and these costs were used to work out the estimated B/C ratio. A B/C ratio > 1 means that the program benefits exceed their costs. A B/C value less than one suggests the costs are higher than the economic benefits. Lastly, benefits were assessed over a 10–year time period, using a discounting rate of 3% discount per year for the costs, as is common for healthcare discounting [19]. Thus:

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

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%).

6.4 Benefit–cost analyses results

The estimated vaccinaton rates, with percentages are shown in Table 19.

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 the equation 5 are shown in Figure 45.

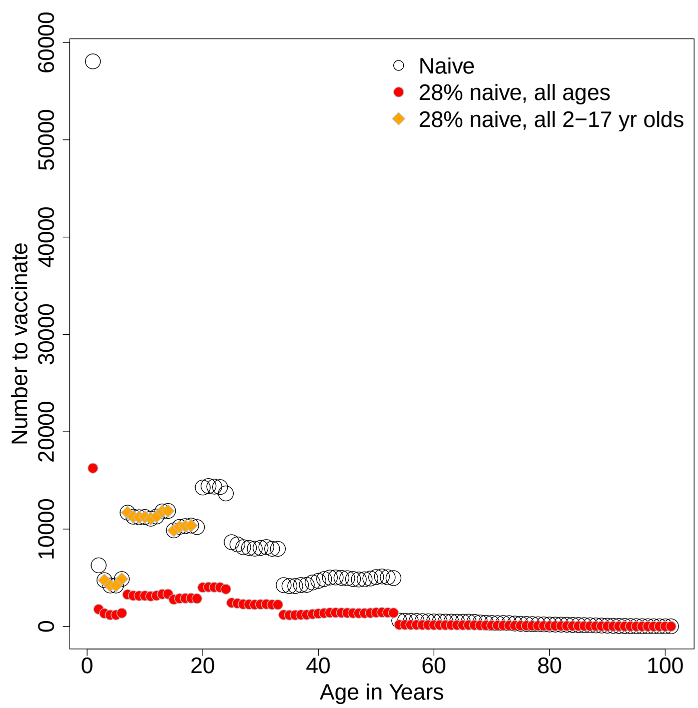

Figure 45: The estimated proportion of the currently naïve New Zealand population requiring additional vaccination given alternative R_v values to reduce the R_v to one (Section 5, Tables **??** and **??**)

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 were <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 stochastically 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

Table 19: DHB and National level catch up vaccination rates and estimated outbreak sizes post 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

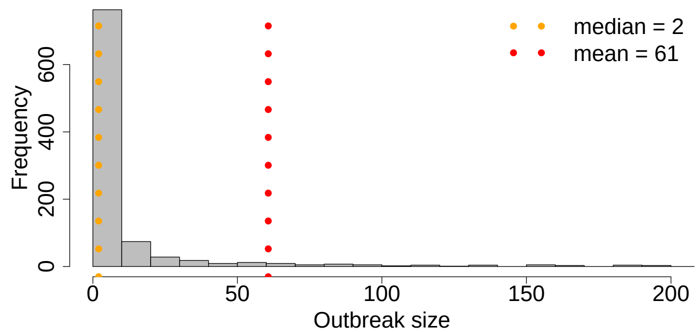

Figure 46: A subset of the expected number of measles cases from 1000 simulations of a model (Section 5) in a homogeneously mixed population in New Zealand with 28% of the currently 11% susceptible to measles infection vaccinated, using an R_v <1. The full distribution of results can be seen in Figure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

1000 simulations low (2 cases). Thus most measles introductions will be single cases 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 were very rarely predicted and this does not take into account spatial variation or heterogeneous contact rates.

Vacc Vacc.costs Wages.saved Manage.saved Hospitalised Hosp.saved Costs.save Outbreak OB.costs Benefit/cost

For the cost analyses we used the values from the above cost section (Section 6.2). Specifically, we used the average cost of a case for the analyses to be \$839 lost in wages and \$1710 in hospitalisation costs for those attending hospital, with 17% of cases predicted to be hospitalised (Table 15). 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 19. The benefit–cost results are in Table 20 and Table 21, 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 (Tables 20 and 21).

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

Table 20: Benefit–cost analyses with 20 dollars per vaccine. *Vacc* is numbers to vaccinate; *Vacc.costs* is cost for the catch up vaccination programme; *Wages.saved* is wages of care givers and cases saved; *Manage.saved* is management costs saved; *Hospitalised* is number of hospitalisations saved; *Hosp.saved* is the hospitalisation costs saved; *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 the same discounted costs as before; *Benefit/cost* is the benefit–cost ratio.

DHB	Vacc	Vacc.costs	Wages.saved	Manage.saved	Hospitalised	Hosp.saved	Costs.save	Outbreak	OB.costs	Benefit.cost
Auckland	17920	358400	26142401	55010965	5297	9057921	79260619	82	209524	139.56
Bay of Plenty	4585	91700	7078643	14895456	1434	2452636	21461595	71	181417	78.58
Canterbury	13687	273740	20719105	43598824	4198	7178837	62817837	62	158420	145.36
Capital and Coast	10461	209220	15440117	32490349	3129	5349752	46812580	96	245296	102.99
Counties Manukau	18880	377600	27605617	58089983	5594	9564902	83696914	50	127758	165.62
Hawke's Bay	3751	75020	5743794	12086558	1164	1990132	17414493	56	143089	79.84
Hutt Valley	4388	87760	6574404	13834395	1332	2277925	19932803	86	219745	64.82
Lakes	2886	57720	4356088	9166434	883	1509314	13207136	62	158420	61.10
MidCentral	4628	92560	7003972	14738327	1419	2426764	21235202	75	191638	74.72
Nelson Marlborough	2356	47120	3700829	7787585	750	1282278	11220469	90	229965	40.49
Northland	3071	61420	4772232	10042118	967	1653502	14468834	70	178862	60.22
South Canterbury	893	17860	1407842	2962496	285	487795	4268408	72	183972	21.15
Southern	8371	167420	12681485	26685411	2570	4393931	38448739	102	260627	89.82
Tairawhiti	1359	27180	2039609	4291911	413	706692	6183849	47	120093	41.99
Taranaki	2899	57980	4414818	9290019	895	1529663	13385198	68	173752	57.76
Waikato	11331	226620	16988072	35747682	3442	5886094	51505793	95	242741	109.74
Wairarapa	720	14400	1129294	2376352	229	391282	3423884	59	150755	20.73
Waitemata	17291	345820	25819386	54331250	5232	8946002	78281277	70	178862	149.20
West Coast	685	13700	1061335	2233347	215	367736	3217840	50	127758	22.75
Whanganui	1378	27560	2122670	4466695	430	735471	6435680	58	148200	36.62

For numbers to vaccinate see Table 13
Proportion of cases hospitalised 0.17
Wage losses per case $839 and cost per hospitalised case $1710
Based on 10 introductions of measles, one per year

Table 21: Benefit–costs analyses with 50 dollars per vaccine. *Vacc* is numbers to vaccinate; *Vacc.costs* is cost for the catch up vaccination programme; *Wages.saved* is wages of care givers and cases saved; *Manage.saved* is management costs saved; *Hospitalised* is number of hospitalisations saved; *Hosp.saved* is the hospitalisation costs saved; *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 the same discounted costs as before; *Benefit/cost* is the benefit–cost ratio.

DHB	Vacc	Vacc.costs	Wages.saved	Manage.saved	Hospitalised	Hosp.saved	Costs.save	Outbreak	OB.costs	Benefit.cost
Auckland	17920	896000	26142401	55010965	5297	9057921	79260619	82	209524	71.70
Bay of Plenty	4585	229250	7078643	14895456	1434	2452636	21461595	71	181417	52.26
Canterbury	13687	684350	20719105	43598824	4198	7178837	62817837	62	158420	74.54
Capital and Coast	10461	523050	15440117	32490349	3129	5349752	46812580	96	245296	60.93
Counties Manukau	18880	944000	27605617	58089983	5594	9564902	83696914	50	127758	78.09
Hawke's Bay	3751	187550	5743794	12086558	1164	1990132	17414493	56	143089	52.67
Hutt Valley	4388	219400	6574404	13834395	1332	2277925	19932803	86	219745	45.39
Lakes	2886	144300	4356088	9166434	883	1509314	13207136	62	158420	43.63
MidCentral	4628	231400	7003972	14738327	1419	2426764	21235202	75	191638	50.20
Nelson Marlborough	2356	117800	3700829	7787585	750	1282278	11220469	90	229965	32.26
Northland	3071	153550	4772232	10042118	967	1653502	14468834	70	178862	43.53
South Canterbury	893	44650	1407842	2962496	285	487795	4268408	72	183972	18.67
Southern	8371	418550	12681485	26685411	2570	4393931	38448739	102	260627	56.61
Tairawhiti	1359	67950	2039609	4291911	413	706692	6183849	47	120093	32.89
Taranaki	2899	144950	4414818	9290019	895	1529663	13385198	68	173752	42.00
Waikato	11331	566550	16988072	35747682	3442	5886094	51505793	95	242741	63.64
Wairarapa	720	36000	1129294	2376352	229	391282	3423884	59	150755	18.33
Waitemata	17291	864550	25819386	54331250	5232	8946002	78281277	70	178862	75.02
West Coast	685	34250	1061335	2233347	215	367736	3217840	50	127758	19.86
Whanganui	1378	68900	2122670	4466695	430	735471	6435680	58	148200	29.64

For numbers to vaccinate see Table 13
Proportion of cases hospitalised 0.17
Wage losses per case $839 and cost per hospitalised case $1710
Based on 10 introductions of measles, one per year

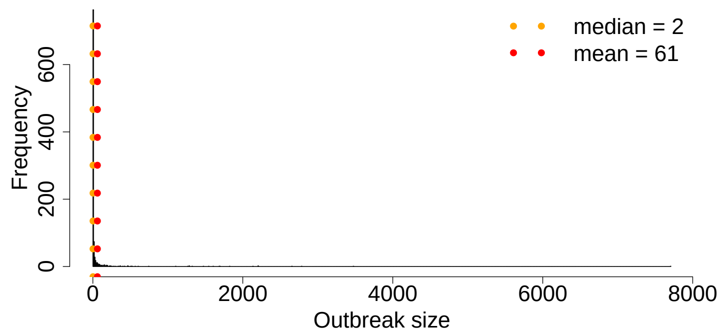

Figure 47: The distribution of the expected number of measles cases from 1000 simulations of a model (Section 5) in a homogeneously mixed population in New Zealand with 28% of the currently 11% susceptible to measles infection vaccinated, using an R_v <1, showing the rare but possible large epidemic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

the appropriate figure (28% of currently naïve) by vaccinating all the currently naïve 2–17 year olds, so pre-school and school age children.

6.5 Benefit–cost analyses discussion

Our estimates of the costs of the measles outbreaks in New Zealand suggest that measles management 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 Tables 20 and 21).

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. In addition to this information, similar data would be needed for cases occurring outside the period 2011–2013 at publicly funded hospitals. In addition, similar data would be needed for non-publicly funded hospitals, e.g. 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. However, other studies have demonstrated direct costs required to manage measles are not linear.

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 (Dayan et al., 2005). They estimated direct costs per case to be less than US$500. 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 [27]. 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) [40]. The work by [40] also finds that measles vaccination is extremely cost effective, however, in their analyses they also include the costs of mumps and rubella (see Table 22). However, the cost of measles in their analyses was substantially higher than mumps and rubella (Table 22).

Our estimates for the benefit–cost ratio of catch up vaccination are also much higher than those in some studies. If we presume the R_0 estimated for measles in New Zealand is representative and following 28% vaccination of the naïve 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, [40] estimate the B/C ratio to be much greater than one for MMR vaccination (see Table 23). As stated above, these authors also consider the costs and benefits of mumps and rubella, so making direct comparison difficult without reanalysis.

Our results 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]). The benefits of catch up vaccination are clear once R_v is greater than one (Tables **??** and **??**, and previous interim report). However, as noted in our previous report,

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 22: Summary of all measles, mumps, and rubella diseases and measles-mumps-rubella vaccination costs, USA, from [40]

if 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.

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 23: Benefit–cost ratios, USA, from [40]

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 (see previous report) 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 $1,710
- 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.

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