

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

David T S Hayman^{*1}, Jonathan C Marshall¹, Nigel P French¹,
Tim Carpenter², and Mick G Roberts³

^{1m}EpiLab, Infectious Diseases Research Centre, Massey University,
Palmerston North 4442, New Zealand

²EpiCentre, Infectious Diseases Research Centre, Massey
University, Palmerston North 4442, New Zealand

³Institute of Natural & Mathematical Sciences, New Zealand
Institute for Advanced Study and the Infectious Disease Research
Centre, Massey University, Private Bag 102 904, North Shore Mail
Centre, Auckland, New Zealand

1 Abstract

New Zealand has been working towards elimination of endemic (domestic) measles virus transmission, but has suffered from small, yet significant outbreaks after measles introductions from abroad. In this draft final report we review the draft *Progress Towards Measles Elimination in New Zealand - Final* report from the New Zealand Ministry of Health to the World Health Organization (WHO) Western Pacific Region. We identify additional analyses that may help understand risk of infection in New Zealand. Here we present the results of statistical analyses of risk factors for measles cases in New Zealand during outbreaks since 2007 until mid-2014. We provide cost analyses for the measles outbreaks in New Zealand, and include modelling of measles outbreaks, including pre- and post-vaccination scenarios, based on the numbers of naïve people at the District Health Board (DHB) and national level. We provide benefit–cost analyses using the results from those model simulations, along with a number of alternative vaccination strategies to achieve different vaccination coverage levels. Our key findings are:

^{*}D.T.S.Hayman@massey.ac.nz

- The *Progress Towards Measles Elimination in New Zealand - Final* report was of high quality and contained substantial information and useful analyses.
- The regression analyses suggest that age is a particularly strong risk factor for measles. People of European ethnicity make up the majority of cases. However, our analyses also highlight other groups that are at greater risk of measles on a per capita basis. Increased wealth (NZDep 1–3) was a risk factor. Pacific people are at greater risk per capita. However, this was driven by young Pacific children, as 2–24 year old Pacific people are less at risk than European and Maori, as are 5–17 year old Asian children.
- Of the 11% of the overall population of New Zealand that are currently considered to be immunologically naïve, it was estimated that approximately 28% would require additional vaccination to ensure measles does not persist, leading to an additional 131,500 vaccinations.
- New Zealand is at risk of frequent measles importation due to travel and endemic measles elsewhere in the globe.
- Peak overall overseas travel rates, and thus presumably risk from measles importation, is in December. However, New Zealander and immigrant or non-New Zealander travel is otherwise out of phase, with peak travel for New Zealanders during winter, and non-New Zealanders during summer.
- Analyses of outbreak data suggest that measles basic reproduction number (R_v , the number of secondary infections in a partially vaccinated population) values often include or exceed one, including 2013–2014 outbreaks. As analysed from data until June, the last outbreak to end in 2014 had an R_v well above 1 (mean estimate 3.66, range 3.4–3.92). The range of estimates for R_v between 2009–2014 was 0.18–3.92. This analysis suggests improved vaccination is a requisite to prevent measles persisting in the population and that large outbreaks could occur.
- The cost of 2014 measles cases is estimated to be approximately \$1,041,186 due to earnings lost relating to cases and contacts, case management and hospitalisation costs.
- The mean wage loss per measles case is estimated to be approximately \$839.
- The mean cost per measles case attending hospital is estimated to be \$1,877 per case, and approximately 17% of measles cases attend hospital
- The mean public health service cost per case is \$1,765 excluding hospitalisation costs.
- The average number of contacts requiring quarantine was 2.11, requiring 7.3 days of quarantine on average, at a cost of \$170.4 per day.

- The benefit–cost (B/C) ratio analyses suggest additional vaccination is extremely beneficial financially ($B/C > 1$), with vaccine costs required to exceed approximately \$8,214 per vaccine before the costs exceed the benefits.
- Measles introductions to New Zealand with a median size of 2 cases per year were predicted by simulation following catch up vaccination to ensure R_v is < 1 . Thus, typically individual cases and secondary cases will be the expectation. However, the mean of 61 cases was predicted, because peak outbreak sizes of tens, hundreds, and very rarely up to many thousands are predicted following importation, despite R_v being one and the outbreak predicted to die out following additional vaccinations. Thus, increased vaccination beyond the 28% of the currently 11% naïve population required may be useful.

2 Background

As a member of the World Health Organization (WHO) Western Pacific Region, New Zealand is committed to work towards measles elimination, defined as the interruption of endemic (domestic) measles virus transmission, as achieved in the Americas in 2002. The Western Pacific Region is expected to be the second WHO region to achieve measles elimination and it was announced in March 2014 that Australia, Macao, Mongolia and the Republic of Korea have achieved measles elimination.

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

Previous measles analyses, including two in New Zealand by Prof. Roberts, estimated the interruption of measles virus transmission can be achieved by herd immunity when approximately 95 percent of the population is homogeneously immune to measles [28, 27]. Thus, while New Zealand immunisation activities have led to measles outbreaks becoming less frequent, with decreasing numbers of cases, outbreaks still occur (as described above). Current estimates suggest that approximately 85 to 90 percent of the population is immune to measles (see subsection 4.3), thus the reasons for the ongoing outbreaks are likely due to overall population immunity being less than 95 percent and there being pockets of susceptible, non-immune population remaining. Since 2009, all the outbreaks in New Zealand have been linked to infections acquired (imported) from overseas,

though previous work suggests these outbreaks still largely affect school-aged children (especially young adults) and children under two years of age. Those under two year olds are thought to 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 size of the 2013–2014 outbreaks, prevention of further measles outbreaks is a priority for the Ministry.

- In this section we review the confidential report to the Western Pacific Regional Verification Commission for Measles Elimination risk assessment provided by the Ministry, titled *Progress Towards Measles Elimination in New Zealand - Final*.

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

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

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

The report concludes that New Zealand's surveillance system has been performing well and that the Ministry is confident that measles has not been circulating since June 2012 and has not become endemic in NZ. We agree with the statement that measles did not become endemic and provide some preliminary analyses on the outbreaks since endemic measles elimination (see section 5) that give information regarding the likelihood of measles persisting within the population and becoming endemic, including analysis of the 2013–2014 outbreaks.

We agree with the *Progress Towards Measles Elimination in New Zealand - Final* report conclusions that testing for measles is performed appropriately

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

Thus in this report we include regression analyses that help understand risk factors for being measles cases in New Zealand (section 4), descriptions of the New Zealand population in terms of vaccination coverage and immunity (subsection 4.3), and we use those data to model the likely measles outbreak sizes in each District Health Board (DHB) and the country (section 5). We estimate the costs of previous and the 2013–2014 measles outbreaks (subsection 6.1) and use these estimates, the modelling results and the population data to estimate the benefit–cost ratio for catch-up vaccination programmes (subsection 6.3). This report includes further developments of the analyses provided in previous interim reports.

4 Risk analyses

In this section we provide work that we believe will help inform the Ministry of Health regarding the understanding of risk from measles. These analyses are intended to build on the analyses already included in the *Progress Towards Measles Elimination in New Zealand - Final* report reviewed above. We include multivariate modelling to account for confounding within the univariate analyses for measles cases in New Zealand (subsection 4.1), descriptive analyses of risk of infection due to previous vaccination history (subsection 4.3), and current rates of immunity within the population (subsection 4.3). In light of the apparent increasing trend in measles incidence in the last few years (Figure 1), we reviewed the information on measles importation and the origins of the introductions of measles into New Zealand. To help understand the risk of measles importation, with a particular goal of enabling the Ministry to better inform travellers and understand high risk periods, we sought to quantitatively evaluate the risk of measles importation from travel (subsection 4.6). The details of the methods and approaches are given in the text below for each section.

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 analy-

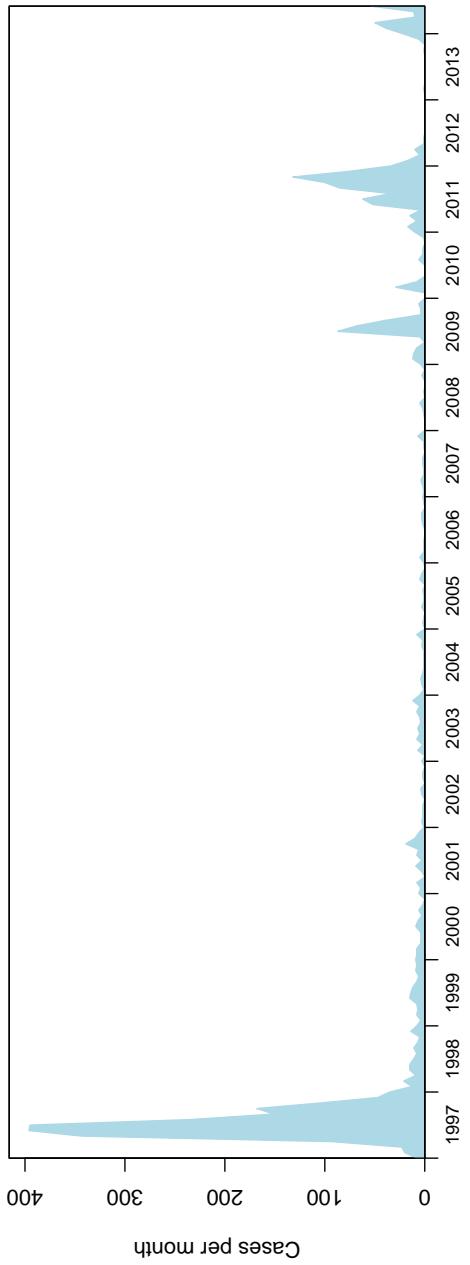


Figure 1: Measles incidence in New Zealand from 1997 to 2014

ses of those ESR data (not shown) suggested that denominator data were required to perform multivariate analyses to adjust for confounding due to a lack of independence among risk factors. Specifically Age \times Prioritised Ethnicity \times NZDep data for New Zealand were required to adjust for confounding and test whether interactions among covariates provide additional information on risk in demographically-defined subgroups over the univariate analyses performed in the *Progress Towards Measles Elimination in New Zealand - Final report*. These Age \times Prioritised Ethnicity \times NZDep data were provided to us on 3 July 2014 by the University of Otago. We used these denominator data to determine if there were interactions among specific age categories, Prioritized Ethnicities, and NZDep that might exist among cases allowing better understanding of measles infection risk.

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

With the 10 NZDep classes, Prioritized Ethnicities, and the age classes above, the numerous combinations of variables led us to have 250 categories. Because for measles cases the very young appear to be disproportionately affected (Figure 2), we split the 0–5 age category into additional classes. Following discussion with the Ministry, these were 0–1, 2–4, and 5 years old for each of the University of Otago denominator data, assuming equal numbers of young were born into each age group over the last five years (which is supported by data from NZ statistics [32]). The 5 year olds were added to the 6–17 year old category. No breakdown of 6–17 year category was performed as constant birth rates for the period could not be assumed.

This large number of categories, some with small population sizes, leads to both overdispersion and zeroinflation, as there are many categories with zero cases in, particularly in the adult age classes. Furthermore, initial preliminary analyses, including multi- and univariate analyses (not shown) suggested little effect of *individual* NZDep classifications and several higher order interactions, and therefore we reduced the number of NZDep categories from ten to three: NZDep 1–3 (least deprived), NZDep 4–7, and NZDep 8–10 (most deprived) (www.otago.ac.nz) following discussion with the Ministry regarding the most appropriate categories. We also incorporated the 65+ age classes into the 25–64 age category, to make a 25+ age category. By doing so, we reduce the zeroinflation present in the data.

The Prioritized Ethnicities for cases are: European; Maori; Pacific Peoples; Asian; Middle Eastern/Latin American/African (MLA); Other Ethnicity; Residual Categories. For the analyses in this report only the first five are used, as these categories cover the overwhelming number of cases, with only 1.9%

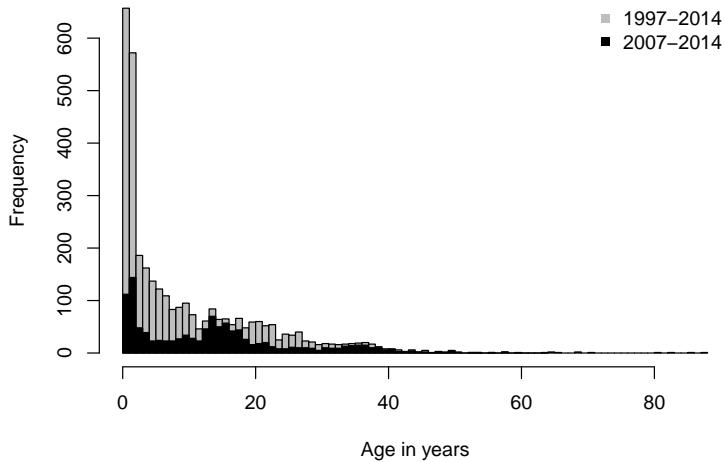


Figure 2: Numbers and age of measles cases in years in New Zealand for two periods, 1997–2014 and 2007–2014

(22/1137) of cases having no Prioritized Ethnicity.

The numbers of cases per category and population sizes for the complete data set from 2007–2014 can be seen in Table 1. Subsequent regression analyses (not shown) also suggested that the MLA category was over- or underrepresented in per capita rates given the very small sample sizes for this classification (Figure 4, Table 1), leading to very large standard error in regression analyses. However, there are numerous issues with the data for MLA ethnicity category above and beyond the small population sizes (see Table 1), creating issues for estimating the denominator data for this group (University of Otago, personal communication). Thus, we removed this grouping for our subsequent analyses and are left with Asian, European, Maori and Pacific as Prioritized Ethnicities. This left us with 1102/1115 (99%) of the measles cases with Prioritized Ethnicity recorded from 2007, and 1102/1137 (97%) of all measles cases recorded since 2007 (Table 1). The breakdown of cases and per capita measles values can be see in Figure 3 and Figure 4. Two way interactions are shown in the Appendix (section 8, Figure 32, Figure 33, Figure 34, Figure 35, Figure 36, Figure 37).

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 quasipoisson regression model. We also account for differences in population sizes by using an offset term, the $\log(\text{population size})$. We used a model simplification approach, by beginning our analyses with all terms and all interactions, and then simplifying

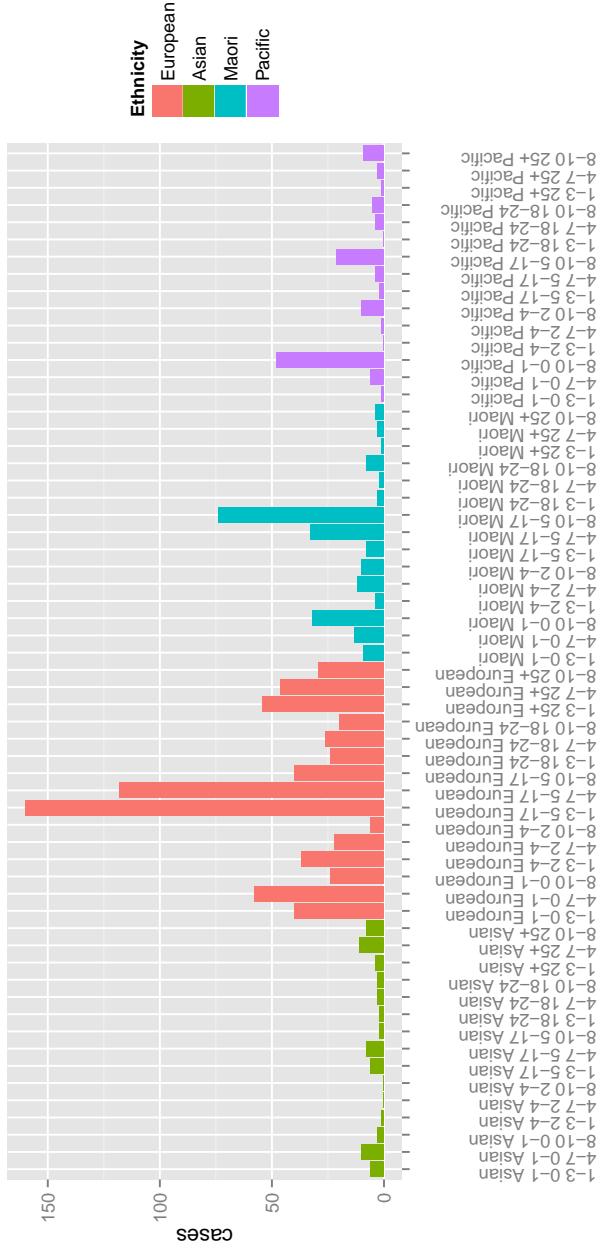


Figure 3: Measles cases from 2007–2014 (Table 1). The x-axis shows NZDep:Age Range:Prioritized ethnicity. Per capita values are in Figure 4

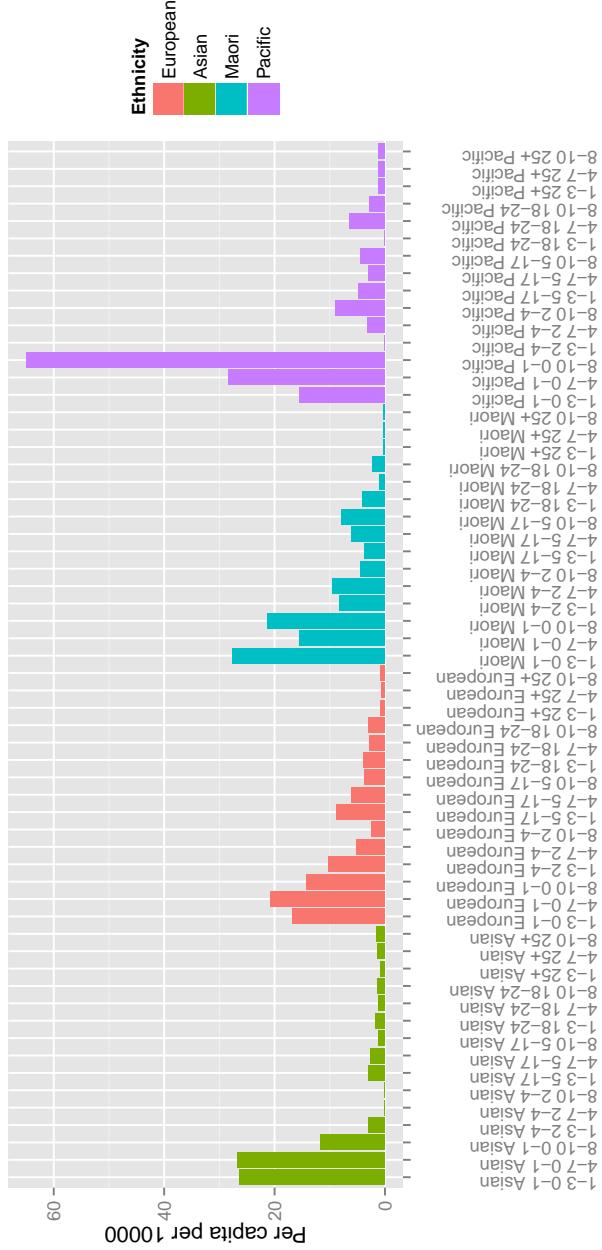


Figure 4: Per capita measles values from 2007–2014 (Table 1). The x-axis shows NZDep:Age Range:Prioritized ethnicity. Absolute cases are in Figure 3

NZDep	Age	Ethnicity	Population	Cases	Per capita
1-3	0-1	Asian	2269	6	26.4434
4-7	0-1	Asian	3748	10	26.6809
8-10	0-1	Asian	2583	3	11.6144
1-3	2-4	Asian	3403	1	2.9386
4-7	2-4	Asian	5623	0	0.0000
8-10	2-4	Asian	3874	0	0.0000
1-3	5-17	Asian	20625	6	2.9091
4-7	5-17	Asian	29721	8	2.6917
8-10	5-17	Asian	16777	2	1.1921
1-3	18-24	Asian	12057	2	1.6588
4-7	18-24	Asian	23904	3	1.2550
8-10	18-24	Asian	21063	3	1.4243
1-3	25+	Asian	54258	4	0.7372
4-7	25+	Asian	86055	11	1.2783
8-10	25+	Asian	54759	8	1.4609
1-3	0-1	European	23961	40	16.6938
4-7	0-1	European	28051	58	20.6766
8-10	0-1	European	16866	24	14.2298
1-3	2-4	European	35942	37	10.2944
4-7	2-4	European	42076	22	5.2286
8-10	2-4	European	25299	6	2.3716
1-3	5-17	European	180875	160	8.8459
4-7	5-17	European	194100	118	6.0793
8-10	5-17	European	106731	40	3.7477
1-3	18-24	European	63051	24	3.8064
4-7	18-24	European	94422	26	2.7536
8-10	18-24	European	68016	20	2.9405
1-3	25+	European	619698	54	0.8714
4-7	25+	European	734550	46	0.6262
8-10	25+	European	371985	29	0.7796
1-3	0-1	Maori	3265	9	27.5651
4-7	0-1	Maori	8378	13	15.5168
8-10	0-1	Maori	15094	32	21.2005
1-3	2-4	Maori	4897	4	8.1683
4-7	2-4	Maori	12568	12	9.5481
8-10	2-4	Maori	22642	10	4.4166
1-3	5-17	Maori	21750	8	3.6782
4-7	5-17	Maori	53963	33	6.1153
8-10	5-17	Maori	94758	74	7.8094
1-3	18-24	Maori	7329	3	4.0933
4-7	18-24	Maori	20862	2	0.9587
8-10	18-24	Maori	35664	8	2.2432
1-3	25+	Maori	35934	1	0.2783
4-7	25+	Maori	87192	3	0.3441
8-10	25+	Maori	140820	4	0.2841
1-3	0-1	MLA	273	0	0.0000
4-7	0-1	MLA	519	2	38.5356
8-10	0-1	MLA	553	1	18.0832
1-3	2-4	MLA	410	0	0.0000
4-7	2-4	MLA	778	0	0.0000
8-10	2-4	MLA	830	1	12.0482
1-3	5-17	MLA	1832	0	0.0000
4-7	5-17	MLA	3121	0	0.0000
8-10	5-17	MLA	3250	1	3.0769
1-3	18-24	MLA	906	0	0.0000
4-7	18-24	MLA	1806	0	0.0000
8-10	18-24	MLA	2076	2	9.6339
1-3	25+	MLA	4569	0	0.0000
4-7	25+	MLA	7452	5	6.7096
8-10	25+	MLA	6342	1	1.5768
1-3	0-1	Pacific	643	1	15.5521
4-7	0-1	Pacific	2113	6	28.3956
8-10	0-1	Pacific	7389	48	64.9614
1-3	2-4	Pacific	964	0	0.0000
4-7	2-4	Pacific	3169	1	3.1556
8-10	2-4	Pacific	11084	10	9.0220
1-3	5-17	Pacific	4212	2	4.7483
4-7	5-17	Pacific	13419	4	2.9808
8-10	5-17	Pacific	47165	21	4.4525
1-3	18-24	Pacific	1707	0	0.0000
4-7	18-24	Pacific	6174	4	6.4788
8-10	18-24	Pacific	18189	5	2.7489
1-3	25+	Pacific	8580	1	1.1655
4-7	25+	Pacific	26688	3	1.1241
8-10	25+	Pacific	74757	9	1.2039

Table 1: Measles cases (Cases), population sizes (Population) and per capita rates per 10,000 (Per capita) of measles in specific age (Age), ethnicity (Ethnicity) and socio-economic deprivation (NZDep) categories from 2007-2014

Age range	Proportion
2-5	0.04
5-11	0.15
5-16	0.27
5-18	0.31
11-16	0.14
11-18	0.18
0-29	0.72
0-44	0.89
>8	0.8

Table 2: Proportions of the naïve population the would be covered if vaccinated by age groups

	Df	Deviance	Resid. Df	Resid. Dev	F	Pr(>F)
NULL			59	1532.80		
Age	4	1345.17	55	187.63	204.01	0.0000
Ethnicity	3	19.88	52	167.75	4.02	0.0141
NZDep	2	17.10	50	150.65	5.19	0.0102
Age:Ethnicity	12	80.80	38	69.85	4.09	0.0004

Table 3: Significance of different predictor variables for measles risk factors from 2007-2014, estimated using Equation 1 and a quasipoisson error structure

the models through removal of non-significant higher order interaction terms. Thus, the final model that remained with all significant interaction terms had the following linear predictor:

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

Where α is the intercept, y signifies cases, a signifies age, e signifies Prioritized Ethnicity, n signifies NZDep, and ϵ is the error term.

4.2 Regression analyses results

The cases and per capita measles values are in Figure 3 and Figure 4. The distribution of the measles cases per category used in the regression analyses are in Figure 5. The predicted values from the regression model plotted against the reported cases are shown in Figure 6, and the residuals are shown in Figure 7. The significance of the different predictor variables can be seen in the ANOVA results (Table 3). 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 4.

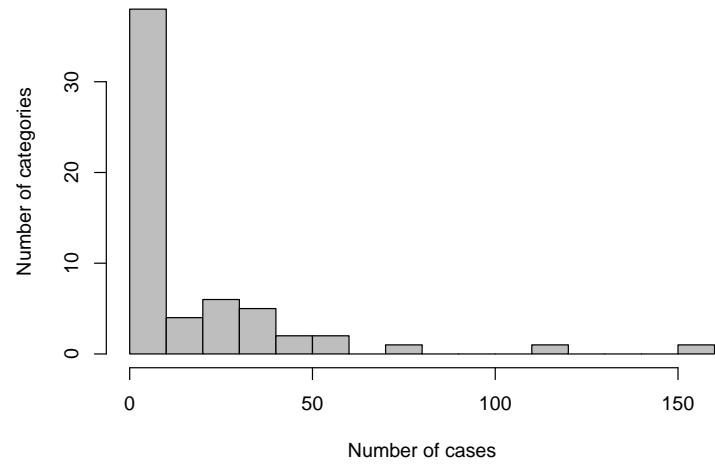


Figure 5: Distribution of measles cases per category (Table 1) used in the final regression model (Equation 1)

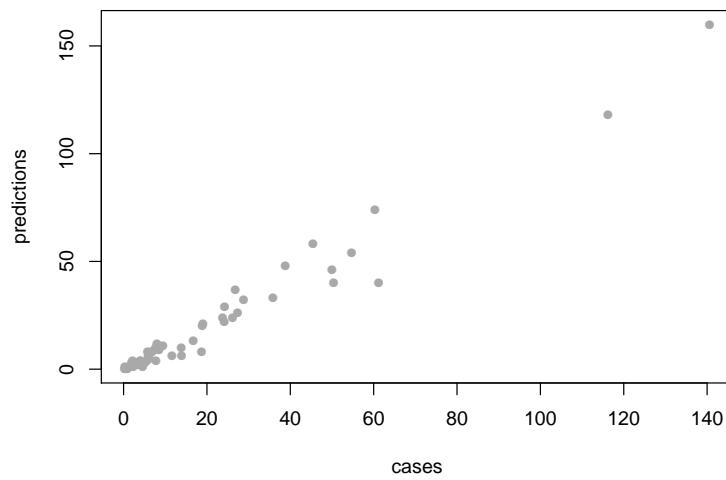


Figure 6: Regression model predictions plotted against the case data (Table 1), estimated using Equation 1 and a quasipoisson error structure

	Estimate	Std. Error	t value	Pr(> t)
(Intercept)	-6.1644	0.1267	-48.65	0.0000
Age2-4	-1.0351	0.1972	-5.25	0.0000
Age5-17	-0.9954	0.1368	-7.28	0.0000
Age18-24	-1.7204	0.1926	-8.93	0.0000
Age25+	-3.1697	0.1622	-19.55	0.0000
EthnicityAsian	0.2464	0.3168	0.78	0.4415
EthnicityMaori	0.2081	0.2121	0.98	0.3327
EthnicityPacific	1.2200	0.2134	5.72	0.0000
NZDep4-7	-0.2609	0.0948	-2.75	0.0090
NZDep8-10	-0.3043	0.1040	-2.93	0.0058
Age2-4:EthnicityAsian	-2.3148	1.3319	-1.74	0.0903
Age5-17:EthnicityAsian	-1.2453	0.4566	-2.73	0.0096
Age18-24:EthnicityAsian	-1.0187	0.5743	-1.77	0.0841
Age25+:EthnicityAsian	0.2344	0.4298	0.55	0.5887
Age2-4:EthnicityMaori	-0.1013	0.3644	-0.28	0.7826
Age5-17:EthnicityMaori	-0.1032	0.2521	-0.41	0.6846
Age18-24:EthnicityMaori	-0.5723	0.4409	-1.30	0.2022
Age25+:EthnicityMaori	-1.0349	0.5127	-2.02	0.0506
Age2-4:EthnicityPacific	-0.9798	0.4676	-2.10	0.0429
Age5-17:EthnicityPacific	-1.5709	0.3312	-4.74	0.0000
Age18-24:EthnicityPacific	-1.0354	0.5003	-2.07	0.0453
Age25+:EthnicityPacific	-0.6629	0.4279	-1.55	0.1296

Table 4: Summary of the regression model results, estimated using Equation 1 and a quasipoisson error structure, for measles risk factors for cases from 2007-2014

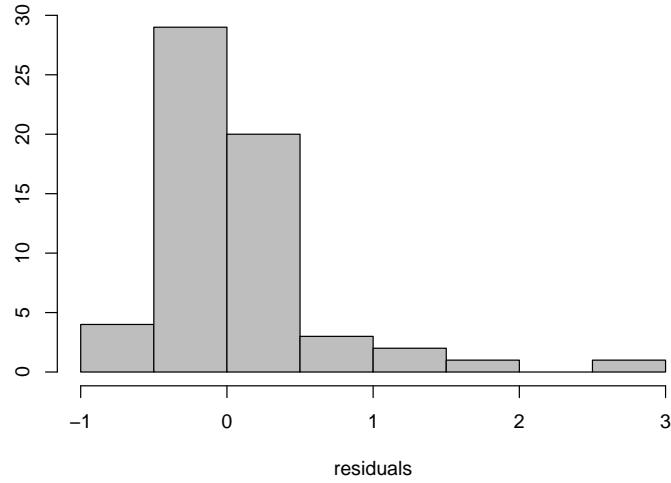


Figure 7: Histogram of residuals from the regression model (Equation 1) and a quasipoisson error structure

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 (Table 4). Indeed, all age categories are significantly less likely to be measles cases compared to 0–1 year olds, and the likelihood generally decreases with age (Table 4, Figure 3, Figure 4, see also Figure 2).

The majority of measles cases are among people of European ancestry (Table 1 and Figure 3). Indeed, the majority of cases were in more wealthy European 5–17 year olds (Figure 3). However, per capita rates for this large age class were lower than in the very young (0–1 year olds, Figure 4). People of Pacific origin are over-represented as measles cases on a per capita basis ($\beta = 1.22$, standard error (SE) = 0.21, p-value < 0.0001; Table 4), and in particular the 0–1 year old less wealthy (NZDep 8–10) (Figure 4). Note however that generally those people in NZDep levels 4–10 are less represented on a per capita basis (NZDep 4–7 $\beta = -0.26$, SE = 0.09, p-value 0.009; NZDep 8–10 $\beta = -0.3$, SE = 0.1, p-value == 0.006; Table 4), and in European and Maori ethnicities there is a trend in the opposite way than Pacific peoples, with the more wealthy more likely to be cases (Figure 4 and Figure 3).

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 5–17 age classes. In later measles outbreaks (since 2007) there has been a shift in the distribution of ages infected. The very young (<2 years old) are still

most likely to be infected, but school aged children and older teenagers are more likely to be represented than the under tens (Figure 2 and Figure 8). This pattern suggests that improving vaccination coverage in the young is reducing the burden of measles in those age categories (Table 1, Table 5, and subsection 4.5). Interestingly the regression results suggest risk of measles in the 5–17 year age category was greater for Europeans and Maori (Table 1, Table 4, Figure 4).

4.3 Vaccination history of measles infection and population immunity estimation methods

In this section we describe the vaccination history of the measles cases from 2007–2014 outbreaks using the data provided by ESR. We describe the population immunity levels at both a national level and for each DHB in New Zealand. To do this we use the census data from NZ statistics (Statistics New Zealand, 2013) and the vaccination and serosurvey data provided by the Ministry of Health at the commencement of this work. Specifically, we use the data in Table 5, derived from the serosurvey results and the National Immunisation Register (NIR) for under 6 year olds.

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

Table 5: Vaccination coverage (0–5 years) and serosurvey estimates of immunity (> 5 years) among different age classes used in these analyses, as provided by the Ministry of Health. Note these values are from vaccination records and serosurveys. Vaccine efficacy for 0–5 year olds was 99%, 6–13 year olds 96%, and for ≤ 14 equivocal serological results were considered non-immune

4.4 Vaccination history and measles infection results

The majority of the measles cases (82.8%, 955/1154) from 2007–2014 were in unvaccinated people (Figure 8). However, 12.6% (154/1154) cases had received their first dose of vaccine and 4.7% had received their second. A further

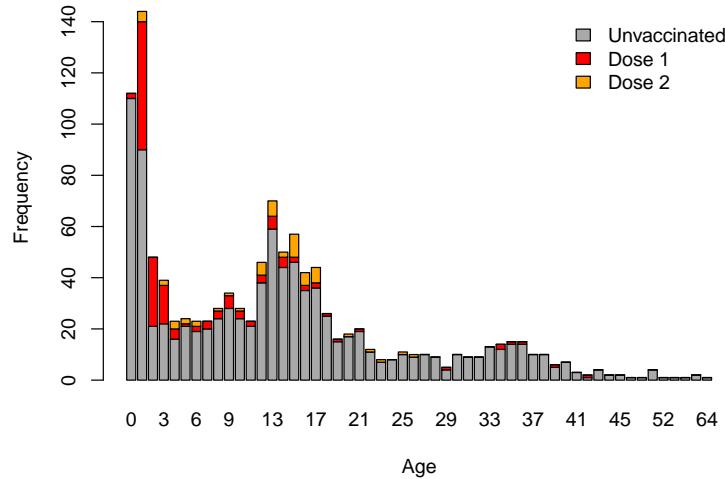


Figure 8: Age and vaccination status of measles cases, 2007–2014

breakdown of those data suggest that majority of those 'vaccine failures' were vaccinated around the first year of age (Figure 9). Plotting the cases (Figure 10) and vaccine failures (Figure 11) by year of birth to look at cohort effects appears to simply reflect the age of vaccine data (Figure 8).

4.5 Population immunity results

The majority of the naïve among the general New Zealand population are in their first years of life (Figure 14). However, the distribution of naïve at a national level shows that the recent MMR vaccination schemes are reducing the proportions of naïve population in the 3–5 year old age group to greater levels than in older young people (Figure 14). 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 15). The distribution of the numbers of naïve and the total naïve populations per DHB, assuming national immunisation and immunity rates are representative, are given in the following figures in the appendix (section 8):

- Northland: Figure 38
- Waitemata: Figure 39
- Auckland: Figure 40
- Counties Manukau: Figure 41
- Waikato: Figure 42
- Lakes: Figure 43

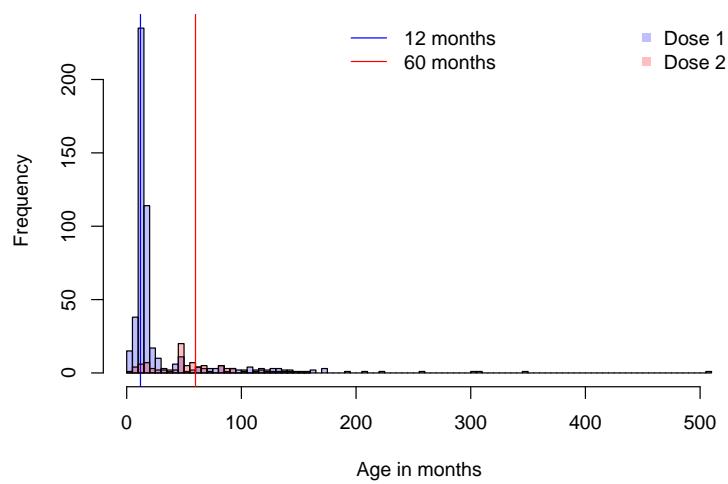


Figure 9: Age of vaccination of vaccinated measles cases, 2007–2014. Recommended vaccination age in months is shown for the measles, mumps, rubella (MMR) dose 1 (12 months) and MMR dose 2 (60 months)

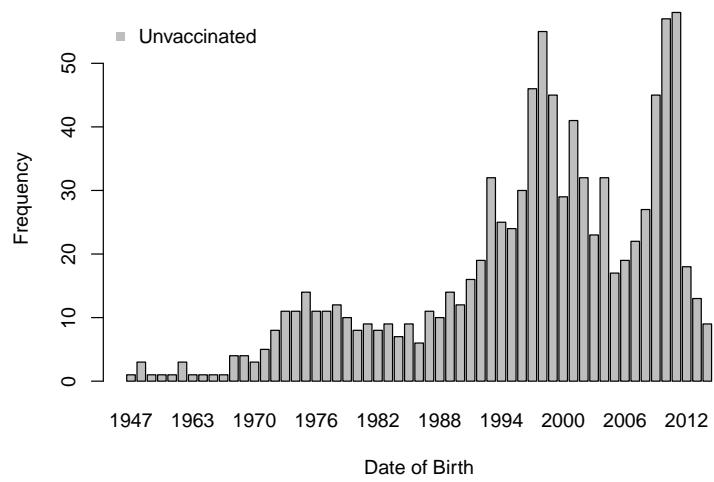


Figure 10: Year of birth and vaccination status of measles cases, 2007–2014

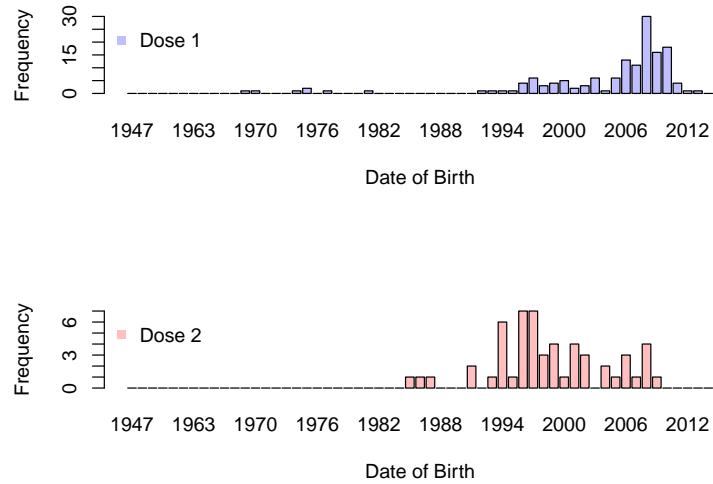


Figure 11: Year of birth and vaccination status of measles cases, 2007–2014

- Bay of Plenty: Figure 44
- Tairawhiti: Figure 45
- Taranaki: Figure 46
- Hawke's Bay: Figure 47
- Whanganui: Figure 48
- Mid-Central: Figure 49
- Hutt: Figure 50
- Capital and Coast: Figure 51
- Wairarapa: Figure 52
- Nelson Marlborough: Figure 53
- West Coast: Figure 54
- Canterbury: Figure 55
- South Canterbury: Figure 56
- Southern: Figure 57

Plotting the lower level data available from the NIR database highlights the issue of surveillance data requiring appropriate denominator data, as these analyses show that there is a lack of correspondence between the national census data and the NIR data (Figure 12, Figure 13)

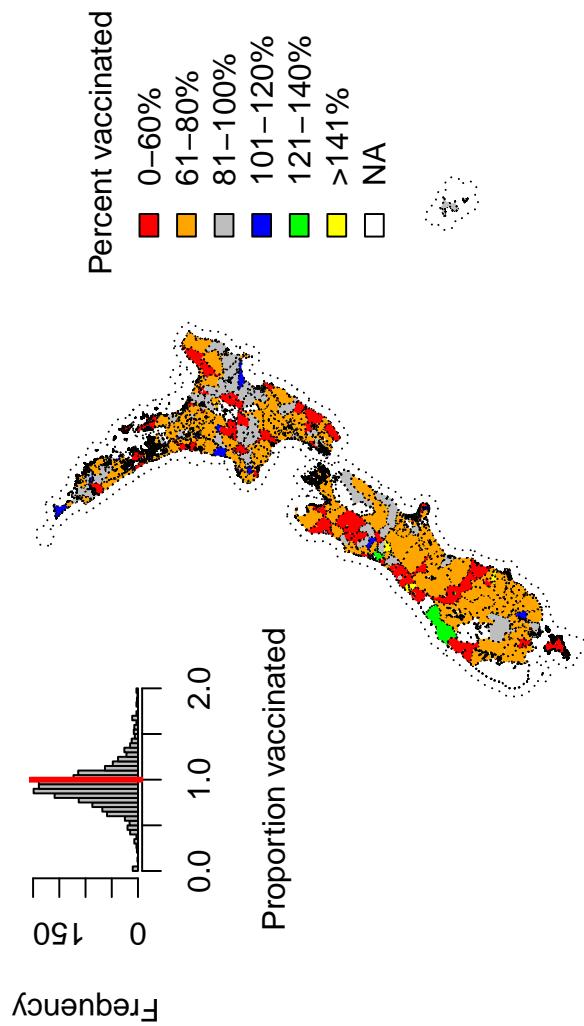


Figure 12: New Zealand population by age and estimated numbers of naïve people in each age class using National Immunisation Register (NIR) level data and national census data as the denominator. Note no values should be greater than 1 in the frequency distribution (upper left) or 100% on the map, demonstrating a lack of concordance between NIR and census data. The full distribution is shown in Figure 13

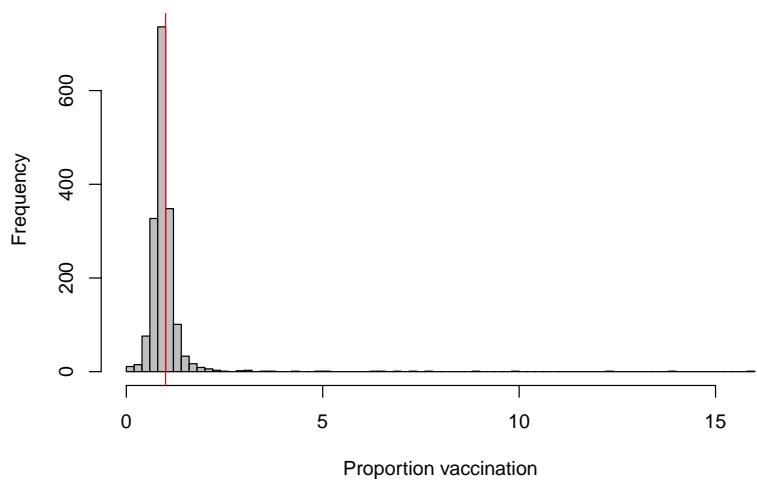


Figure 13: New Zealand population by age and estimated numbers of naïve people in each age class using National Immunisation Register level data and national census data as the denominator. Note no values should be greater than 1 (100% vaccine cover), and the maximum discordance in > 1600%.

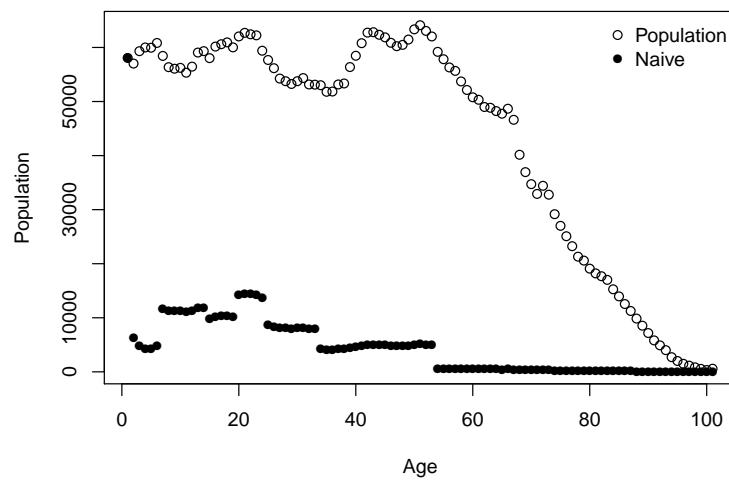


Figure 14: New Zealand population by age and estimated numbers of naïve people in each age class using national immunity data (Table 5)

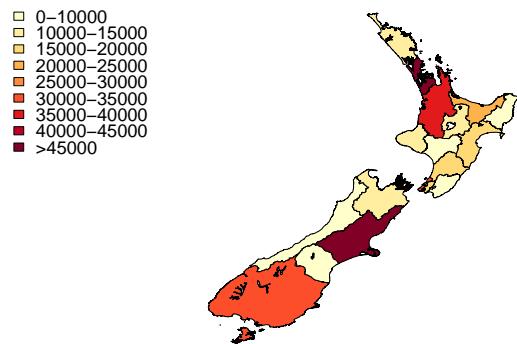


Figure 15: Numbers of naïve individuals per District Health Board, using national immunity data (Table 5)

4.6 Measles importation risk methods

For our measles importation risk analyses, we use arrivals data from New Zealand immigration and New Zealander travel destination data by country and year (www.immigration.govt.nz), to measure human movement to and from New Zealand. We collated country population size, measles incidence and measles vaccination cover from the WHO (www.who.int/research/en/). WHO measles coverage is the percent of children that receive one dose of measles vaccine by their second birthday. Note the immigration figures use all immigration of foreign nationals, coming for whatever purpose, and includes non-New Zealanders resident in New Zealand, but not yet holders of New Zealand passports. We use the WHO data to determine per capita measles cases for each year and use these data and the number of immigrants to New Zealand to begin to understand where measles is likely to be imported from. We use simple per capita rates for measles and the number of travellers to each country to score and map the risk of measles importation. We use 0–19 year old data for the immigration figures, as this is the only category available and it was determined this was more appropriate than using all age classes as > 19 year olds are believed to be immune to measles more or less globally. These data were not available for New Zealand travellers, so we use all travel. We present the data from 2013 because this year was the most recent with the most complete WHO measles data, and thus accounts for improved measles vaccination coverage following the United Nations Millennium Development Goals' improvements in measles vaccination coverage. Data for 2013 are incomplete, but substantially better than 2014.

4.7 Measles importation risk results

Globally, analyses of the most complete and recent year of data available, 2013, suggest measles incidence highest and vaccination coverage is lowest in less developed nations (Table 6 and Table 7, and Figure 16 and Figure 17). Immigration by 0–19 year old non-New Zealanders (whether for work, pleasure, etc.) is dominated by people from Australia Table 8 and Figure 18. A number of other countries then follow, including United Kingdom, China, Japan and the United States. Travel by New Zealanders is also dominated by that to Australia (Table 9 and Figure 19). Together, these mean that the greatest travel location for New Zealanders and immigration origin is from Australia (Table 10 and Figure 18). However, many South Pacific nations also appear in the most visited country list by New Zealanders. Though the precise interactions between these different risk factors are unknown, the most simple, a product of measles incidence in 2013 and immigration numbers of 0–19 year olds in 2013, suggest that those countries with greatest international travel, Australia, UK, China and South East Asian countries, pose the greatest risk to New Zealand for measles importation. Though immigration from and travel to some Asian countries is lower, some Asian countries also pose a high risk of measles importation to New Zealand. Note the South Pacific island do not appear to pose a greater risk, despite large numbers of travellers of New Zealand origin, perhaps because

country	incidence
Georgia	1806
Namibia	455
Equatorial Guinea	436
Angola	409
Lebanon	379
Nigeria	313
Somalia	311
Sudan	260
Lesotho	251
Uganda	217
Netherlands	159
Central African Republic	132
Turkey	100
Sri Lanka	100
Togo	85
Sudan	76
Gabon	75
Niger	71
Nepal	68
Benin	63
Ethiopia	57
Romania	51
Pakistan	49
Thailand	40
Indonesia	39
Qatar	36
Cameroon	35
Syrian Arab Republic	34
Djibouti	33
United Kingdom	31

Table 6: Highest measles incidence per million (2013)

country	cover
Central African Republic	29
Somalia	29
Equatorial Guinea	41
South Sudan	55
Lesotho	61
Pakistan	61
Vanuatu	65
Gabon	70
Marshall Islands	70
Papua New Guinea	70
Timor-Leste	70
Mali	72
Togo	72
Nigeria	73
Liberia	74
San Marino	74
Eritrea	75
Paraguay	75
Solomon Islands	76
Iraq	77
Ethiopia	78
Haiti	78
Yemen	78
Chad	79
Kenya	79
Congo	80
Djibouti	80
Mauritania	80
Zambia	80
Afghanistan	82

Table 7: Lowest national measles vaccine cover (%), 2013

country	immigration
Australia	130703
China	26380
United Kingdom	25155
Japan	20534
United States	20247
Germany	14793
France	12173
Korea, Republic of	10398
India	7013
Fiji	6040
Malaysia	5981
Thailand	5233
Canada	5013
Singapore	4887
Samoa	4047
South Africa	3763
Tonga	3477
Hong Kong	3281
Philippines	3147
Taiwan	2915
Indonesia	2580
Netherlands	2509
Brazil	2265
Sweden	1862
Denmark	1605
Switzerland	1376
Ireland	1331
Chile	1157
Saudi Arabia	1141
Russia	1068

Table 8: Non-New Zealander travel and immigration numbers, 0–19 year olds, 2013

country	immigration
Australia	1017540
United States	142200
Fiji	112260
United Kingdom	96680
China	73340
Cook Islands	72820
Samoa	44060
Thailand	42060
India	40760
Indonesia	25100
Japan	21840
Canada	21720
Tonga	20120
Singapore	18300
Hong Kong	18000
Malaysia	17480
Philippines	17260
France	15980
Vanuatu	15580
South Africa	14000
Korea, Republic of	13980
Italy	13620
Germany	12800
Viet Nam	12640
Taiwan	10300
New Caledonia	7620
Spain	6560
Netherlands	6260
Papua New Guinea	6200
Ireland	6160

Table 9: New Zealander travel numbers by destination, 2013

country	immigration
Australia	1148243
United States	162447
United Kingdom	121835
Fiji	118300
China	99720
Samoa	48107
India	47773
Thailand	47293
Japan	42374
France	28153
Indonesia	27680
Germany	27593
Canada	26733
Korea, Republic of	24378
Tonga	23597
Malaysia	23461
Singapore	23187
Hong Kong	21281
Philippines	20407
South Africa	17763
Vanuatu	15748
Italy	14617
Viet Nam	13680
Taiwan	13215
Netherlands	8769
Ireland	7491
Spain	7118
Papua New Guinea	6457
Sri Lanka	5764
Brazil	5245

Table 10: Total New Zealand traveller numbers by country (New Zealand nationals and 0–19 year old immigrants, 2013)

country	risk
Australia	7870820
United Kingdom	3723960
China	1928613
Thailand	1870193
Netherlands	1391896
Indonesia	1071788
Philippines	616175
Germany	590184
Sri Lanka	575635
India	532515
Turkey	350451
Viet Nam	169200
Malaysia	156460
Namibia	151083
Nepal	134525
France	119768
Switzerland	109766
Nigeria	101638
Angola	98652
Japan	76407
Pakistan	73853
Uganda	70444
Canada	62923
Lebanon	57601
Russia	55743
Romania	34971
Ethiopia	21876
Sweden	21674
Sudan	21024
Spain	20552

Table 11: Risk of measles importation to New Zealand in 2013, estimated by 0–19 year old international and all New Zealander traveller numbers multiplied by measles incidence in the source or destination location, see also Table 12 and Table 13

country	risk
Australia	6974895
United Kingdom	2955082
Thailand	1663255
China	1418417
Netherlands	993645
Indonesia	971888
Philippines	521154
Sri Lanka	499336
India	454343
Turkey	342245
Germany	273778
Viet Nam	156336
Namibia	145622
Nepal	125990
Malaysia	116573
Angola	98243
Nigeria	87565
Switzerland	79655
Uganda	69360
France	67982
Pakistan	53765
Lebanon	53054
Canada	51123
Japan	39381
Russia	38275
Georgia	36127
Romania	31378
Ethiopia	19471
Spain	18941
Qatar	16373

Table 12: Risk of measles importation to New Zealand due to New Zealander travel in 2013, estimated by all traveller numbers multiplied by measles incidence in the source or destination location, see also Table 13 and Table 11

country	risk
Australia	895925
United Kingdom	768878
China	510197
Netherlands	398252
Germany	316406
Thailand	206938
Indonesia	99899
Philippines	95021
India	78172
Sri Lanka	76299
France	51786
Malaysia	39887
Japan	37026
Switzerland	30111
Pakistan	20088
Russia	17469
Nigeria	14073
Viet Nam	12863
Canada	11799
Sweden	9984
Nepal	8535
Turkey	8206
Namibia	5461
Sudan	5451
Denmark	4874
Lebanon	4547
Somalia	4046
Romania	3593
Afghanistan	2437
Ethiopia	2405

Table 13: Risk of measles importation to New Zealand due to non-New Zealander 0–19 year old travel and immigration in 2013, estimated by traveller numbers multiplied by measles incidence in the source or destination location, see also Table 12 and Table 11

country	incidence	cover	immigration
Australia	7	94	1148243
United Kingdom	31	95	121835
China	19	99	99720
Thailand	40	99	47293
Netherlands	159	96	8769
Indonesia	39	89	27680
Philippines	30	90	20407
Germany	21	97	27593
Sri Lanka	100	99	5764
India	11	88	47773

Table 14: Measles and travel data from 2013 for the top 10 countries identified as high risk for measles importation. incidence: measles incidence per million; cover: percent vaccination cover (% children that receive one dose of measles vaccine by their second birthday.); immigration: the number of 0–19 year old travellers entering New Zealand from the country

of low measles incidence in these nations. These data are shown in Table 11. The breakdown of risk of measles importation by New Zealander and non-New Zealander travellers is in Table 12 and Table 13 and Figure 22 and Figure 23. The measles incidence and vaccination coverage for those countries identified as posing the greatest risk for measles importation to New Zealand are in Table 14.

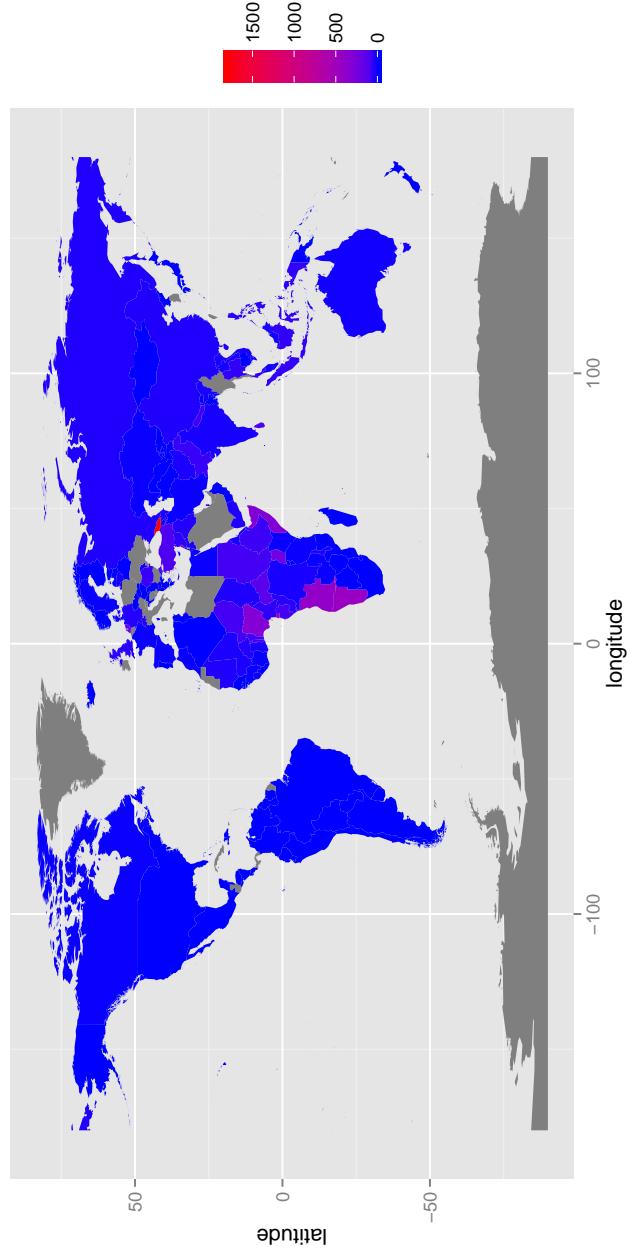


Figure 16: Measles incidence per million, 2013. Data: WHO (www.who.int/research/en/). Grey indicates not reported.

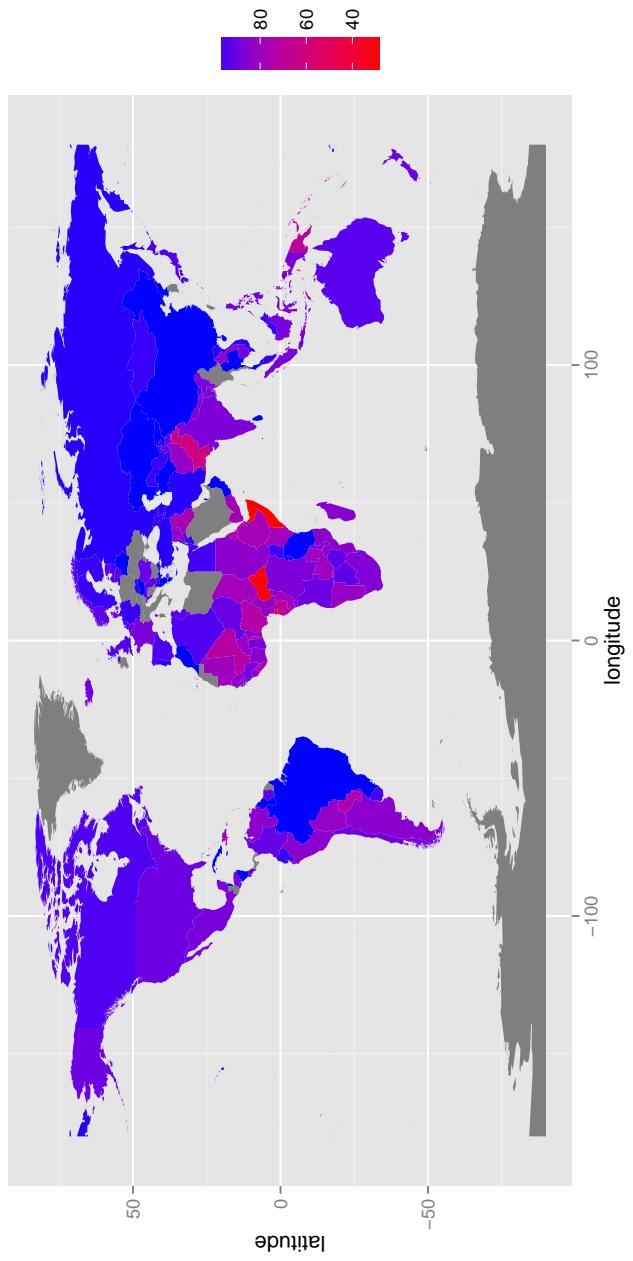


Figure 17: Measles vaccination cover (% coverage of children that receive one dose of measles vaccine by their second birthday.), 2013. Data: WHO (www.who.int/research/en/). Grey indicates not reported.

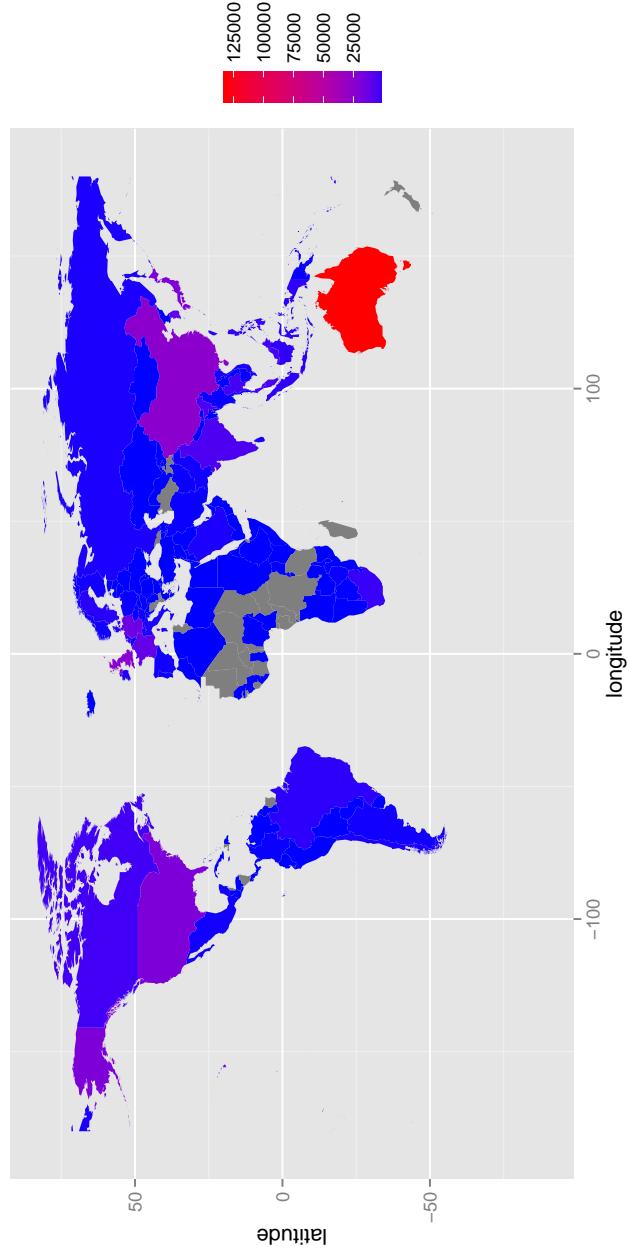


Figure 18: Non-New Zealander international travel and immigration by 0-19 year olds, 2013)

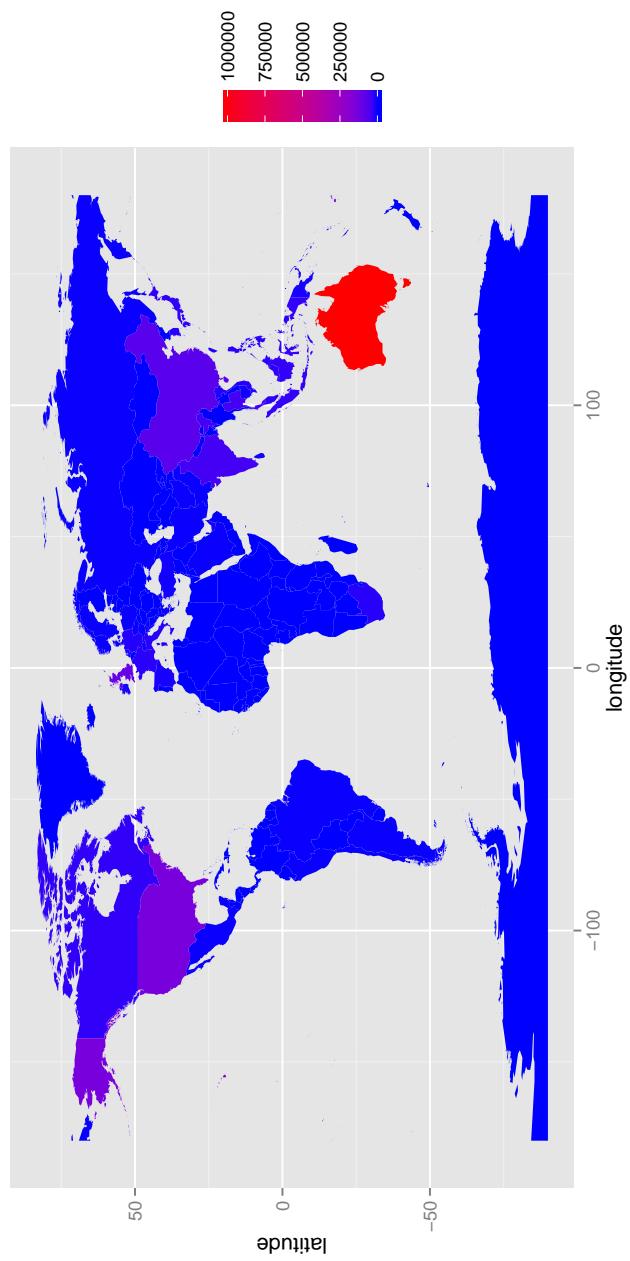


Figure 19: New Zealander international travel, 2013

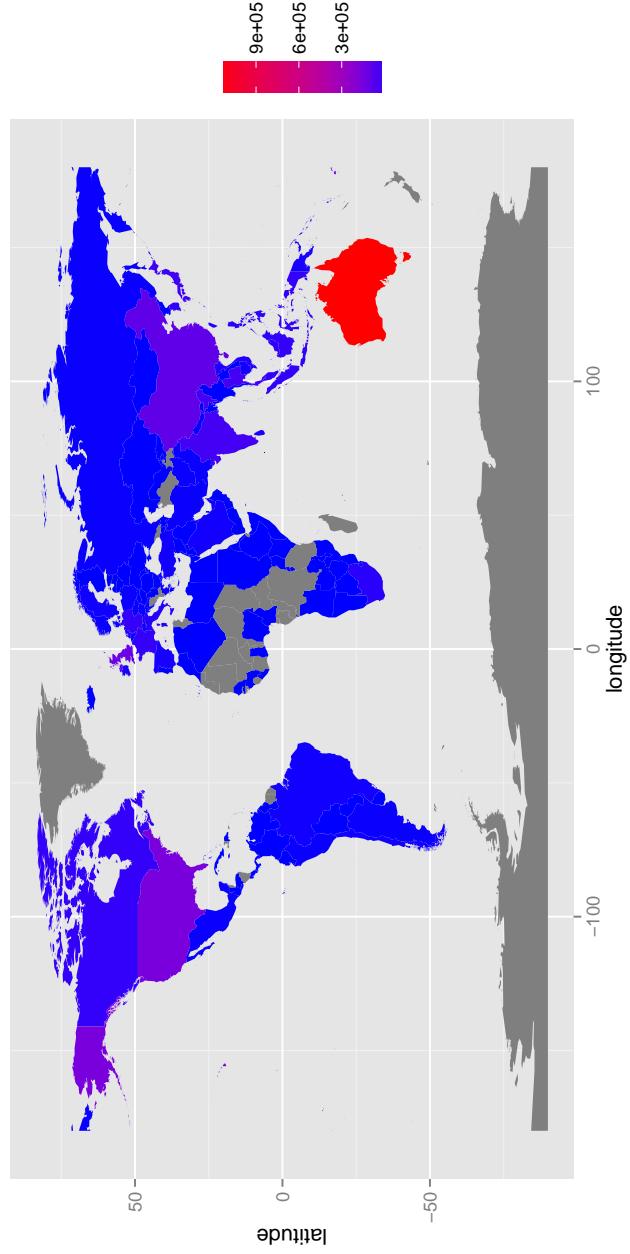


Figure 20: Total international travel by 0–19 year old non New Zealanders and all ages of New Zealanders, 2013

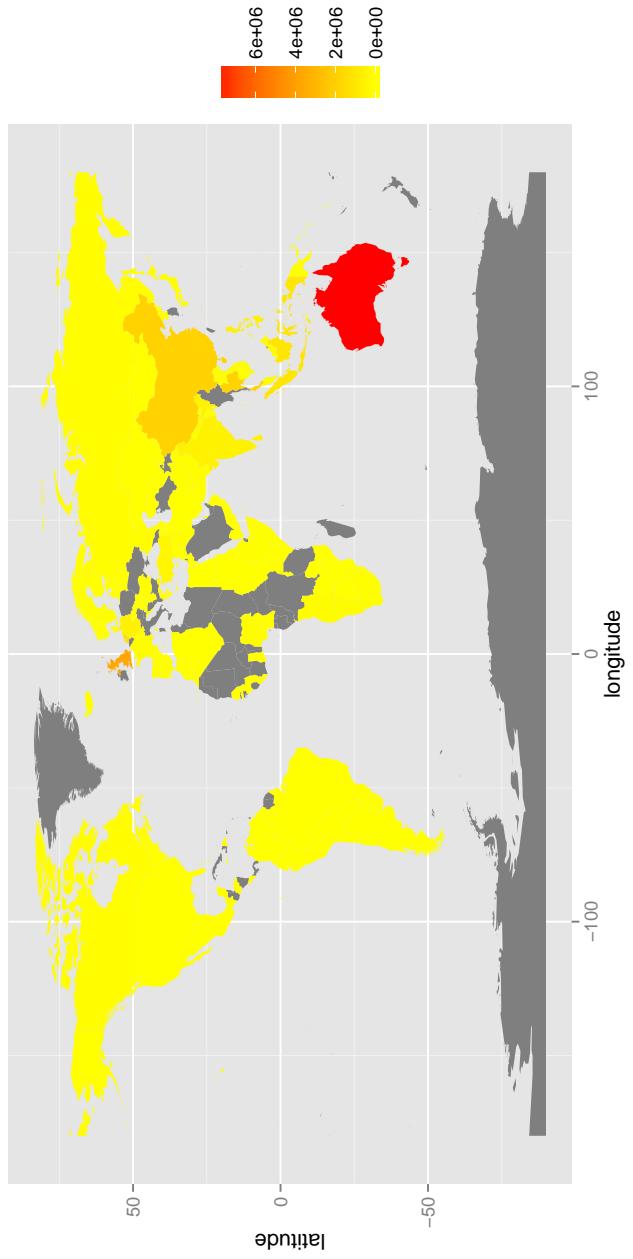


Figure 21: Risk map for measles importation, based on measles incidence and non New Zealander 0–19 year old and all ages of New Zealander travel figures, 2013)

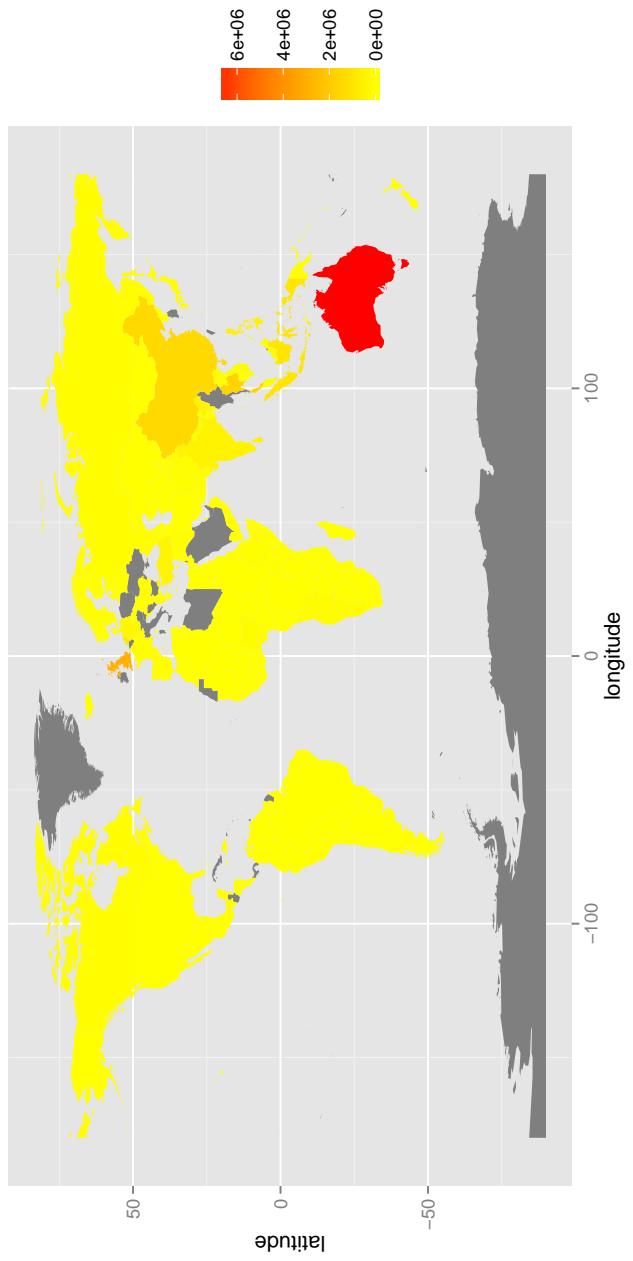


Figure 22: Risk map for measles importation from New Zealander international travel, based on measles incidence and travel figures, 2013

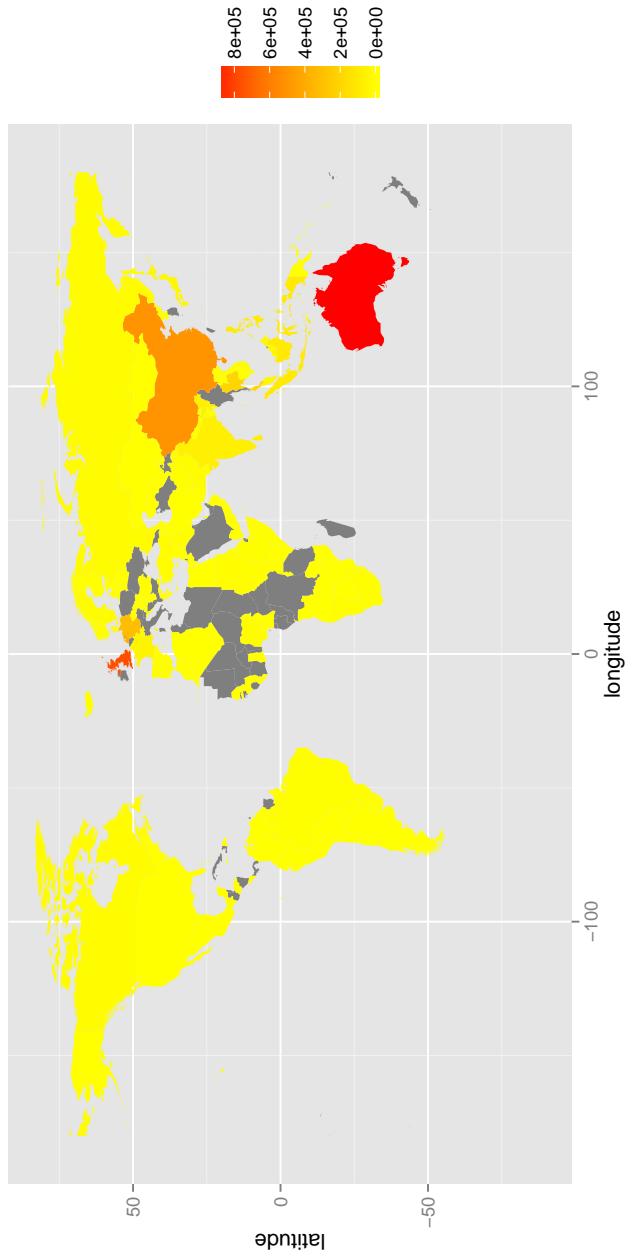


Figure 23: Risk map for measles importation from 0–19 year old non-New Zealander international travel and immigration and measles incidence, 2013

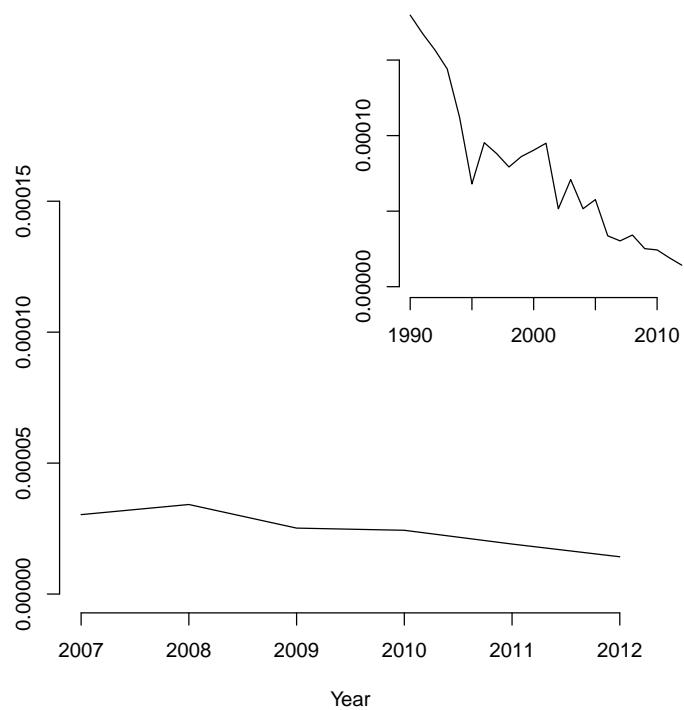


Figure 24: Trend in global per capita measles incidence

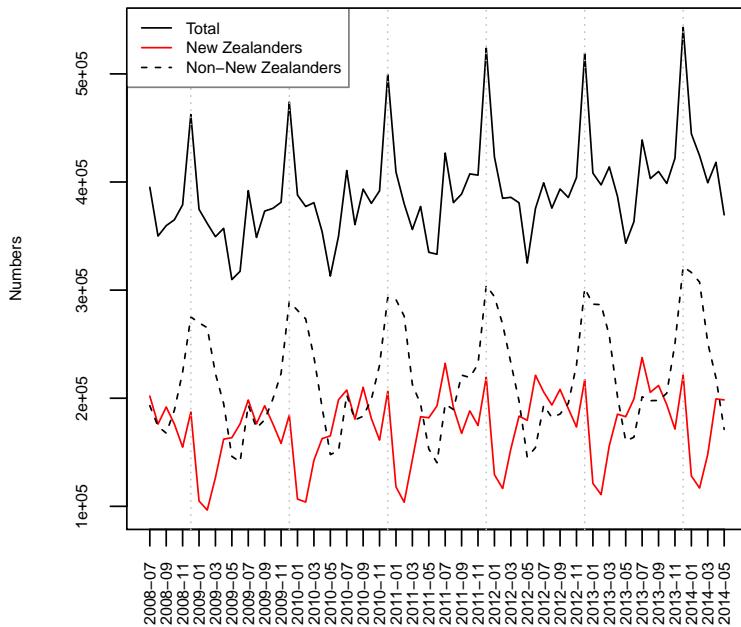


Figure 25: Trends in international travel, determined by immigration arrival data and New Zealander travel departure destinations. Note this is for all age categories.

Though the global incidence of measles is declining, in recent years that decline has slowed (Figure 24) and immigration rates to New Zealand have risen (Figure 25). This suggests that the risk of measles importation could increase, though further analyses are required to understand the interaction between these variables. Of note, however, is the clear seasonality in immigration and travel (Figure 25). This seasonality suggests that there may be periods of increased risk of measles importation, though again the interactions with seasonal measles transmission from the nations of origin will be an important factor in determining the risk of measles importation. Of interest is the asynchrony, or lack of phase, between peak non-New Zealander immigration and New Zealanders travelling. The Christmas summer period being an exception to this, when there is substantial New Zealander travel and combined these lead to a very sharp peak in travel rates in December (Figure 25).

Risk analysis discussion

The regression analyses suggest that age is a particularly strong risk factor for measles. This comes as no surprise to epidemiologists or health care providers. However, our analyses also highlight other groups that are at greater risk of measles. In particular, Pacific people are at greater risk per capita, as are the less deprived (NZDep 1–3), and European and Maori 5–17 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. For example, increased numbers of more wealthy Europeans were measles cases, as was true for Maori. However, the alternative situation was clear for Pacific people, especially of the 0–1 year olds (Figure 4 and Figure 3). Results such as this may simply due to the spatial effects due the communities the outbreaks were occurring in, rather than an effect of wealth. A key issue with incorporating the spatial immunisation data has been the denominator data and the NIR data. The data suggest that census data and NIR data are recording children living in different DHBs to that in which they are vaccinated, or subsequent to the census or NIR data moving. This leads to some area census units having more than 100% children vaccinated, with some many times more, and some with very low levels reportedly vaccinated. Another issue was how to deal with people of greater age than those recorded in the NIR. Thus, these analyses are possible future directions for this work and a focus of future data collection could be to better understand the link between denominator data and NIR data.

The distribution of the measles cases (Figure 8) appears to reflect the distribution of naïve individuals in the population (Figure 14). The vaccination history of the cases suggests that lack of vaccination cover is the main contributor to the outbreak, though it is noticeable that a number ($> 16\%$) of cases had been vaccinated at least once. However, the majority of these received only one vaccination, and were vaccinated when they were young (Figure 9). The majority of naïve among the New Zealand population is clearly focused in the DHB with large urban areas (Figure 15).

Unfortunately, additional data we received from the Ministry that we hoped would allow us to provide finer scale results (lower than DHB) immunisation coverage data are not able to provide reliable results, as discussed above. Frequently the numbers of vaccinated children in a census area provided in the NIR was greater than the number reported in the census area unit population census (Figure 13). Given these data gaps we are unable to provide finer scale risk maps (Figure 12).

The distribution of naïve among the DHBs also varies (subsection 4.5, Figure 38, Figure 39, Figure 40, Figure 41, Figure 42, Figure 43, Figure 44, Figure 45, Figure 46, Figure 47, Figure 48, Figure 49, Figure 50, Figure 51, Figure 52, Figure 53, Figure 54, Figure 55, Figure 56, Figure 57). We hope that the Ministry will find these informative, as they indicate which age classes may be the focus of vaccination efforts for each DHB. However, it is worth bearing in mind that the data here assume that the national NIR vaccination coverage

and serosurvey results are appropriate for all DHB.

Further analyses are required to see if the seasonal patterns in travel match seasonality in measles incidence in the countries from which most individuals come from when travelling to, or back to, New Zealand. However, the strong seasonality in travel around the summer vacation in December suggests this may be a time where extra effort and vigilance is required for measles vaccination and control efforts. The area identified as greatest risk for measles importation, Australia, simply reflects the enormous amount of travel between Australia and New Zealand (Table 10 and Figure 18). However, recently Australia was declared free of endemic measles and so the 2013 data must reflect imported measles there. Other interaction terms beyond the product of travel and infection incidence may be more appropriate but this will require substantial further analyses. Other areas of high risk include the United Kingdom, where measles persists, and South, Southeast and East Asia, where measles is endemic (Table 11 and Figure 21). The 2012 data were more complete than the 2013 data, which suffers from data deficiencies, but due to the dynamic nature of measles epidemiology and consultation with the Ministry we present the 2013 data. Lastly, more refined data on the age of travellers may improve the risk assessment, but these are currently unavailable.

4.8 Risk analysis summary

- Risk of measles infection decreases significantly with age.
- European ethnicity comprise the largest number of measles cases.
- Pacific people are statistically more at risk per capita of measles infection.
- There is some statistical support for those living in better socio-economic situations being at greater risk of measles.
- There is some statistical support for 2–24 year old Pacific people being less at risk than European and Maori of the same age, as are 5–17 year old Asian children.
- The majority of cases are unvaccinated.
- The majority of vaccine failures occur in those people which received single vaccinations around 1 year old.
- Distribution of numbers of naïve among New Zealand is uneven, with the majority predictably in DHBs with larger urban areas.
- There is a continued, and perhaps increasing, risk of measles importation due to travel and endemic measles elsewhere in the world.
- There may be seasonal changes in risk of measles importation, with travel numbers peaking in December.

5 Modelling measles epidemics

A previously-published model of the dynamics of measles infections in New Zealand has been used to evaluate the vaccination strategy in New Zealand of MMR1 at 15 months and MMR2 before 5 years [28, 27, 33]. The results show that achieving coverage of greater than 90% at both vaccination opportunities is necessary if future epidemics of measles are to be prevented.

The original mathematical model for the dynamics of measles in New Zealand prepared in 1996 [33] successfully predicted the 1997 epidemic, which was curtailed by a mass vaccination campaign [22, 28]. Subsequent extension of this work in 1998 showed that the then current schedule of MMR1 at 15 months and MMR2 at 11 years was insufficient to prevent further epidemics [28]. The model supported the change in the immunisation schedule that took effect in January 2001, at which time MMR2 was changed from delivery at 11 years to delivery before the age of five. The schedule was changed in 2000 with MMR2 now being administered before 5 years [3]. Later analyses suggested high levels of vaccination coverage (but less than 95%) could eliminate measles, but emphasised that it is necessary to maintain high coverage rates in order to prevent future epidemics and poor schedules were not considered [27].

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

Numerous models for measles vaccination strategies for various regions [1, 5, 13, 16, 34] based on sets of nonlinear ordinary differential equation (ODE) models have reached similar conclusions. The differences in the models have been in the details of the representation of the infectious period, and in the ways in which the age and contact structures of the population have been specified. While analyses suggest that 85% coverage at MMR1 and MMR2 could be sufficient to prevent future measles epidemics, in the Netherlands analyses showed that high overall levels of measles vaccination can obscure pockets of poor coverage, resulting in localised regions with increased risk of infection and effective immunisation difficult to evaluate [17]. No such models exist for New Zealand currently.

The quantity that determines whether an epidemic will occur is the basic reproduction number of the infection, R_0 . This is defined as the expected number of secondary infections that would arise from a single primary infection introduced into a fully susceptible population [2, 12]. If $R_0 > 1$ an epidemic will

occur following an introduction of infection. The best estimate for measles in New Zealand was $R_0 = 12.8$ [27]. The basic reproduction number of the infection under vaccination, R_v , is the expected number of secondary infections that would arise from a single primary infection introduced into a vaccinated population at equilibrium and is a robust indicator of the performance of a vaccination schedule. If $R_v < 1$ epidemics are prevented. The case reproduction number of the infection at time t , R_t , is the expected number of secondary infections that arise from a single infection at a particular time and depends on the number in the population who are susceptible.

5.1 Modelling methods

To understand the transmission dynamics of measles in the partially immune population and how likely an outbreak was of becoming endemic, we estimated R_v from all the outbreaks in New Zealand since 2009. To do this we estimated R_t , following an adaptation of the methods in [24, 35]. We are required to compute the generation time for measles to do so. The generation time is the average time an index case infects others after becoming infected. We used a lognormal distribution with mean 12.0 and standard deviation (s.d.) 3.5 from [19]. We then estimated R_t from the incidence data for each outbreak, defining outbreaks in the dataset given their reported outbreak numbers. The geographic locations of cases are shown in Figure 26. The outbreaks we used in our analyses are shown in Figure 27. Note these analyses do not use those sporadic cases not linked to other outbreaks.

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

$$\log(1 - \mathcal{P}) + R_0\mathcal{P} = 0 \quad (2)$$

where 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 $R_V = x_0 R_0$, and the final size equation becomes

$$\log\left(1 - \frac{\mathcal{P}}{x_0}\right) + R_0\mathcal{P} = 0 \quad (3)$$

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

$$x_0 = \frac{\mathcal{P}}{1 - e^{-R_0\mathcal{P}}} \quad (4)$$

In order to prevent future epidemics, it is necessary that $R_V < 1$. Hence, the proportion of the population that must be vaccinated to prevent future

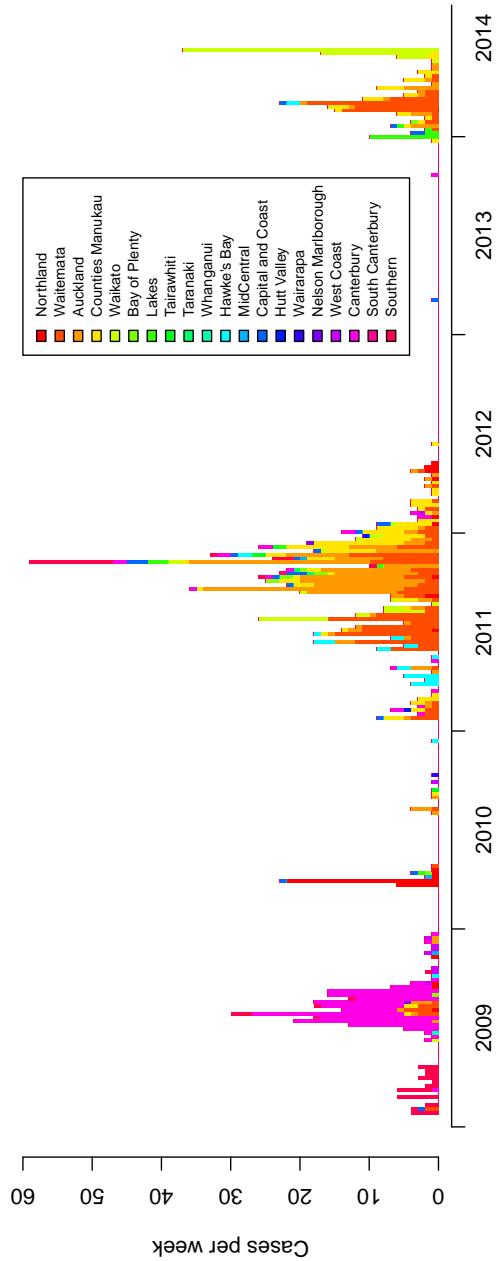


Figure 26: Measles cases by District Health Board (DHB) from 2009 to 2014

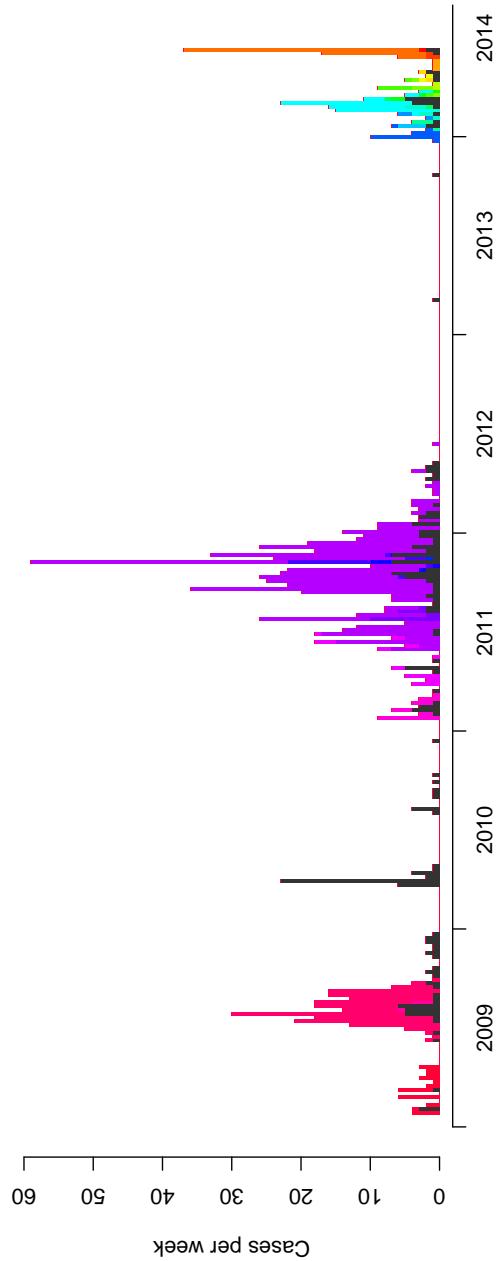


Figure 27: Measles data classified as outbreaks for reproduction number of the infection (R_v) estimation from 2009 to 2014. Outbreaks are coloured by reported outbreak number and sporadic cases not given a number are in grey.

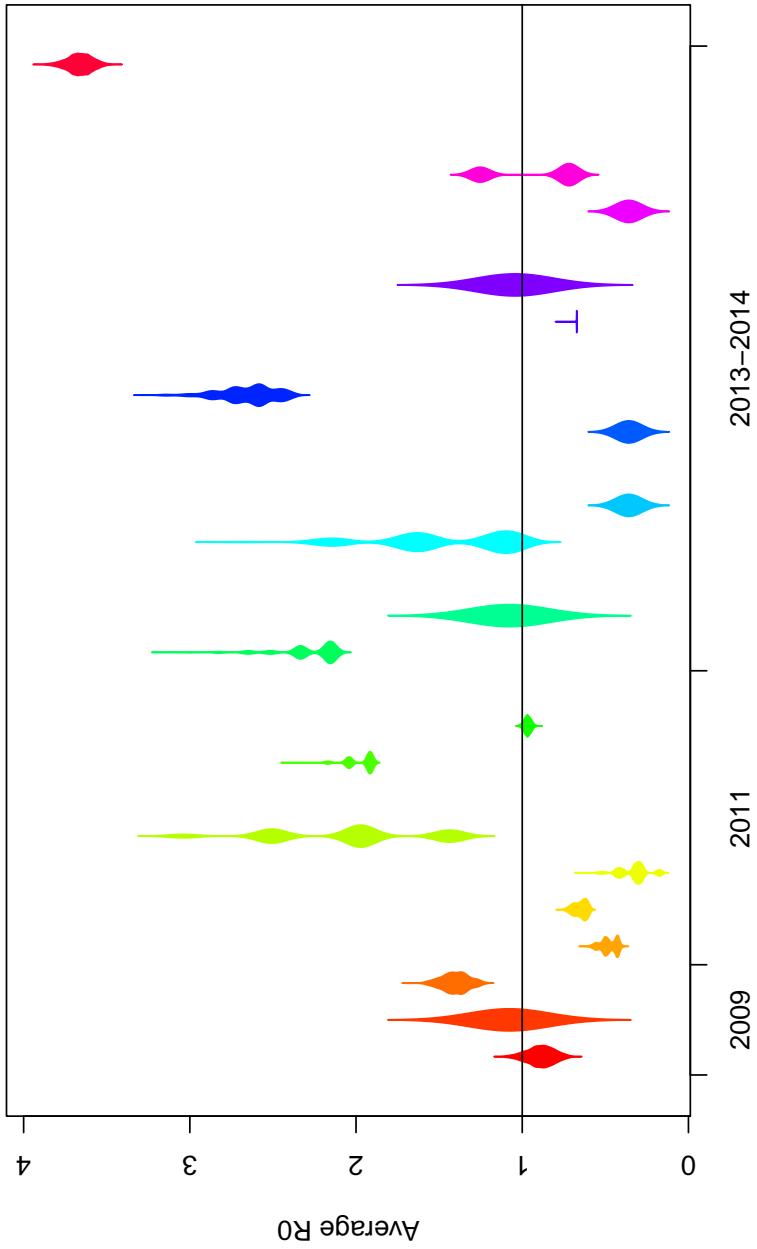


Figure 28: Estimates of R_v for the outbreaks each year, as classified by outbreaks in Figure 27. Sporadic cases are excluded.

outbreaks, \mathcal{P}_v is

$$\mathcal{P}_v = x_0 - 1/\mathcal{R}_0 \quad (5)$$

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

5.2 Modelling results and discussion

The estimated R_v for each outbreak is shown in Figure 28. Our analyses suggest the R_v for the 2009–2014 outbreaks range between 0.18–3.92, and for the last outbreak that ended in August 2014, but for which data were available until 12 June, a mean estimate of 3.66 (range 3.4–3.92). The probability density of the R_v estimates for 13 of 20 outbreaks for which we had outbreak numbers include one. Of particular note there have been a number of outbreaks for which our estimated R_v was well above one and thus we may expect outbreaks to occur if conditions remain the same. An important caveat to the analysis of the last outbreak is that because this outbreak that ended in August was ongoing when the data were collected, and not in decline, R_v is necessarily over one, and so the comparison with others must be cautious. However, this is not the only case for which the R_v is greater than one (Figure 28).

These analyses also imply that the regular importation of measles is an ongoing process. Given the risk of importation of measles as highlighted in subsection 4.6 is likely to continue, these analyses suggest substantial efforts are required to increase immunisation to high enough levels that measles does not become endemic and large outbreaks prevented. The measles outbreaks in 2011–2012 had an R_v of just greater than one, and yet it persisted for over 12 months. This implies that outbreaks may persist within the population for a substantial period, even if R_v values are not much greater than one. A caveat to this and other R_v estimates is that the outbreaks may include some sporadic cases misclassified, but also exclude some sporadic cases as yet not associated with another outbreak. Thus the true basic reproduction numbers may differ to those estimated. However, undetected cases may lower the estimate. The relative contributions of both to our estimates are currently unknown.

To use the results from our modelling exercise to help inform the appropriate measles vaccination coverage, we use Equation 5. The proportion of the population requiring additional vaccination to make $R_v < 1$ ranged from 17% to 34% at the DHB level, with a national average of approximately 28% (Table 15). These additional vaccination numbers can be calculated in a number of different ways, as discussed in the benefit–cost section (subsection 6.3). However, they require differing numbers of vaccinations per DHB. Estimates for West Coast, Wairarapa, and South Canterbury, for example, are fewer than 1000 (Table 15). The estimated numbers to vaccinate in the Auckland area, however, are higher for each DHB, with those estimated for Waitemata, Auckland, and Counties Manukau DHBs all over 17,000 (Table 15). Note that there is also evidence for vaccine failure (Figure 9) and pockets of susceptible populations [17] may

require greater vaccination effort than these estimates and this is considered further in the section 6.

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 28). However, the naïve population (Figure 14 and Figure 15) and the higher R_v for some of the 2009–2014 outbreaks (Figure 28) suggests that catch up vaccination is necessary (Table 15). The results of these analyses support other studies that suggest very high rates of vaccination are required to eliminate measles and prevent epidemics. Vaccinating 85% of susceptible children aged one to seven years at five-yearly intervals was suggested to be sufficient to prevent epidemics in Israel [1], but nearly all other studies in Europe suggest no strategies succeeded if coverage rates were below approximately 87%, which the population level immunity in New Zealand has only just reached, with approximately 11% currently naïve. Analysis of measles vaccination in various regions suggest that 85% coverage at MMR1 and MMR2 could be sufficient to prevent future measles epidemics [1, 5, 13, 16, 34], whereas [17] showed that high overall levels of measles vaccination can obscure pockets of poor coverage, resulting in localised regions with increased risk of infection making effective immunisation difficult. Future analyses at a smaller, more local level would be useful, but the lack of appropriate data matching between the NIR data and the census unit area data currently prevent these.

5.3 Summary of modelling

- Regular introductions of measles pose an ongoing threat to New Zealand’s efforts to eliminate measles (also see section 4).
- The reproduction number for measles in the partially immune New Zealand population is often close to and exceeding one, suggesting increased population level immunity is required to ensure prevention of measles persistence following importation.
- Additional vaccination levels to push R_v below one among the currently naïve population in New Zealand range from 17% to 34% among DHBs, and 28% at the national level (approximately 131,500 vaccinations).

6 Cost analyses

In this section we provide a review of the costs of measles from other locations and an analysis of the costs involved with the current 2013–2014 measles outbreak. All exchange rates are from the Reserve Bank of New Zealand.¹

About 50 years ago, approximately 135 million cases of measles causing 7–8 million deaths were believed to occur in the world [9]. Thirty years later, it was estimated there were still approximately 45 million cases of measles occurring

¹<http://www.rbnz.govt.nz/statistics/tables/b1/>

DHB	Size	Naïve	Attack	Vacc	Vacc (%)
Auckland	436350	52010	31159	17920	34
Bay of Plenty	206000	20679	8437	4585	22
Canterbury	482180	51357	24695	13687	27
Capital and Coast	283700	32625	18403	10461	32
Counties Manukau	469300	55544	32903	18880	33
Hawke's Bay	151700	15602	6846	3751	24
Hutt Valley	138380	15198	7836	4388	29
Lakes	98196	10558	5192	2886	27
MidCentral	162560	17328	8348	4628	27
Nelson Marlborough	137000	13059	4411	2356	18
Northland	151690	14921	5688	3071	21
South Canterbury	55620	5238	1678	893	17
Southern	297420	31607	15115	8371	26
Tairawhiti	43650	4769	2431	1359	28
Taranaki	109750	11473	5262	2899	25
Waikato	359310	39402	20248	11331	29
Wairarapa	41112	3932	1346	720	18
Waitemata	525550	58350	30774	17291	30
West Coast	32151	3197	1265	685	21
Whanganui	60120	6075	2530	1378	23
TOTAL	4241739	462924	234567	131539	28

Table 15: Epidemic size calculations. *Size*: DHB Population, Statistics NZ 2013; *Naïve*: DHB naïve population ($x_0 \times \text{Size}$); *Attack*: Number infected in DHB in an outbreak of measles in the absence of any vaccination (\mathcal{P}); *Vacc*: Number of the currently naïve to be vaccinated in DHB to reduce \mathcal{R}_V below one ($(x_0 - 1/\mathcal{R}_0) \times \text{Size}$); *Vacc (%)*: Proportion of the currently naïve population to vaccinate. These simulations assume homogeneous mixing.

annually, including 6 million measles-related fatalities. It was estimated that in 1999 measles was responsible for more than 30 million disability adjusted life years (DALYs) lost and 12 million in 2005 [37]. The incidence of cases was reduced by more than 50% from 43 million in 1999 to approximately 20 million in 2005. Approximately 7.5 million deaths from measles were avoided from 2000–05 due vaccination [37]. The World Health Organization (WHO) estimated 158,000 deaths from approximately 355,000 measles cases in 2011 [38]. In addition to the substantial losses occurring in measles-endemic countries, a significant impact is felt in heavily measles-vaccinated countries, which may be considered measles-free, due to contact with cases either in the country of origin or in the previously measles-free country.

The annual cost of treating and controlling measles in 11 industrialised countries was estimated to be more than US\$150 million² [8]. The estimated cost for a case ranged from US\$189–344³ [8]; however, the average estimated cost of a typical hospital case ranges from US\$967–1,755⁴ [7]. [31] estimated the economic benefits from cases averted due to measles vaccination. They estimated that the expanded vaccination from 2005 to 2015 in 72 of the world's poorest countries could result in nearly US\$10 billion⁵ 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.⁶ The economic impact of a large measles outbreak in Italy, 2002–03, has been evaluated. The costs associated with 5,154 hospitalisations where measles was the main discharge diagnosis was calculated. The mean length of hospital stay was 5.2 days (median = 4 days and range = 1 to 303 days). The total cost of these hospitalisations amounted to €8.83 million⁷, or approximately €1,700⁸ per case. The average cost per non-complicated measles case was €1,429,⁹ while the mean cost of a case with complicated measles was €2,721.¹⁰ The average daily cost of a hospital stay was €327.¹¹

An outbreak of measles occurred in Sydney, Australia, lasting nearly 2 months in 2011 and resulted in 26 confirmed cases [15]. Seven (27%) of the cases required hospitalisation for more than 1 day and 10 (38%) resulted in management within a hospital emergency department. During this outbreak, a total of 1,395 contacts were identified and managed by a public health unit

²Jan 2001 \$ to US\$ rate 0.4445: \$337.5million

³Jan 2001 \$ to US\$ rate 0.4445: \$425–774

⁴Jan 2001 \$ to US\$ rate 0.4445: \$2175–3948

⁵Jan 2009 \$ to US\$ rate 0.5526: \$18.1billion

⁶Jan 2001 \$ to US\$ rate 0.4445: \$112.5million

⁷Jan 2005 \$ to € rate 0.5375: \$18.4million

⁸Jan 2005 \$ to € rate 0.5375: \$3539

⁹Jan 2005 \$ to € rate 0.5375: \$2975

¹⁰Jan 2005 \$ to € rate 0.5375: \$5664

¹¹Jan 2005 \$ to € rate 0.5375: \$681

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, Jan 2005 \$ to AUS\$ rate 0.7692: \$62,400 with 90% of this being associated with staff time.

Germany implemented a two-dose measles vaccination program in 1991 and has seen the benefits in recent years. In 2001 more than 6,000 cases were reported, but by 2004 this number fell to 122 [36]. However, in 2005 more than 500 cases were reported by the middle of the year in two German states, with the vast majority (>95%) in non-vaccinated children [30]. An economic analysis was performed of the 614 measles cases reported in an 8-month period in Duisburg in the state of North Rhine-Wesphalia (NRW). In that study, they estimated the health-care provider costs to be approximately €229,000,¹² or €373¹³ 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 €1,877,¹⁴ including one patient with encephalitis at a cost of €35,623.¹⁵ In addition to the health-care provider costs, additional costs of €89,400¹⁶ were incurred by the district public health office, the majority (€85,000,¹⁷ 95.1%) for personnel, €2,300¹⁸ (2.6%) for vaccination, and €2,100¹⁹ (2.3%) for serologic testing. Therefore the combined direct costs of these 612 cases amounted to €318,400,²⁰ or €520²¹ per case. To determine the total impact, it would be necessary to include the indirect losses associated with lost production of cases and care givers.

Although measles was declared eliminated from the United States in 2000, it remains a concern due to its endemic nature around the world [25]. Several studies have been conducted in the United States to assess the economic impact of recent measles outbreaks due to imported cases. The economic impact to public health departments in the US as the result of 16 outbreaks in 2011 has been estimated [23]. The outbreaks lasted an average of 22 days and resulted in 107 confirmed cases; however, from these 107 cases, they estimated between approximately 8,900 and 17,500 contacts with confirmed cases, requiring between 42,600 and 83,100 personnel hours at a cost of between US\$2.7²² and 5.3²³ million. Overall, it was estimated that each contact required 4.7 personnel hours at a cost of US\$298²⁴ 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

¹²Jan 2005 \$ to € rate 0.5375: \$426046

¹³Jan 2005 \$ to € rate 0.5375: \$694

¹⁴Jan 2005 \$ to € rate 0.5375: \$3492

¹⁵Jan 2005 \$ to € rate 0.5375: \$66275

¹⁶Jan 2005 \$ to € rate 0.5375: \$166325

¹⁷Jan 2005 \$ to € rate 0.5375: \$158140

¹⁸Jan 2005 \$ to € rate 0.5375: \$4279

¹⁹Jan 2005 \$ to € rate 0.5375: \$3907

²⁰Jan 2005 \$ to € rate 0.5375: \$592372

²¹Jan 2005 \$ to € rate 0.5375: \$967

²²Jan 2011 \$ to US\$ rate 0.7653: \$3.53million

²³Jan 2011 \$ to US\$ rate 0.7653: \$6.93million

²⁴Jan 2011 \$ to US\$ rate 0.7653: \$389

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\$142,452,²⁵ or nearly US\$50,000²⁶ per case.

The impact of a measles outbreak due to a non-autochthonous case in Indiana was also reported [25], and a total of 34 cases, 94% of which were not vaccinated against measles, were reported in the outbreak. Direct cost information was obtained from approximately 100 public health officers and infection-control officials needed to control the outbreak. Direct cost for those completing a survey showed the outbreak cost at least US\$167,685,²⁷ 83% of which (US\$139,023²⁸) was for wages, salaries and overheads. This amounted to a direct cost of US\$4,932²⁹ 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\$11,881.³⁰ In addition, per-contact costs amounted to US\$264.³¹ The cost of hospitalisation for the 3-day stay by the index case was US\$931.³² Additional costs were associated with physician visits (US\$294³³), vaccine and immunoglobulin (US\$1,765³⁴), mileage (US\$205³⁵) and immunologic screening tests for the parents exposed to measles (US\$240³⁶) for a total of US\$23,816.³⁷

Economic analyses of measles control programs have shown them to be financially effective. In the Republic of Korea, the economics of alternative measles vaccination programs were compared. All of the alternatives were found to be economically efficient (benefit/cost ratio (B/C) > 1.0), with the alternative using two doses of the MMR program, with a catch-up campaign for measles and rubella being the most favourable (B/C = 1.27), and B/C values 10.8 – 54.2 have been estimated for MMR vaccination in the USA [39].

The purpose of the current study is to estimate the cost of the 2013–2014 measles outbreaks in New Zealand. Using this information, we will then evaluate the economics of alternative measles control strategies in order to provide

²⁵Jan 2004 \$ to US\$ rate 0.6724: \$211856

²⁶Jan 2004 \$ to US\$ rate 0.6724: \$74360

²⁷Jan 2005 \$ to US\$ rate 0.704: \$238189

²⁸Jan 2005 \$ to US\$ rate 0.704: \$197476

²⁹Jan 2005 \$ to US\$ rate 0.704: \$7006

³⁰Jan 2010 \$ to US\$ rate 0.7277: \$16327

³¹Jan 2010 \$ to US\$ rate 0.7277: \$363

³²Jan 2010 \$ to US\$ rate 0.7277: \$1279

³³Jan 2010 \$ to US\$ rate 0.7277: \$404

³⁴Jan 2010 \$ to US\$ rate 0.7277: \$2425

³⁵Jan 2010 \$ to US\$ rate 0.7277: \$282

³⁶Jan 2010 \$ to US\$ rate 0.7277: \$330

³⁷Jan 2010 \$ to US\$ rate 0.7277: \$32728

additional information to public health officials and decision makers.

6.1 Cost analyses methods

Costs are evaluated as either direct or indirect. Direct costs included physician/general practitioner (GP) consultations, hospitalisations, laboratory testing, drugs, vaccination, long-term care for chronic sequelae, special education costs. Direct costs can be divided into medical and non-medical [29]. Direct medical costs include costs for diagnosis, treatment, continuing care, rehabilitation and terminal care. Personnel time (investigation and emergency response, including primary care), 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, as well as those relating to case-contacts. Indirect costs included work loss for cases and caregivers. This could also include the economic value of premature life lost, costs associated with permanent disability, e.g. deafness and mental retardation. Commonly the human value approach (HVA) has been used to estimate economic impact of life. The HVA measures the potential future earnings of an individual and discounts it into a present value. Typically this is 3% but 5% has also been used in a sensitivity analysis, which will tend to reduce the present value of the future earnings (saved by avoiding a case).

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

To determine the cost per case for the direct medical costs, cost of the Auckland Regional Public Health Service (ARPHS) for measles response were obtained from the Ministry of Health. These figures are representative for the most recent outbreaks as most cases were from North Island, and in particular Auckland and Waikato regions. However, results benefit-cost analyses are relatively robust to changes in this. Data, for the period January 1 - March 9, 2014, reported salaries for people involved with the measles outbreak management medical team. The costs are reported as direct, additional (above normal budgeting) costs required to enable the management of measles. The data includes a breakdown by individual performing the work and whether it was during the normal work schedule (Monday to Friday, M-F) or weekends. Normal work is calculated as $1.2 \times$ full time equivalent (FTE) \times number of days worked. Overtime is calculated as $1.6 \times$ FTE (M-F) and $2.0 \times$ FTE (weekend). A full day is considered as 8 hours worked. Salary (hourly) rates are calculated for the following: public health nurse (PHN, \$36), public health assistant (PHA, \$22), data support (\$26), data support (temporary) (\$33), management and programme supervisors (\$40), incident management team (IMT), which have

the following work titles: incident controller (\$96), administrator (\$24), planning and intel (\$40), logistics (\$36), communications (\$45), informatics (\$40), operations (\$40), and safety/security officer (SSO) (\$26). In addition, measles operations personnel are calculated at a daily rate of \$600 and operations partners and IMT controller partners at \$729. Senior medical officer (SMO) costs for GP visits were estimated as approximately \$20 per consultation,³⁸ though we allow flexibility in this value for the benefit–cost analyses later. These costs are applied on a per case basis below.

Wages lost due to measles are calculated for the period January 2008 - August 2014. We assume that the losses to the economy are the same, whether the employee is able to obtain sick leave pay, as this is the general loss to the economy as work days are lost. Calculations are based on the assumptions that 5 days of work are lost for each case; however, individuals between 0-14 years of age are not assumed to be employed and therefore did not suffer an income loss and the employment rate of teenagers 15-19 years of age was 41.9% (Statistics New Zealand, 2013). If the case is < 20 years of age, it was assumed there was an income loss of 5 days for the care giver, in addition to the wage loss of the case if 15-19 years of age. Case contact data was used to estimate further wage loss costs. These data were provided by the Ministry of Health. The data included the number and duration of school exclusions.

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

The total cost for the 293 publicly funded hospital discharges with a measles primary diagnosis that spent 470 nights in hospital from 2001–2014 (part year) was \$550,024 (Table 17). The mean cost per case was \$1,877. The mean cost per day of stay in the hospital was \$1,170.

From 16 December, 2013 through 19 June, 2014 there were 201 confirmed measles cases in New Zealand (note 14 of these occurred before 1 January 2014, so 187 occurred from Jan 2013 – 19 June 2014). The number of cases by age group is shown in Table 18. Of these 201 cases, 34 (17%) were admitted to hospital with the highest proportion occurring in the youngest (< 15 months) and oldest (> 19 years) age groups, 47% and 33%, respectively.

The length of hospital stay for the 293 cases reported between 2000 and 2014 ranged from 0 to 19 days, with a male patient, who was discharged in 2011 at age 57, after a stay of 19 days (Figure 29) and a cost of \$8,213.

Nearly 40% (114/293) of the cases did not spend a night in the hospital, while

³⁸personal communication with Ministry of Health

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

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

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

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

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

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

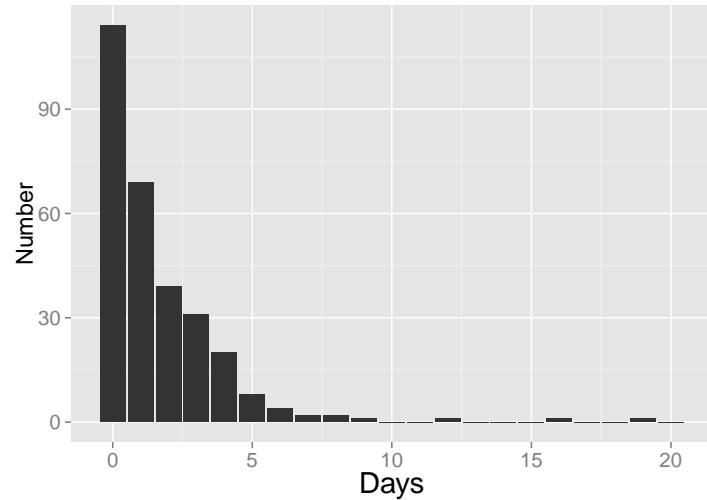


Figure 29: Number of measles cases attending hospital and stay duration from 2000–2014 ($n = 288$) in New Zealand

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 19.

Regression analyses showed statistically significant associations between cost of hospitalisation and three variables: length of hospitalisation, case age and year of case, and a less strong association with case gender (Table 20). Results showed the expected hospitalisation costs in 2000 of a female measles patient who did not stay overnight in the hospital was \$582. The cost was \$256 less if the case was a male. It increased of approximately \$406 per night of hospitalisation and \$64 per year over the time period of 2000–2014. The cost of a case decreased with the age of the patient by approximately \$8 per year of case age.

Wages lost for the period January 2008 – August 2014 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 under 15 years of age. Overall, the cost per case from 2008–2014 was estimated to be \$2923.27 (\$839 in forgone wages, \$1,765 in management costs, and \$1,710 in hospital costs). This figure brings an approximate estimate of \$546650.78 for 187 cases for the current outbreak in 2014 alone, which is comprised of earnings lost, case management and hospitalisation costs for 17%.

The average number of contacts quarantined per case was calculated to be 2.11. Average number of days a contact is quarantined was calculated to be 7.3. The average wage of a contact per day was estimated to be \$170.39. This leads to the estimate of wage losses of \$490794.86 relating to case contacts.

In total, with additional \$20 costs per GP consultation, we estimate that the 2014 measles cases alone cost the New Zealand economy \$1041185.63.

6.3 Benefit–cost analyses methods

To estimate the benefits from additional vaccinations, as estimated from the above modelling section (section 5), we carried out a number of analyses. Primarily, we used Equation 5 to estimate the proportion of the naïve populations in each DHB (Figure 15 and Table 15) and the national level requiring vaccination to reduce the R_v to <1 (section 5). We assume that the number of cases prevented by this is proportional to the outbreak size. However, there is a continued risk of introduction and despite R_v being <1 , smaller outbreaks may occur. Thus, we simulated expected outbreak sizes with $R_v < 1$. We use these values of numbers of predicted cases prevented and numbers expected despite additional vaccination to calculate the savings.

The cost figures above are used to estimate the savings for vaccinating additional populations, using estimated per case costs saved. The costs of the catch up vaccination schemes are estimated to be two different values, to determine

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

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

As of 7 August, 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

Table 20: Regression results ($R^2_{\text{adj}} = 0.43$, p-value < 0.001) for measles hospitalisation cost based on length of stay (days), gender, case age and year of case ($n = 288$) in New Zealand, 2000 – 2014

how sensitive the benefit–cost ratio ((B/C) was to differing vaccination costs. Values of \$20 and \$50 per vaccine are used, based on US literature, however, this assumes all costs are included with the vaccine delivery. Therefore, we also estimate approximate cost a vaccine (including the delivery costs) would need to be before the vaccination costs exceed the benefits. Thus the expected measles-related costs due to constant introduction of measles despite increased population immunity and the costs of the vaccination schemes are used to estimate the costs of additional vaccine programs for the B/C analysis. The financial savings from reduced measles cases are used to work out the benefits for the additional vaccination programs. The costs for the catch up vaccination programs are presumed to be over a single year. The benefits for the cases saved are presumed to be over a ten year period. Because benefits are assessed over a 10-year time period, a discounting rate of 3% discount per year for the costs saved was used, as is common for healthcare discounting [18]. Measles introductions are expected to be annually occurring events, though the costs per year for each event was also discounted. Thus, the B/C ratio was:

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

Where B is the benefit in saved funds from cases prevented and C is the cost of vaccination, discounted over time, where n is the year and r the annual discount rate of 0.03 (3%). A B/C ratio > 1 means that the program benefits exceed their costs. A B/C value less than one suggests the costs are higher than the economic benefits.

6.4 Benefit–cost analyses results

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

The numbers of susceptible people to vaccinate in New Zealand, assuming a homogeneously mixed population to achieve the 28% currently naïve catch up in vaccination numbers and using Equation 5 are shown in Table 21.

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
Waitomatā	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

Table 21: DHB and national level catch up vaccination rates and estimated outbreak sizes post catch-up vaccination.
Size: DHB Population, Statistics NZ 2013; *Naïve*: DHB naïve population ($x_0 \times \text{Size}$); *Attack*: Number infected in DHB in an outbreak of measles in the absence of any vaccination (\mathcal{P}); *Vacc*: Number to be vaccinated in DHB to reduce \mathcal{R}_V below one ($(x_0 - 1/\mathcal{R}_0) \times \text{Size}$); *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

^aNote that the median value is what is expected, however, the mean values from 1000 simulations are especially skewed by the small numbers of large outbreaks. The distribution of these outbreaks sizes can be seen in Figure 31 and Figure 30

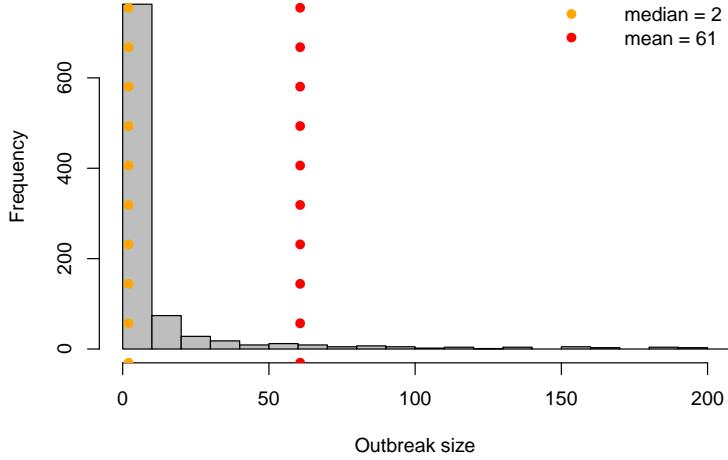


Figure 30: A subset of the expected number of measles cases from 1000 simulations of a model (section 5) in a homogeneously mixed population in New Zealand with 28% of the currently 11% susceptible to measles infection vaccinated, using an $R_v < 1$. The full distribution of rare results can be seen in Figure 31

The expected number of cases in New Zealand, assuming homogenous mixing, in a naïve population of subsequently lower (approximately 8%) numbers of naïve of the population and assuming measles R_v is < 1 is shown in Figure 30 and Figure 31. These simulations show that even in scenarios when R_v is lower than one, and thus deterministically should fail to persist (i.e. become endemic or cause an outbreak), outbreaks can occur due to stochastic processes following measles importation. The most likely scenario is that very few cases occur, with the median value from 1000 simulations low (2 cases). Thus most measles introductions will be single cases or lead to minor outbreaks with single secondary cases. In this modelling exercise the mean value was 61 cases, suggesting there is likely to be an outbreak of a larger size given enough introductions. The maximum predicted number of cases was nearly 8,000 cases (Figure 31). Note, however, that larger values are very rarely predicted and this does not take into account spatial variation or heterogeneous contact rates.

For the cost analyses we used the values from the above cost section (subsection 6.3). Specifically, we used the average cost of a case for the analyses to be \$839 lost in wages, \$1765.49 in case management costs, and \$1877 in hospitalisation costs for those attending hospital, with 17% of cases predicted to be hospitalised (Table 17). We estimated there would be approximately one introduction of measles per year (section 4). We provide two costs for measles

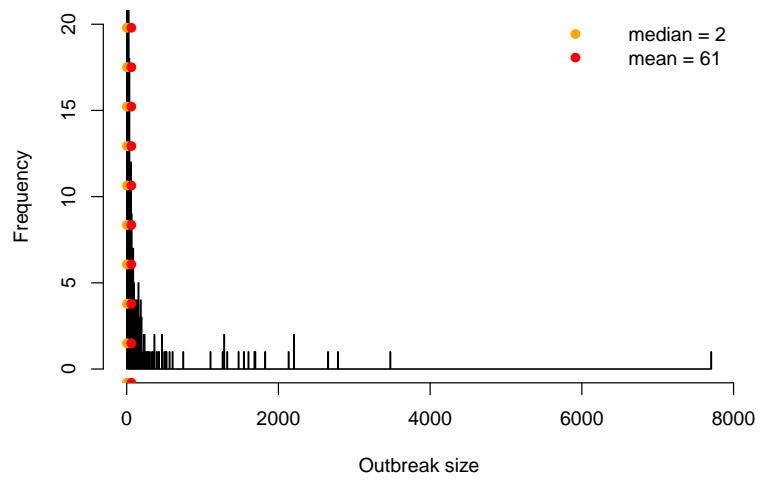


Figure 31: The distribution of the expected number of measles cases from 1000 simulations of a model (section 5) in a homogeneously mixed population in New Zealand with 28% of the currently 11% susceptible to measles infection vaccinated, using an $R_v < 1$, showing the rare but possible large epidemic sizes possible. The full distribution of common results can be seen in Figure 30

DHB	Vacc	Vacc costs	Wages saved	Manage saved	Hosp saved	Contacts	Costs saved	Outbreak	OB costs	B/C
Auckland	17920	358400	26132561	55634145	9942525	81779021	152428668	82	4011409	34.88
Bay of Plenty	4585	91700	7075979	15064196	2692162	22143509	41273490	71	3473294	11.58
Canterbury	13687	273740	20711307	44092724	7879928	64813791	120807021	62	3033017	36.53
Capital and Coast	10461	209220	15434306	32858409	5872213	48299988	90026791	96	4696284	18.35
Counties Manukau	18880	377000	27595227	58748043	10499018	86356274	160960251	50	2445981	57.01
Hawke's Bay	3751	75020	5741632	12223478	2184490	17967816	33490377	56	2739499	11.90
Hutt Valley	4388	87760	6571929	13991115	2500389	20566142	38333420	86	4207088	8.93
Lakes	2886	57720	4354448	9270274	1656715	13626775	25399071	62	3033017	8.22
MidCentral	4628	92560	7001336	14905287	2663763	21909922	40838105	75	3668972	10.86
Nelson Marlborough	2356	47120	3699436	7875805	1407506	11576985	21578448	90	4402766	4.85
Northland	3071	61420	4770436	10155878	1814984	14928562	2782584	70	3424374	7.98
South Canterbury	893	17860	1407312	2996056	535433	4404031	8208714	72	3522213	2.32
Southern	8371	167420	12676712	26987711	4823045	39670397	73942017	102	4989802	14.34
Tairawhiti	1359	27180	2038841	4340531	775708	6380333	11892361	47	2299223	5.11
Taranaki	2899	57380	44113156	9395259	1679052	13810495	25741508	68	3326535	7.61
Waikato	11331	226620	16981678	36152642	6460934	53142322	99032462	95	4647365	20.32
Wairarapa	720	14400	1128869	2403272	429495	3532673	6584582	59	2886258	2.27
Waitamata	17291	345820	25809668	54946730	9819676	80768561	150545262	70	3424374	39.93
West Coast	685	13700	1060936	2258647	403649	3320083	6188333	50	2445981	2.52
Whanganui	1378	27560	2121871	4517295	807298	6640166	1237666	58	2837338	4.32

Table 22: Benefit-cost analyses with 20 dollars per vaccine. *Vacc* is numbers to vaccinate (see Table 15); *Vacc costs* is cost for the catch up vaccination programme; *Wages saved* is wages of care givers and cases saved (\$839 per case); *Contacts* is costs saved through contact exclusion; *Manage saved* is management costs saved (\$1,765 per case), plus \$20 GP costs; *Hosp saved* is the hospitalisation costs saved (\$1,877 per case); *Costs save* is the discounted costs saved; *Outbreak* is the predicted mean outbreak size despite $R_v < 1$ due to measles importation from 1000 simulations^a; *OB costs* is costs expected due to continued measles importations based on 10 introductions of measles, one per year, but costs discounted on the same discounted rate; *B/C* is the benefit-cost ratio.

^anote the mean takes into account rare, but large outbreaks, see Figure 30 and Figure 31. Median values are all 2, thus the expected number of cases will be small

DHB	Vacc	Vacc costs	Wages saved	Manage saved	Hosp saved	Contacts	Costs saved	Outbreak	OB costs	B/C
Auckland	17920	896000	26132561	55634145	9942525	81779021	152428668	82	4011409	31.06
Bay of Plenty	4585	229250	7075979	15064196	2692162	22143509	41273490	71	3473294	11.15
Canterbury	13687	684350	20711307	44092724	7879928	64813791	120807021	62	3033017	32.50
Capital and Coast	10461	523050	15434306	32858409	5872213	48299988	90026791	96	4696284	17.25
Counties Manukau	18880	944000	27595227	58748043	10499018	86356274	160960251	50	2445981	47.48
Hawke's Bay	3751	187550	5741632	12223478	2184490	17967816	33490377	56	2739499	11.44
Hutt Valley	4388	219400	6571929	13991115	2500389	20566142	38333420	86	4207088	8.66
Lakes	2886	144300	4354448	9270274	1656715	13626775	25399071	62	3033017	7.99
MidCentral	4628	231400	7001336	14905287	2663763	21909922	40838105	75	3668972	10.47
Nelson Marlborough	2356	117800	3699436	7875805	1407506	11576985	21578448	90	4402766	4.77
Northland	3071	153550	4770436	10155878	1814984	14928562	27825484	70	3424374	7.78
South Canterbury	893	44650	1407312	2996056	535433	4404031	8208714	72	3522213	2.30
Southern	8371	418550	12676712	26987711	4823045	39670397	73942017	102	4989802	13.67
Tairawhiti	1359	67950	2038841	4340531	775708	6380333	11892361	47	2299223	5.02
Taranaki	2899	144950	44113156	9395259	1679052	13810495	25741508	68	3326535	7.42
Waikato	11331	566550	16981678	36152642	6460934	53142322	99032462	95	4647365	19.00
Wairarapa	720	36000	1128869	2403272	429495	3532673	6584582	59	2886258	2.25
Waitamata	17291	864550	25809668	54946730	9819676	80768561	150545262	70	3424374	35.10
West Coast	685	34250	1060936	2258647	403649	3320083	6188333	50	2445981	2.50
Whanganui	1378	68900	2121871	4517295	807298	6640166	1237666	58	2837338	4.26

Table 23: Benefit-cost analyses with 50 dollars per vaccine. *Vacc* is numbers to vaccinate (see Table 15); *Vacc costs* is cost for the catch up vaccination programme; *Wages saved* is wages of care givers and cases saved (\$839 per case); *Contacts* is costs saved through contact exclusion; *Manage saved* is management costs saved (\$1,765 per case), plus \$20 GP costs; *Hosp saved* is the hospitalisation costs saved (\$1,877 per case); *Costs save* is the discounted costs saved; *Outbreak* is the predicted mean outbreak size despite $R_v < 1$ due to measles importation from 1000 simulations^a; *OB costs* is costs expected due to continued measles importations based on 10 introductions of measles, one per year, but costs discounted on the same discounted rate; *B/C* is the benefit-cost ratio.

^anote the mean takes into account rare, but large outbreaks, see Figure 30 and Figure 31. Median values are all 2, thus the expected number of cases will be small

vaccinations for our cost analyses, \$20 and \$50, based on US literature. We add GP consultation costs of \$20 and the cost of contact exclusions at \$2624.57 (see subsection 6.2). Note vaccination and GP costs can be altered by the Ministry of Health in the spreadsheet provided.

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

It is worth noting that vaccination strategies that target the very young (<1 year old) may be less effective, as our analyses of the vaccinated cases suggests a substantial proportion of vaccinated cases that were vaccinated (Figure 8) were vaccinated with a single vaccine at a very young age (Figure 9). Furthermore, it may be unnecessary to vaccinate very young, as it appears possible to reach the appropriate figure (28% of currently naïve) by vaccinating all the currently naïve 2–17 year olds, so pre-school and school age children. However, there are a number of different vaccination schemes that will lead to sufficient coverage and these are given in Table ???. The appropriate cover could be reached by catch up vaccination of all school aged children.

Age range (yrs)	Proportion of naïve population
2–5	0.04
5–11	0.15
5–16	0.27
5–18	0.31
11–16	0.14
11–18	0.18
0–29	0.72
0–44	0.89
>8	0.8

Table 24: Proportion of the currently naïve New Zealand population that would be vaccinated if all naïve people in each age range were vaccinated. The estimated additional proportion of the population requiring vaccination is 28%

6.5 Benefit–cost analyses discussion

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

The results presented here are based on available data. While some of the

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

Detailed measles outbreak management costs were provided for the period of January 1 – March 9, 2014. Similar data are needed for the period preceding 2014. In the absence of these data we have used mean case data from aggregated data available. It may be unrealistic to assume that these costs would be linearly related with the number of measles cases, making it difficult to extrapolate these costs outside the reported period for 2014, but we have done so for these purposes.

In other outbreaks, the average cost per measles case was estimated to be US\$254³⁹, US\$276⁴⁰, and US\$307⁴¹ for Canada, the Netherlands, and the UK, respectively [7]. These values are substantially lower than our estimates, however, it is noticeable 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\$142,542.⁴² In this outbreak, more than 2500 hours of personnel time were needed to investigate and respond to the outbreak [11]. They estimated direct costs per case to be less than US\$500.⁴³ However, the combined direct costs of €520⁴⁴ per case in Germany [30] suggests costs may be higher. Thus, our estimates of the additional costs, including indirect costs and wages lost may be appropriate.

The annual cost for long-term care of people with moderate or severe mental retardation over a period of 50 years is estimated at US\$31,059⁴⁵ and US\$78,448,⁴⁶ respectively in Minnesota [26]. In 2000 expenditures for care in large state mental retardation/developmental disabilities (MR/DD) facilities continued to increase and reached a national annual average of US\$113,864⁴⁷ per person. In 2000 the average annual expenditures for care in large state MR/DD facilities were US\$113,864.⁴⁸ The cost of a case of measles was es-

³⁹Jan 2001 \$ to US\$ rate 0.4445: \$571

⁴⁰Jan 2001 \$ to US\$ rate 0.4445: \$621

⁴¹Jan 2001 \$ to US\$ rate 0.4445: \$691

⁴²Jan 2004 \$ to US\$ rate 0.6724: \$211990

⁴³Jan 2004 \$ to US\$ rate 0.6724: \$774

⁴⁴Jan 2005 \$ to € rate 0.5375: \$967

⁴⁵Jan 2012 \$ to US\$ rate 0.8007: \$38790

⁴⁶Jan 2012 \$ to US\$ rate 0.8007: \$97974

⁴⁷Jan 2012 \$ to US\$ rate 0.8007: \$221612

⁴⁸Jan 2012 \$ to US\$ rate 0.8007: \$221612

timated to range from US\$71⁴⁹ (no complications and no hospitalisation) to US\$29,556⁵⁰ (encephalitis and hospitalisation for 8.7 days). They estimated the annual cost of measles vaccination in the US with its vaccination program to be US\$1,234,083⁵¹ (52.5% direct cost and 47.5% indirect cost) [39]. Work by others also finds that measles vaccination is extremely cost effective, however, in their analyses they also include the costs of mumps and rubella (see Table 25) [39]. However, the cost of measles in their analyses was substantially higher than mumps and rubella (Table 25) [39].

Our estimates for the benefit–cost ratio of catch up vaccination are also higher than those in some studies. If we presume the R_0 estimated for measles in New Zealand is representative and following 28% vaccination of the naïve population, measles will be unable to persist ($R_v < 1$), our B/C ratio is substantially greater than 1. Estimates in Korea suggest catch up vaccination schemes have a benefit–cost ratio of just over one [6]. However, the estimated B/C ratio for MMR has been estimated to be between 10.2 and 54.2, much greater than one (see Table 26) [39]. As stated above, these authors also consider the costs and benefits of mumps and rubella, so making direct comparison difficult without reanalysis.

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

Finally, our model of measles introductions remains a simple one, and more complex models may predict smaller outbreaks depending on contact structure and other scenarios, such as the size of the local naïve population. The spatial effects of measles transmission may have affected both our multivariate regression analyses (section 4) and will affect the predictions from modelling exercises (section 5). Whatever happens, however, it is clear that there will be ongoing costs to maintain New Zealand free of endemic measles and introductions occurring on an annual basis may produce some larger and costly outbreaks, even if vaccination cover is high and R_v is less than one (Figure 30 and Figure 31). Given that, the greater the vaccination coverage, the smaller the outbreaks will be.

⁴⁹Jan 2012 \$ to US\$ rate 0.8007: \$138

⁵⁰Jan 2012 \$ to US\$ rate 0.8007: \$57524

⁵¹Jan 2012 \$ to US\$ rate 0.8007: \$2401874

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 25: Summary of all measles, mumps, and rubella diseases and measles-mumps-rubella (MMR) vaccination costs, USA, from [39]

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

6.6 Benefit–cost analysis summary

- The mean wage losses per measles case is estimated to be \$839
- The mean cost per measles case attending hospital is estimated to be \$1,877
- Approximately 17% of measles cases attend hospital
- The mean management cost per measles case for the current outbreak, estimated from three months of data is estimated to be \$1,765
- Using R_0 values estimated for measles in New Zealand prior to vaccination and the current naïve population sizes, the benefits of catch up vaccination strategies are clear (>1 B/C ratio).
- Introduction of measles are estimated by simulation to lead to median outbreak size of 2 cases, suggesting most infections will be individuals or lead to single secondary cases. However, mean sizes of 61 cases were predicted, 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 larger sizes.

7 Acknowledgments

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

References

- [1] Agur, Z., L. Cojocaru, G. Mazor, R. M. Anderson and Y. L. Danon (1993). Pulse mass measles vaccination across age cohorts. *Proceedings of the National Academy of Sciences USA*, 90, 11698–11702.
- [2] Anderson, R. M. and R. M. May (1991). *Infectious diseases of humans: dynamics and control*. Oxford: Oxford University Press.
- [3] Anon. (2002a). *Immunisation handbook* Wellington: Ministry of Health. pp. 131–146.
- [4] Anon. (2002b). *Infectious diseases in livestock* The Royal Society. pp. 68.
- [5] Babad, H. R., D. J. Nokes, N. J. Gay, E. Miller, P. Morgan-Capner, and R. M. Anderson (1995). Predicting the impact of measles vaccination in England and Wales: model validation and analysis of policy options. *Epidemiology and Infection*, 114, 319–344.

- [6] Bae, G. R., Y. J. Choe, U. Y. Go, Y. I. Kim, and J. K. Lee (2013). Economic analysis of measles elimination program in the Republic of Korea, 2001: A cost benefit analysis study. *Vaccine*, 31, 2661–2666.
- [7] Carabin, H., W. J. Edmunds, U. Kou, S. van den Hof, and V. H. Nguyen (2002). Measles in industrialized countries: a review of the average costs of adverse events and measles cases. *BMC Public Health*, 2, 22.
- [8] Carabin, H., W. J. Edmunds, M. Gyldmark, P. Beutels, D. Levy-Bruhl, H. Salo, U. K. and Griffiths (2003) The cost of measles in industrialised countries. *Vaccine*, 21, 4167–4177.
- [9] Clements, C. J. and G. D. Hussey (2004). Chapter 4: Measles. In *The Global Epidemiology of Infectious Diseases*, Murray, C., A. D. Lopez, and C. D. Mathers, (eds.), Geneva. World Health Organization, pp. 391.
- [10] Coleman, M. S., L. Garbat-Welch, H. Burke, M. Weinberg, K. Humbaugh, A. Tindall, and J. Cambron (2012). Direct costs of a single case of refugee-imported measles in Kentucky. *Vaccine*, 30, 317–321.
- [11] G. H. Dayan, I. R. Ortega-Sanchez, C. W. LeBaron, M. P. Quinlisk, and the Iowa Measles Response Team (2005). The cost of containing one case of measles: the economic impact on the public health infrastructure - Iowa, 2004. *Pediatrics*, 116:e1; DOI:10/1542/peds.2004-2512.
- [12] Diekmann, O., J. A. P. Heesterbeek, and T. Britton (2013). *Mathematical tools for understanding infectious disease dynamics*. Princeton: Princeton University Press.
- [13] Edmunds, W. J., N. J. Gay, M. Kretzschmar, R. G. Pebody and H. Wachman (2000). The pre-vaccination epidemiology of measles, mumps and rubella in Europe: implications for modelling studies. *Epidemiology and Infection*, 125, 635–650.
- [14] Filia, A., A. Brenna, A. Pana, G. M. Cavallaro, M. Massari and M. L.C. degli Atti (2007). Health burden and economic impact of measles-related hospitalization in Italy, 2002-2003. *BMC Public Health*, 7, 169
- [15] Flego, K. L., D. A. Belshaw, V. Sheppard, and K. M. Weston (2013). Impacts of a measles outbreak in western Sydney on public health resources. *Communicable Diseases Intelligence Quarterly Report*, 37, E240–245.
- [16] Gay, N. J., L. Pelletier, and P. Duclos (1998). Modelling the incidence of measles in Canada: an assessment of the options for vaccination policy. *Vaccine*, 16, 794–801.
- [17] Glass, K., J. Kappey, and B. T. Grenfell (2004). The effect of heterogeneity in measles vaccination population immunity. *Epidemiology and Infection*, 132, 675–683.

- [18] Honeycutt, A. A., L. Clayton, O. Khavjou, E. A. Finkelstein, M. Prabhu, J. L. Blitstein, W. Dougles Evans, and J. M. Renaud (2006). Guide to Analyzing the Cost-Effectiveness of Community Public Health Prevention Approaches. <http://aspe.hhs.gov/health/reports/06/cphpa/report.pdf>
- [19] Klinkenberg, D. and H. Nishiuraa (2011). The correlation between infectivity and incubation period of measles, estimated from households with two cases. *Journal of Theoretical Biology*, 284, 52–60
- [20] Koopmanschap, M. A. (1998). Cost-of-illness studies: useful for health policy? *Pharmacoeconomics*, 14, 143–148.
- [21] Larg, A. and J. R. Moss (2011). Cost-of-illness studies: a guide to critical evaluation. *Pharmacoeconomics*, 29, 653–671.
- [22] Mansoor, O., A. Blakely, M. Baker, M. Tobias, and A. Bloomfield (1998). A measles epidemic controlled by immunisation. *New Zealand Medical Journal*, 111, 467–471.
- [23] Ortega-Sanchez, I. R., M. Vijayaraghavan, A. E. Barskey, and G. S. Wallace (2014). The economic burden of sixteen measles outbreaks on United States public health departments in 2011. *Vaccine*, 32, 1311–1317.
- [24] Obadia, T., R. Haneef and P-Y. Boelle The R0 package: a toolbox to estimate reproduction numbers for epidemic outbreaks. *BMC Medical Informatics and Decision Making*, 2012, 12–147.
- [25] Parker, A. A., W. Staggs, G. H. Dayan, I. R. Ortega-Sanchez, P. A. Rota, L. Lowe, P. Boardman, R. Teclaw, C. Graves, and C. W. LeBaron (2006). Implications of a 2005 measles outbreak in Indiana for sustained elimination of measles in the United States. *The New England Journal of Medicine*, 355, 447–455.
- [26] Prouty, R.W., G. Smith and K. C. Lakin (2001). Residential services for persons with developmental disabilities: status and trends through 2000. *Minneapolis: Institute on Community Integration*, University of Minnesota, pp. 179, rtc.umn.edu/risp00.
- [27] Roberts, M. (2004). A mathematical model for measles vaccination. Wellington: Ministry of Health.
- [28] Roberts, M. G. and M. I. Tobias (2000). Predicting and preventing measles epidemics in New Zealand: Application of a mathematical model. *Epidemiology and Infection*, 124, 279–287.
- [29] Saha, S. and U. G. Gerdtham (2013). Cost of illness studies on reproductive, maternal, newborn, and child health: a systematic literature review. *Health Economics Review*, doi:10.1186/2191-1991-3-24.

- [30] Siedler, A., A. Tischer, A. Mankertz, and S. Santibanez (2006). Two outbreaks of measles in Germany 2005. *Eurosurveillance* 2006;11(4) article 5, www.eurosurveillance.org, accessed 14 June 2014.
- [31] Stack, M. L., S. Ozawa, D. M. Bishai, A. Mirelman, Y. Tam, L. Niessen, D. G. Walker, and O.S. Levine (2011). Estimated economic benefits during the 'decade of vaccine' include treatment savings, gains in labor productivity. *Health Affairs*, 30,1021–1028.
- [32] Statistics New Zealand (2014). <http://nzdotstat.stats.govt.nz/>, accessed 17 June 2014.
- [33] Tobias, M. I. and M. G. Roberts (1998). Predicting and preventing measles epidemics in New Zealand: Application of a mathematical model. Wellington: Ministry of Health.
- [34] Wallinga, J., D. Levy-Bruhl, N. J. Gay, and C. H. Wachman (2001). Estimation of measles reproduction ratios and prospects for elimination of measles by vaccination in some Western European countries. *Epidemiology and Infection*, 127, 281–295.
- [35] Wallinga, J., and P. Teunis (2004). Different Epidemic Curves for Severe Acute Respiratory Syndrome Reveal Similar Impacts of Control Measures. *American Journal of Epidemiology*, 160, 509.
- [36] Wichmann, O., A. Siedler, D. Sagebiel, W. Hellenbrand, S. Santibanez, A. Mankertz, G. Vogt, U. van Treeck, and G. Krause (2009). Further efforts needed to achieve measles elimination in Germany: results of an outbreak investigation. *Bulletin of the World Health Organization*, 87, 108–115.
- [37] Wolfson, L. J., P. M. Strebel, M. Gacic-Dobo, E. J. Hoekstra, J. W. McFarland, and B. S. Hersh (2007). Has the 2005 measles mortality reduction goal been achieved? A natural history modelling study. *Lancet*, 369, 191–200.
- [38] World Health Organisation measles media centre, January (2013) Geneva: World Health Organization. www.who.int, accessed July 1, 2014.
- [39] Zhou, F, S. Reef, M. Massoudi, M. J. Papania, H. R. Yusuf, B. Bardenheier, L. Zimmerman, and M. M. McCauley (2004). An economic analysis of the current universal 2-dose measles-mumps-rubella vaccination program in the United States. *Journal of Infectious Diseases*, 189, S131–45.

8 Appendix

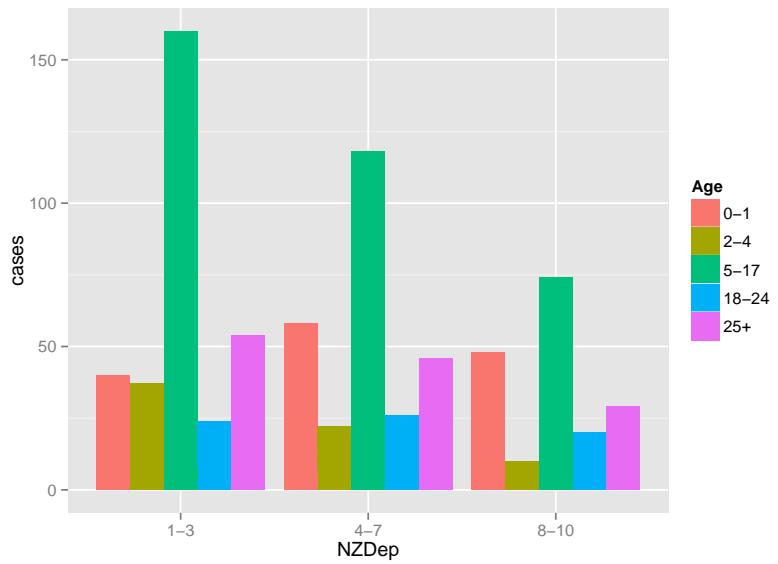


Figure 32: Measles cases by age and NZDep from 2007–2014. Full details are given in (Figure 3)

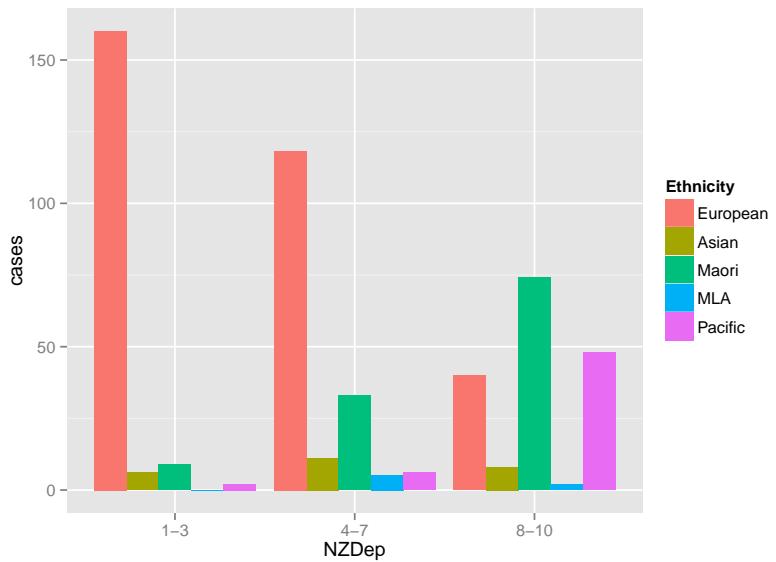


Figure 33: Measles cases by prioritized ethnicity and NZDep from 2007–2014.
Full details are given in (Figure 3)

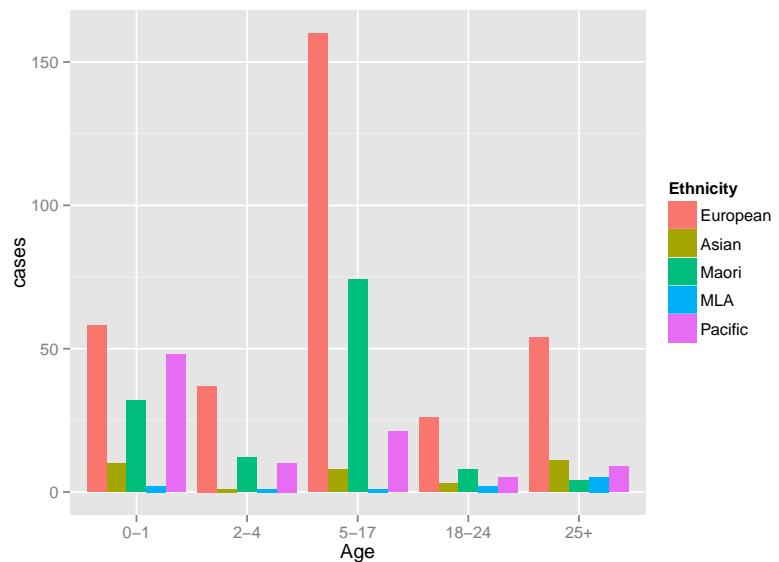


Figure 34: Measles cases by age and prioritized ethnicity from 2007–2014. Full details are given in (Figure 3)

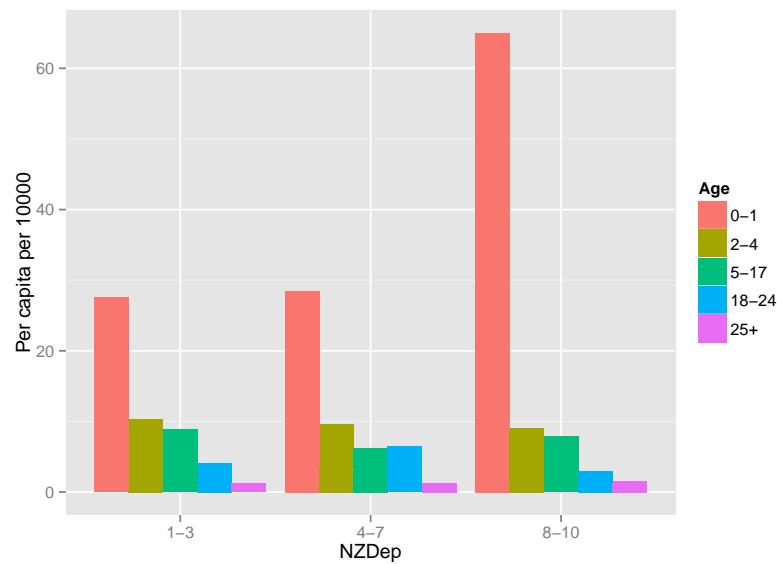


Figure 35: Per capita measles case rates by age and NZDep from 2007–2014.
Full details are given in (Figure 4)

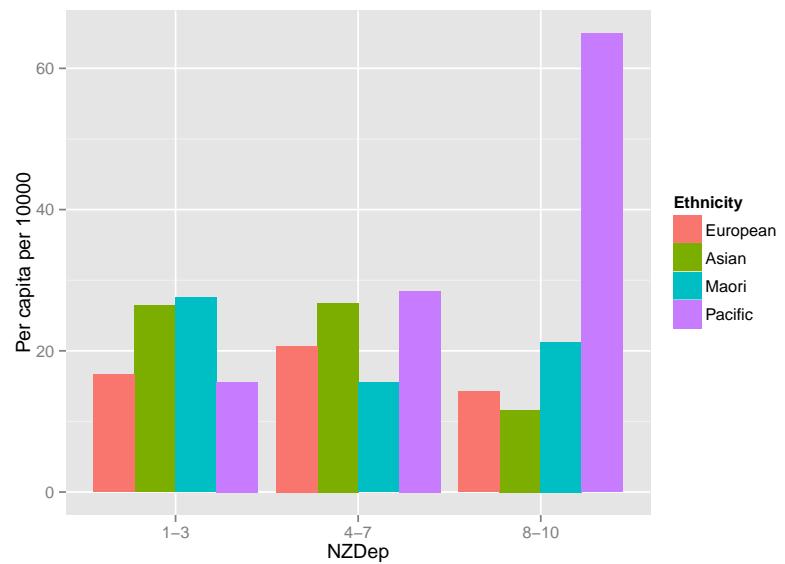


Figure 36: Per capita measles case rates by prioritized ethnicity and NZDep from 2007–2014. Full details are given in (Figure 4)

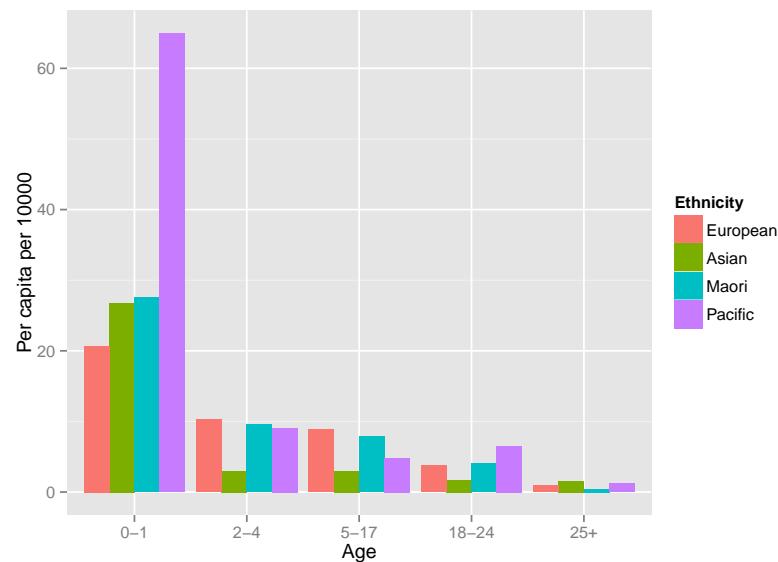


Figure 37: Per capita measles case rates by prioritized ethnicity and age from 2007–2014. Full details are given in (Figure 4)

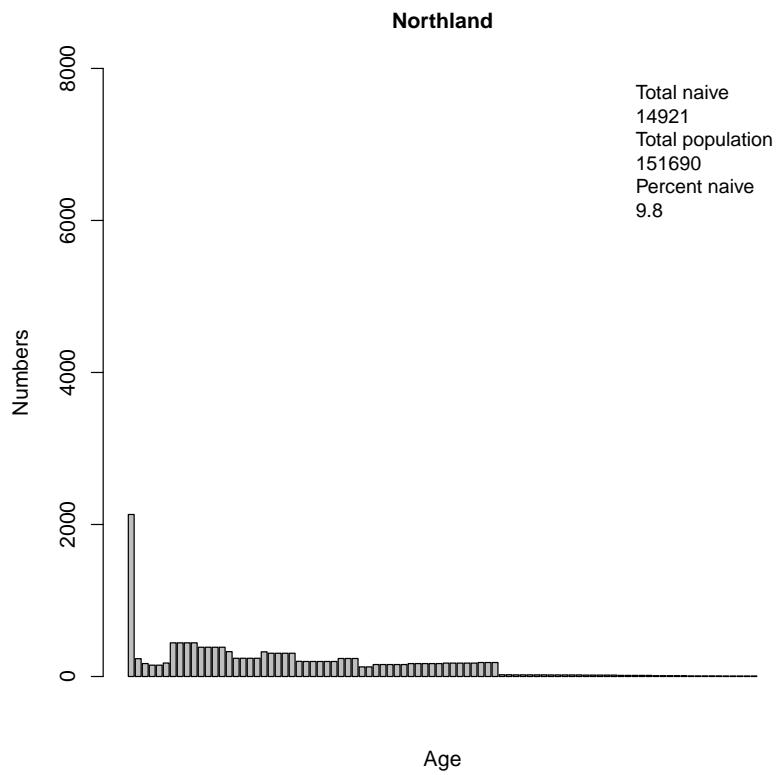


Figure 38: Numbers of naïve individuals per age class, Northland District Health Board, using national immunity data (Table 5)

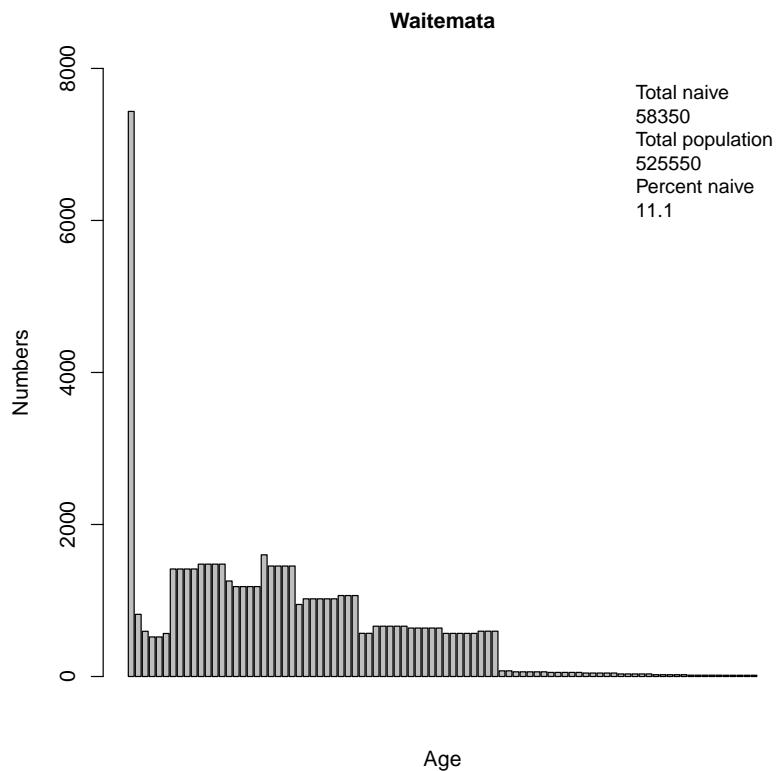


Figure 39: Numbers of naïve individuals per age class, Waitemata District Health Board, using national immunity data (Table 5)

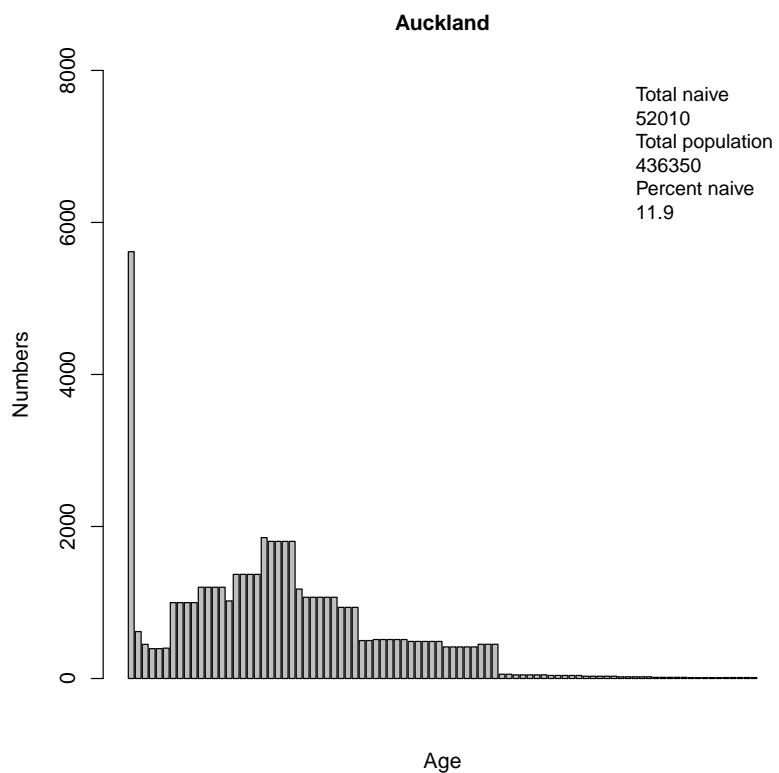


Figure 40: Numbers of naïve individuals per age class, Auckland District Health Board, using national immunity data (Table 5)

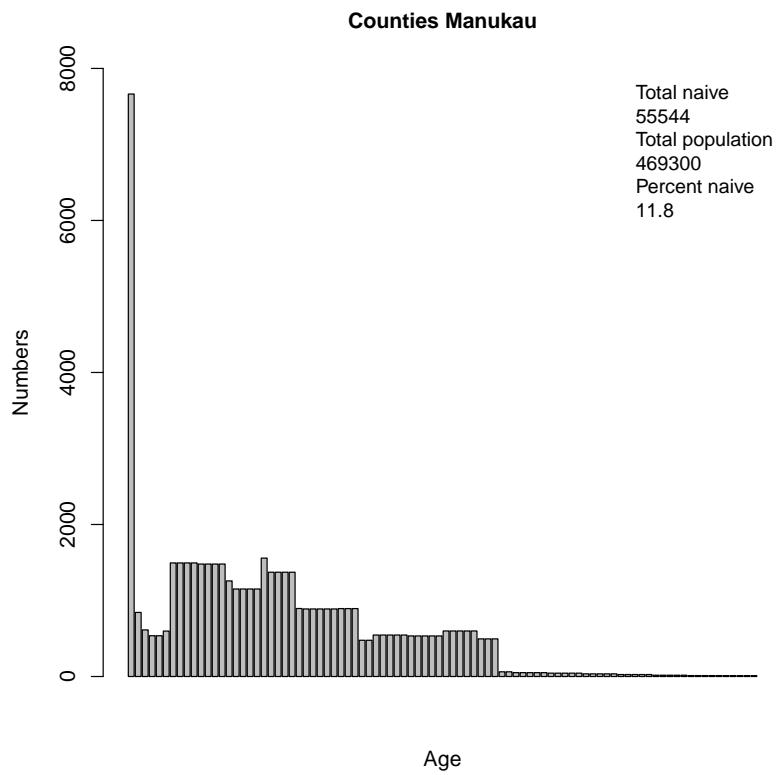


Figure 41: Numbers of naïve individuals per age class, Counties Manukau District Health Board, using national immunity data (Table 5)

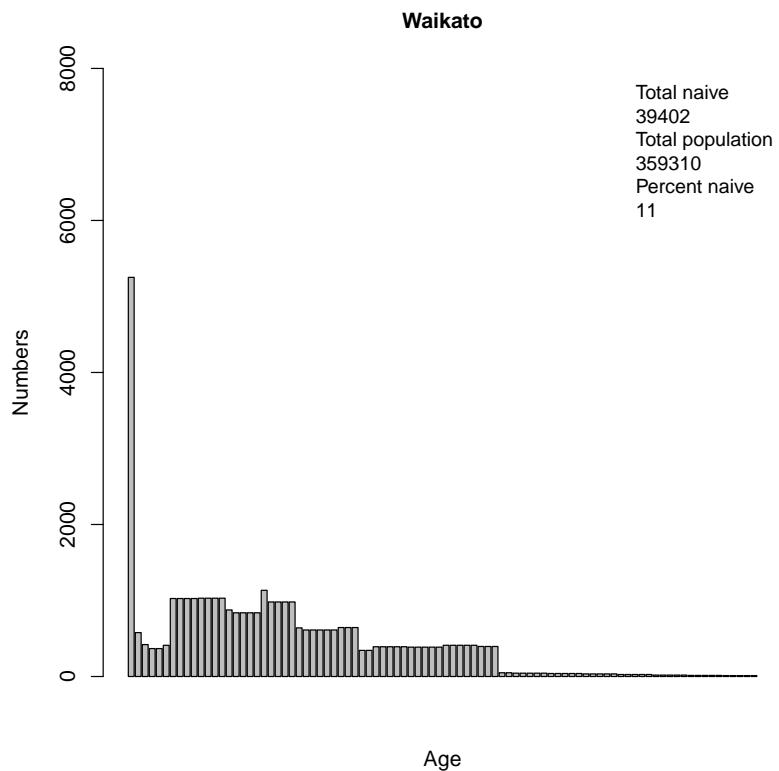


Figure 42: Numbers of naïve individuals per age class, Waikato District Health Board, using national immunity data (Table 5)

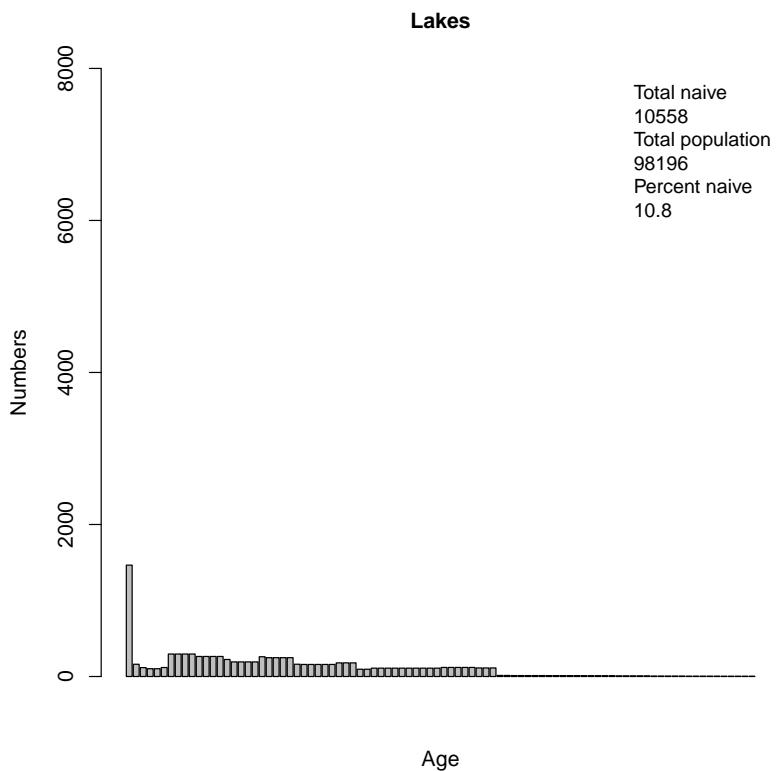


Figure 43: Numbers of naïve individuals per age class, Lakes District Health Board, using national immunity data (Table 5)

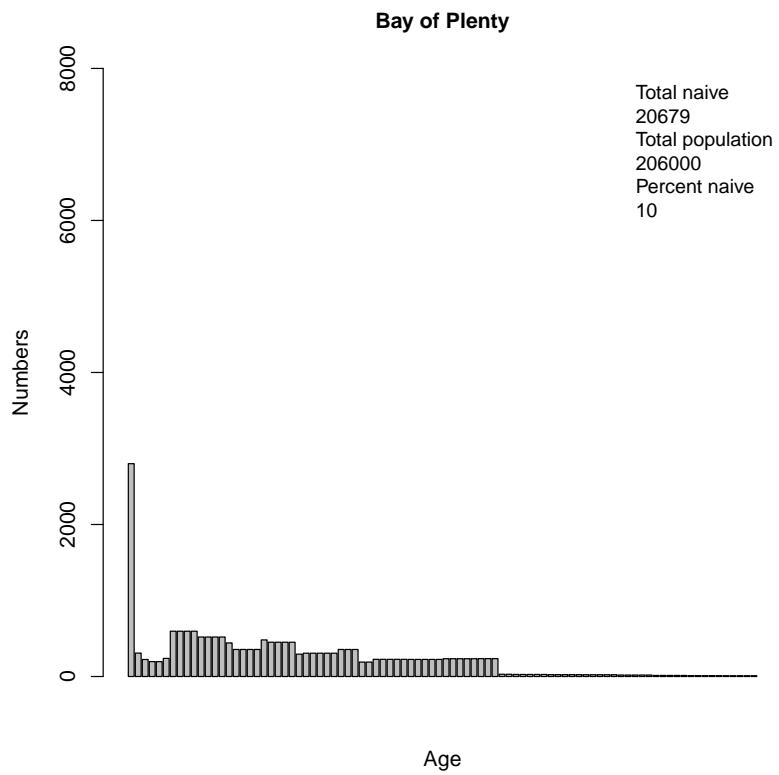


Figure 44: Numbers of naïve individuals per age class, Bay of Plenty District Health Board, using national immunity data (Table 5)

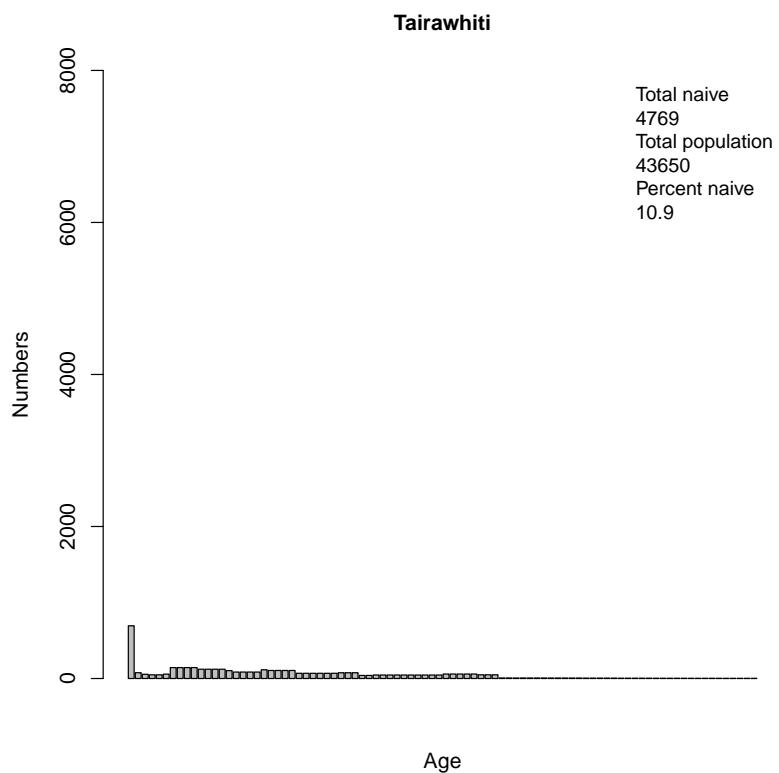


Figure 45: Numbers of naïve individuals per age class, Tairawhiti District Health Board, using national immunity data (Table 5)

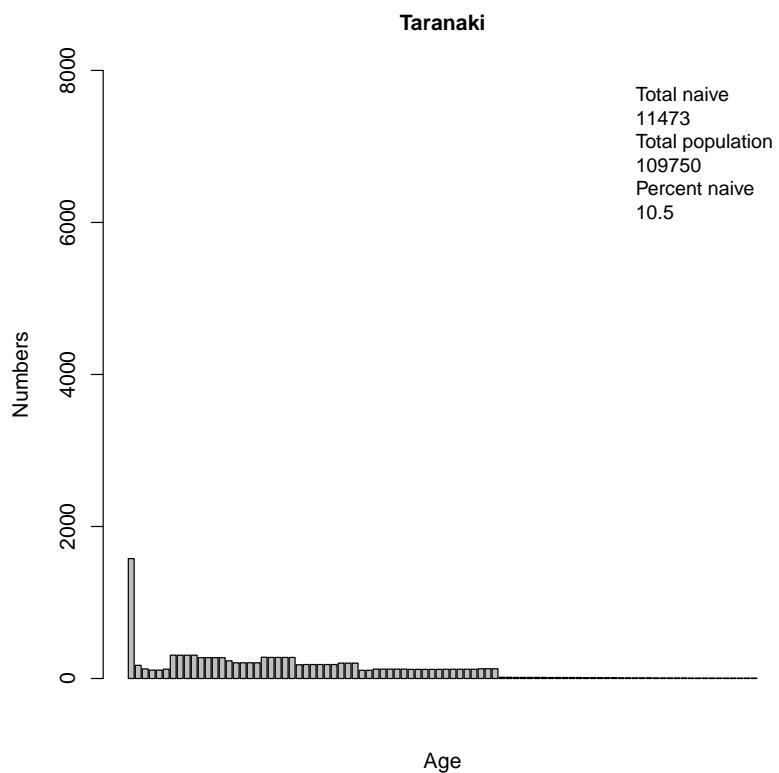


Figure 46: Numbers of naïve individuals per age class, Taranaki District Health Board, using national immunity data (Table 5)

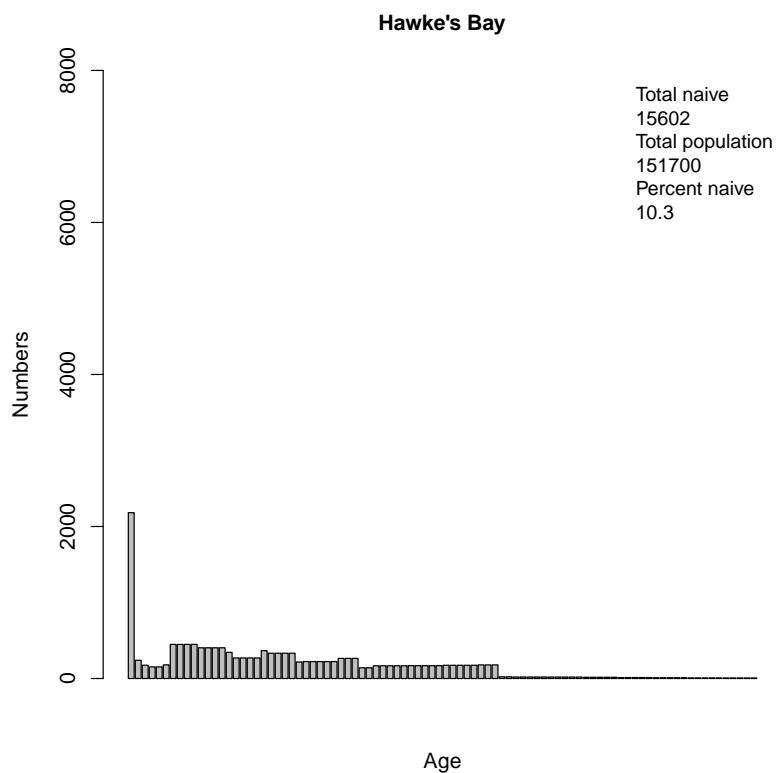


Figure 47: Numbers of naïve individuals per age class, Hawke's Bay District Health Board, using national immunity data (Table 5)

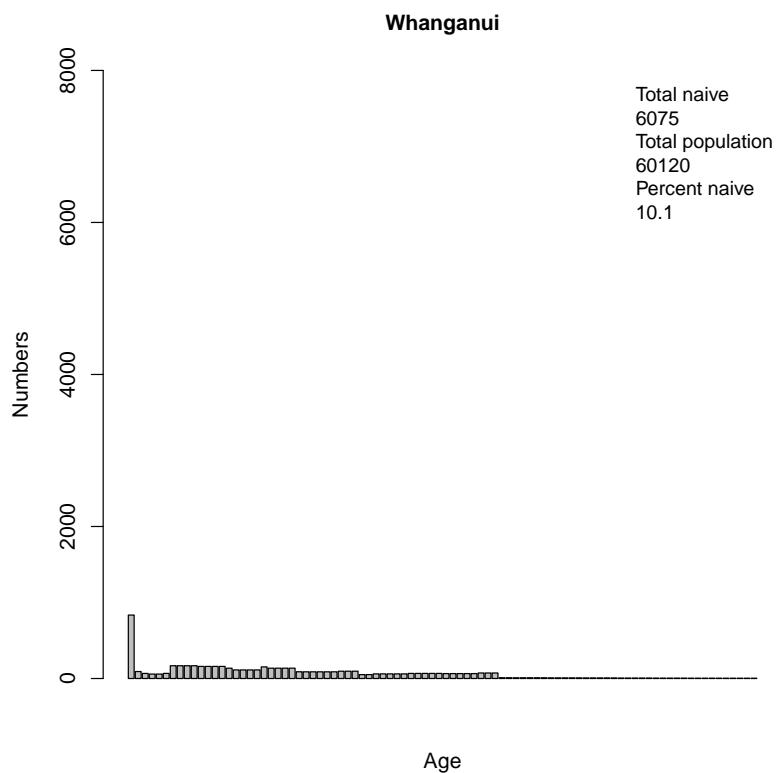


Figure 48: Numbers of naïve individuals per age class, Whanganui District Health Board, using national immunity data (Table 5)

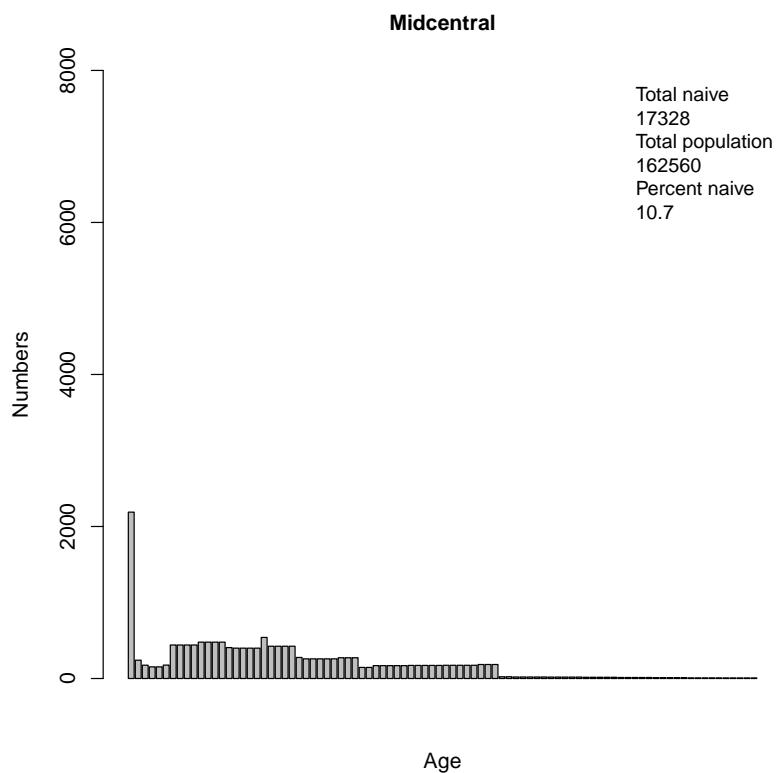


Figure 49: Numbers of naïve individuals per age class, Midcentral District Health Board, using national immunity data (Table 5)

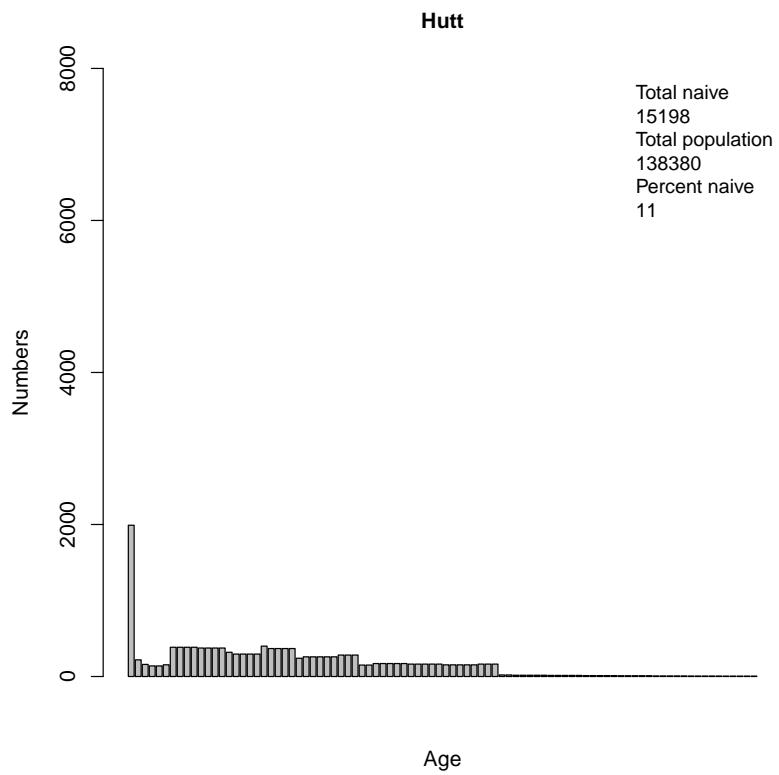


Figure 50: Numbers of naïve individuals per age class, Hutt District Health Board, using national immunity data (Table 5)

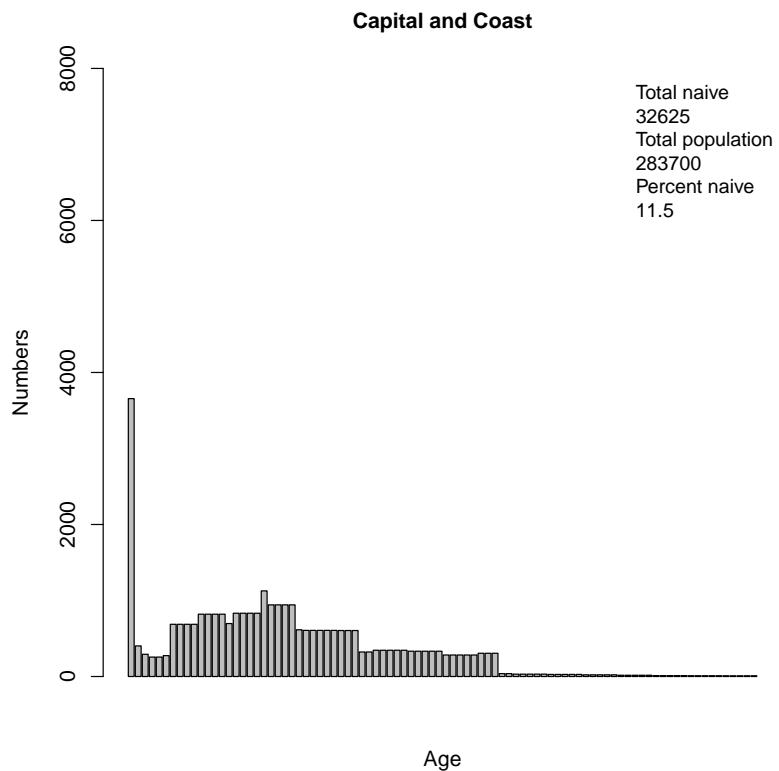


Figure 51: Numbers of naïve individuals per age class, Capital and Coast District Health Board, using national immunity data (Table 5)

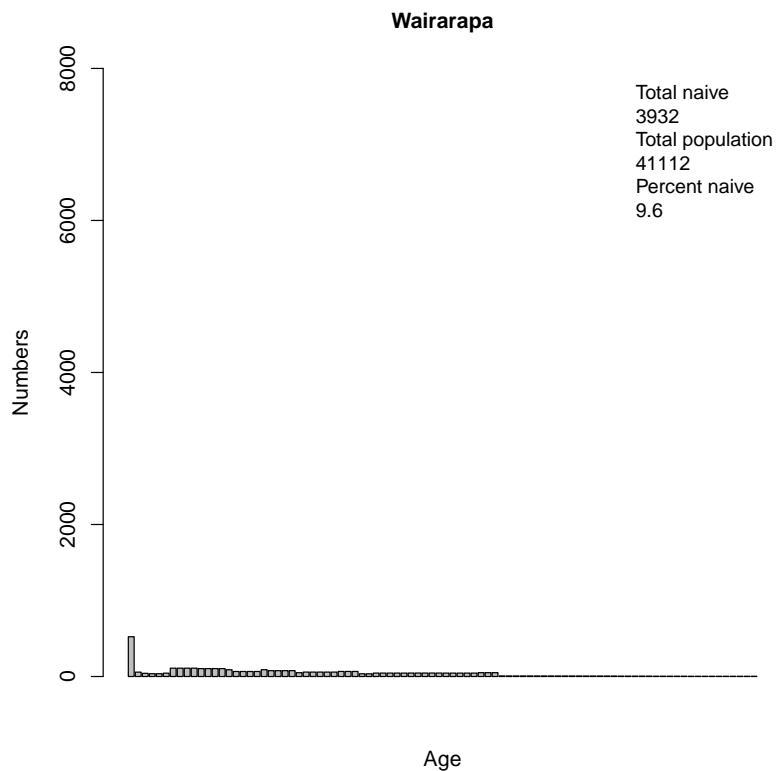


Figure 52: Numbers of naïve individuals per age class, Wairarapa District Health Board, using national immunity data (Table 5)

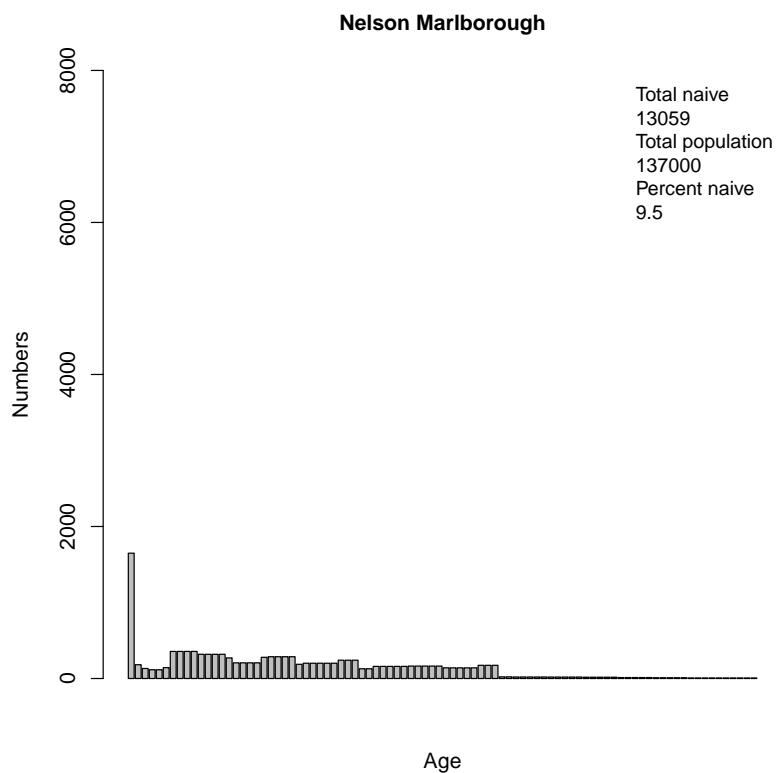


Figure 53: Numbers of naïve individuals per age class, Nelson Marlborough District Health Board, using national immunity data (Table 5)

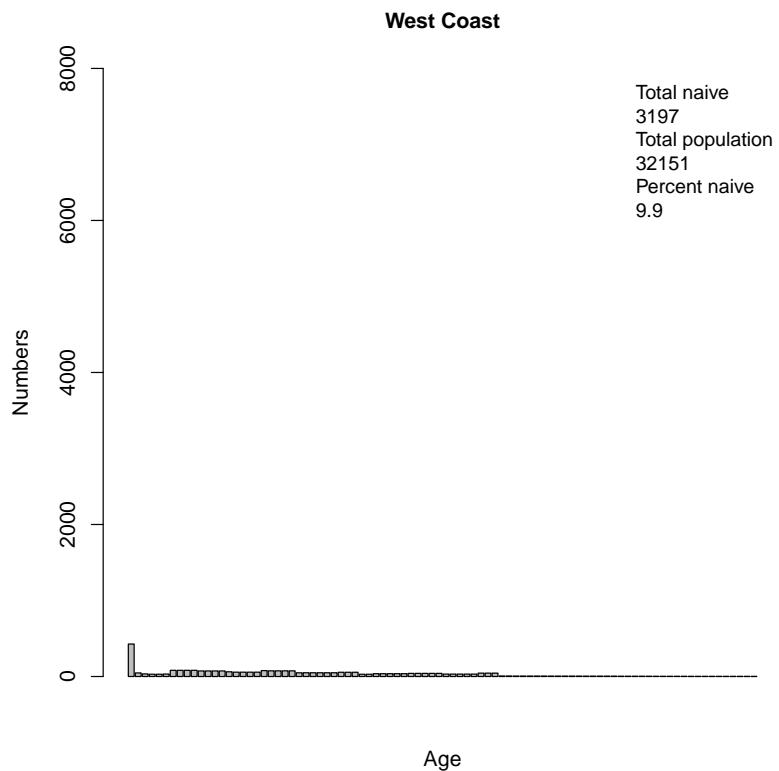


Figure 54: Numbers of naïve individuals per age class, West Coast District Health Board, using national immunity data (Table 5)

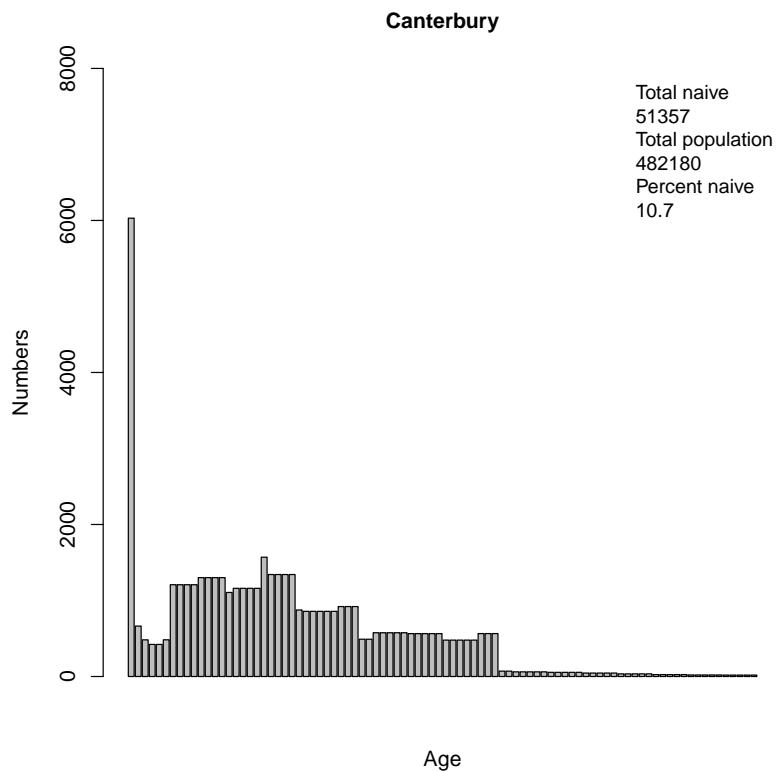


Figure 55: Numbers of naïve individuals per age class, Canterbury District Health Board, using national immunity data (Table 5)

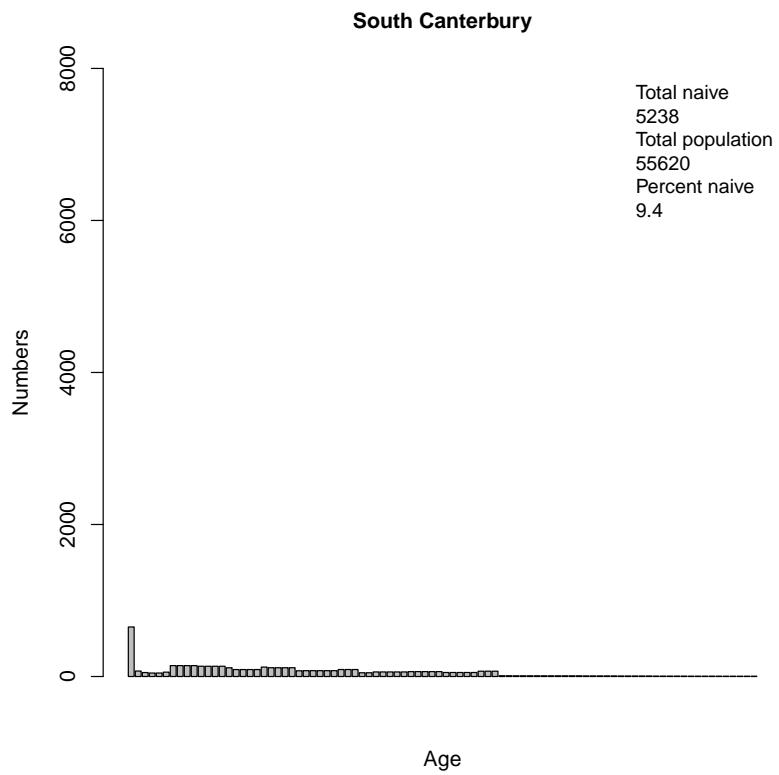


Figure 56: Numbers of naïve individuals per age class, South Canterbury District Health Board, using national immunity data (Table 5)

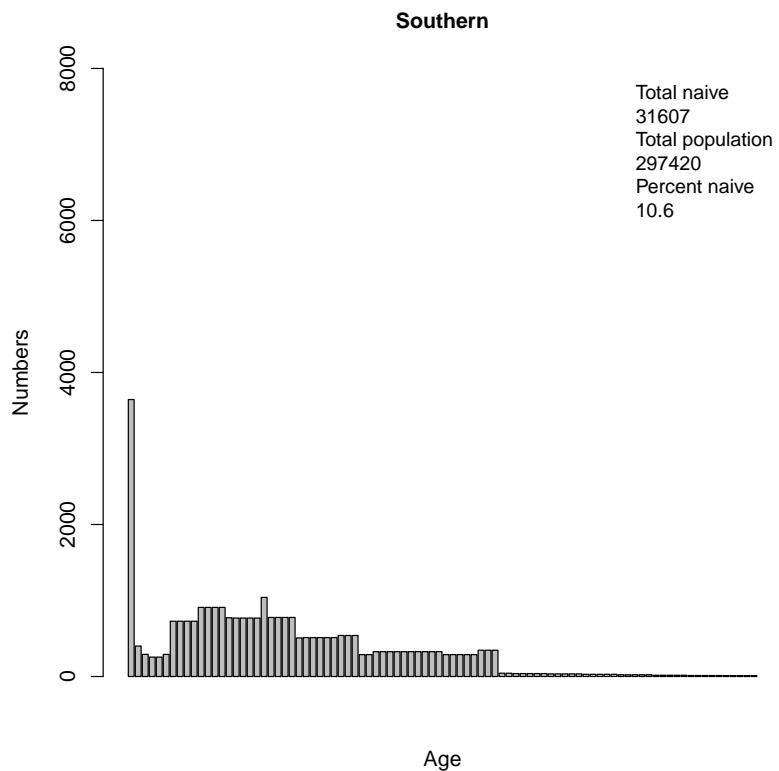


Figure 57: Numbers of naïve individuals per age class, Southern District Health Board, using national immunity data (Table 5)