Interim report
Measles risk assessment, modelling and cost analysis

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1 Abstract

New Zealand has been working towards elimination of endemic (domestic) measles virus transmission, but has suffered from small, but significant outbreaks of measles after measles introductions from abroad. In this interim report we reviewed the draft *Progress Towards Measles Elimination in New Zealand - Final* report from the New Zealand Ministry of Health to the World Health Organization (WHO) Western Pacific Region. We identified additional analyses that may help understand risk of infection in New Zealand, began analyses of the cost of the current 2013–2014 outbreak and began modelling measles outbreaks to understand how they may be controlled, and to evaluate the likelihood that measles may become endemic once more. Our key findings were:

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

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

- The cost of the current 2013–2014 measles outbreak is estimated to be at least $750,000.

- Analyses of outbreak data suggest that measles basic reproductive number (R_v, the number of secondary infections) values often include 1 and this year, 2014, is well above one. This analysis suggests improved vaccination is a requisite to prevent measles becoming endemic again.

2 Background

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

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

Previous measles analyses, including two in New Zealand by Prof. Roberts, estimated the interruption of measles virus transmission can be achieved by herd immunity when approximately 95 percent of the population is homogeneously immune to measles [27, 26]. Thus, while New Zealand immunisation activities have led to measles outbreaks becoming less frequent, with decreasing numbers of cases, outbreaks still occur (as described above). Current overall population immunity estimates suggest that approximately 85 to 90 percent of the population is immune to measles, thus the reasons for the ongoing outbreaks are likely due to overall population immunity being less than 95 percent and there being pockets of susceptible, non-immune population remaining. Since 2009, all the outbreaks in New Zealand were linked to infections acquired (imported) from overseas, though previous work suggests these outbreaks still largely affect school-aged children and children under two years of age. Under two year olds are thought be be consistently among the most affected age groups because the first of two doses of measles, mumps and rubella vaccine (MMR) is not due until fifteen months.

3   Risk analysis review

A measles risk assessment has been undertaken by the Ministry of Health to better assess current and future population immunity and high risk groups. Given the current measles outbreak, measles control is a priority for the Ministry and resources are available to control this outbreak and decrease the risk of future outbreaks.

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

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

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

Specific epidemiological details were provided for the 2011–2012 outbreak including *Figure 4*, the number and classification of measles notifications in New Zealand by month and year (2011 and 2012), with additional breakdown by age group in both years (*Figure 5*) and per 100,000 population (*Figures 6–8*). Similar presentation of the case data are provided for ethnicity (*Figures 9–10*) and New Zealand Index of Deprivation (NZDep) (*Figures 11–13*). Three figures, *Figures 12, 13,* and *28*, show that there is 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 gives information regarding the likelihood of measles persisting within the population and becoming endemic, including important analysis of the current outbreak.

We agree with the report conclusions that testing for measles is performed appropriately within the required timeframe. Clearly improving inter-laboratory communication and collaboration and timeliness of the testing and reporting is necessary for rapid responses to measles introductions following measles control. Vaccination coverage presented in the report and to ourselves confirms that immunisation levels are approaching 94% for MMR dose one (birth cohorts 2009 and 2010) and 89% for MMR dose two (birth cohorts 2006 and 2007). However,
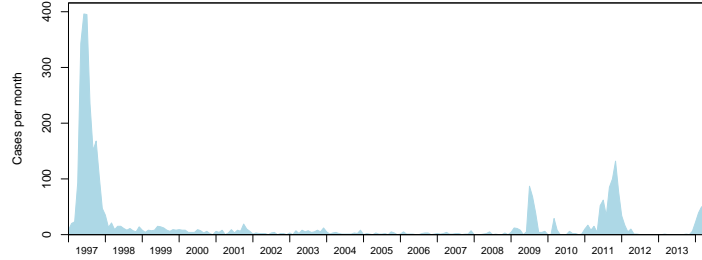
Figure 1: Measles incidence from 1997 to 2014

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 preliminary modelling and risk analyses results (section 3.1 and section 5).

The analyses we believe could further inform the understanding of risk from measles infection are:

- Multivariate modelling to account for confounding within the univariate analyses.

- Inclusion of multivariate model results with local level immunity data to develop a risk map for New Zealand.

- Analyses of changing risk factors through time during outbreaks.

- Modelling transmission chains in the population to understand effective reproduction number.

- Development of risk maps to understand measles importation.

3.1 Additional risk analyses

In this section we provide a brief description of the 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.

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

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Table 1: Immigration numbers to New Zealand (2012)

country	immigration
Australia	809775
United Kingdom	306177
China	256036
United States	194438
Japan	86676
Germany	83608
Korea, Republic of	73459
France	71448
India	69038
Canada	54981

Table 2: Lowest national measles vaccine cover (%, 2012)

country	cover
Equatorial Guinea	34
Somalia	49
Lesotho	60
Central African Republic	65
Papua New Guinea	67
Chad	69
Haiti	69
South Sudan	70
Gabon	71
Yemen	71

to better inform travellers and understand high risk periods, we sought to use quantitative methods to evaluate the risk of measles importation.

For our initial analyses, we use arrivals data from New Zealand immigration (www.immigration.govt.nz) as a proxy for human movement to and from New Zealand. We collated country population size, measles incidence and measles vaccination cover from the WHO (www.who.int/research/en/). Note this uses all immigration of foreign nationals, coming for whatever purpose. We used the WHO data to determine per capita measles cases for each year and used these data and the number of immigrants to New Zealand to begin to understand where measles was likely to be imported from.

Preliminary analyses of 2012 data, the most complete and current year of data, suggest immigration (whether for work, pleasure, etc.) is dominated by Australia, United Kingdom, China, and the United States, as shown in Table

Table 3: Measles incidence per million (2012)

country	incidence
Equatorial Guinea	1617
Nauru	1100
Democratic Republic of the Congo	1096
Somalia	979
Djibouti	824
Sudan	786
Burkina Faso	447
Romania	342
Ukraine	280
Sudan	229

Table 4: Risk of measles importation to New Zealand in 2012

country	risk
United Kingdom	10202161
Australia	6991116
Malaysia	3226580
Thailand	1576414
China	1138900
India	1039356
Indonesia	984022
Ukraine	664315
Ireland	585413
Romania	490731

1. However, vaccination coverage is lowest and measles incidence highest in less developed nations (Table 2 and Table 3). Though the precise interactions between these different risk factors are unknown, the most simple, a product of measles incidence in 2012 and immigration numbers in 2012, suggest that though immigration is lower from some Asian countries, travel from (and thus we presume to) some Asian countries also poses a high risk of measles importation to New Zealand. These data are shown in Table 4. The data for all the variables for each nation state and territories for 2012 are plotted in Figure 2, Figure 3, and Figure 4 and the risk map for measles incidence and immigration in Figure 5.
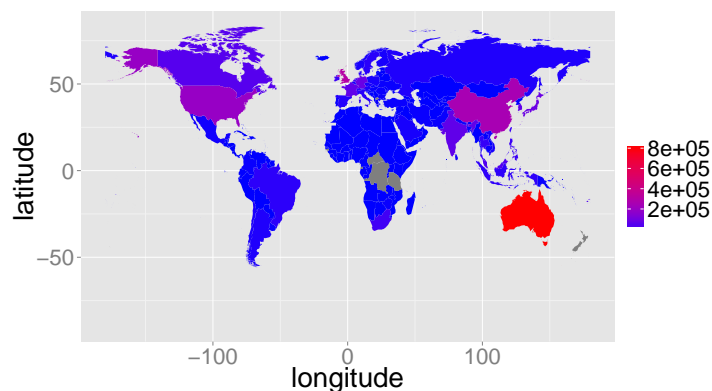

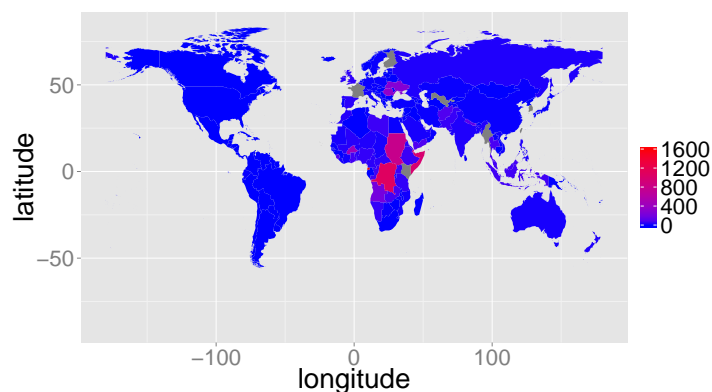Figure 2: Immigration to New Zealand 2012

Figure 3: Measles incidence per million 2012

Though global incidence of measles in declining, in recent years that decline has slowed (Figure 6) and immigration rates to New Zealand have risen
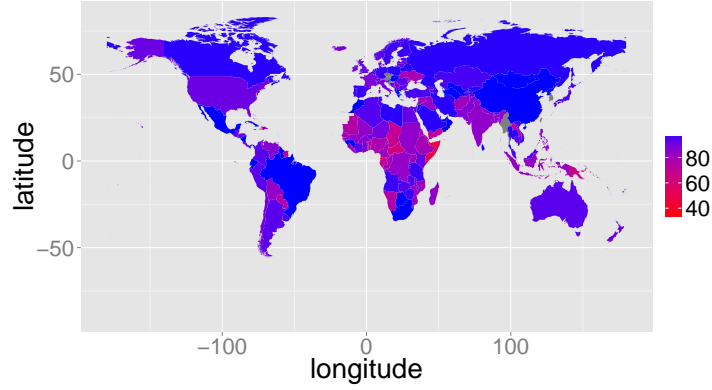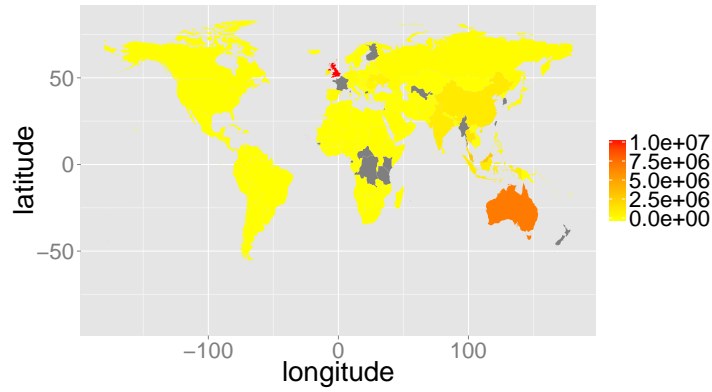
Figure 4: Measles vaccination cover (%) 2012

Figure 5: Risk map from measles incidence and immigration rates

(Figure 7). This suggests that the risk of measles importation could increase, though further analyses are require to understand the interaction between these variables. Of note, however, is the clear seasonality in immigration (Figure 7). This seasonality suggests that there may be period of increased risk of measles importation, though again the interactions with seasonal measles transmission from the nations of origin will be an important factor in determining the risk of measles importation.

3.2   Risk analysis summary

- There is a continued, and perhaps increasing, risk of measles importation due to travel and endemic measles elsewhere in the world.
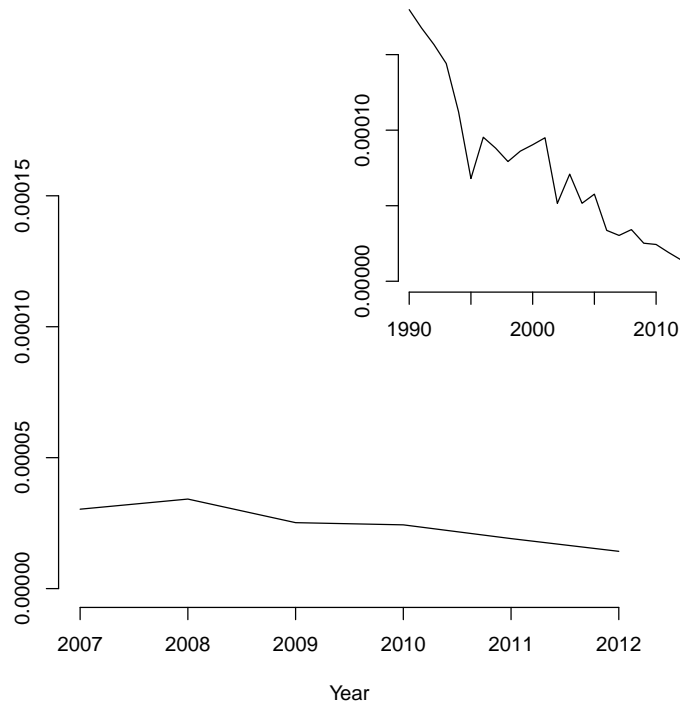
Figure 6: Trend in global per capita measles incidence

- There may be seasonal changes in risk of measles importation, though further analyses are needed.

3.3 Future risk analyses

We received the raw EpiSurv measles case data from The Institute of Environmental Science and Research Ltd (ESR) on 27 June 2014. Initial analyses of those data (not shown) suggest that we require denominator data to perform multivariate analyses to avoid confounding results due to a lack of independence among risk factors. Specifically for the multivariate analyses we wish to perform that detect interactions we require Age × Prioritised Ethnicity × NZDep data for New Zealand to test whether interactions among case covariates provide additional information on risk over the univariate analyses performed in the report reviewed above. These Age × Prioritised Ethnicity × NZDep data only became available to us on 3 July 2014, provided by the University of Otago.

The following analyses are in progress, for inclusion in later reports:

- Multivariate regression analyses to assess interactions between risk factors that may confound the univariate analyses.
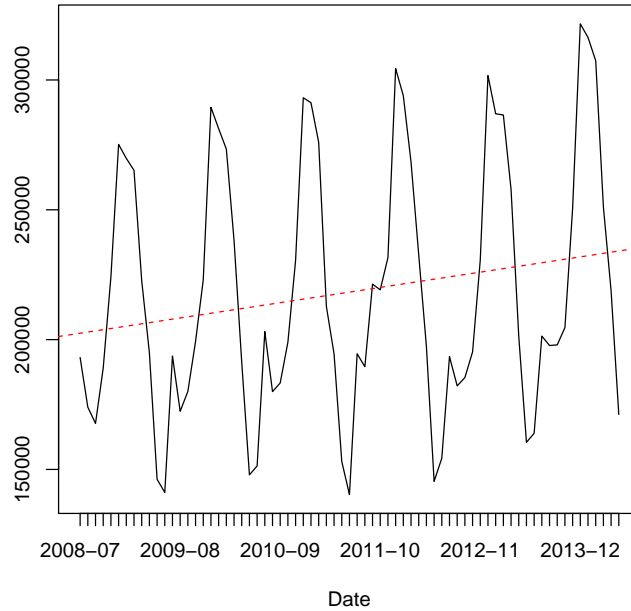
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Figure 7: Trend in total immigrations into New Zealand

- Update of the importation risk analyses using a broader range of years, including modelling the trend in importations.

Additional data we believe would enable us and the Ministry to better understand measles risk is fine scale (lower than District Health Board (DHB)) immunisation coverage data. Thus the data gap that we have that will hinder us providing fine scale risk maps are:

- Meshblock (or census area unit) level immunisation coverage data to allow targeted immunisation and understanding of risk at a fine scale level.

- The number of New Zealanders arriving from abroad each year, the countries to which they travelled, and length of travel.

We understand the National Immunisation Register (NIR) allows tracking of the vaccination status of children and this is very useful, but inclusion of these data at lower (e.g. meshblock, census area unit) level would allow better understanding of risk of measles infection and resource allocation because they may allow targeted immunisation programmes.

4 Cost analyses

In this section we provide a review of the costs of measles from other locations and an analysis of the costs involved with the current measles outbreak.

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

The annual cost of treating and controlling measles in 11 industrialised countries was estimated to cost more than US$150 million

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

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

Germany implemented a two-dose measles vaccination program in 1991 and has seen the benefits in recent years. In 2001 more than 6,000 cases were reported in Germany but by 2004 this number fell to 122 [35]. However, in 2005 more than 500 cases were reported by the middle of the year in two German states, with the vast majority (>95%) in non-vaccinated children [29]. An economic analysis was performed of the 614 measles cases reported in an 8-month period in Duisburg in the state of North Rhine-Wesphalia (NRW). In that study,

they estimated the health-care provider costs to be approximately €229,000, or €373 per case. Approximately 78% of these costs were associated with the 95 (15.5%) of the cases that were hospitalised. The mean costs of the hospitalised patients was €1,877, including one patient with encephalitis at a cost of €35,623. In addition to the health-care provider costs, additional costs of €89,400 were incurred by the district public health office, the majority (€85,000, 95.1%) for personnel, €2,300 (2.6%) for vaccination, and €2,100 (2.3%) for serologic testing. Therefore the combined direct costs of these 612 cases amounted to €318,400, or €520 per case. In addition, to determine the total impact, it would be necessary to include the indirect losses associated with lost production of cases and care givers.

Although measles was declared eliminated from the United States in 2000, it remains a concern due to the endemic nature of it around the world [24]. Several studies have been conducted in the United States to assess the economic impact of recent measles outbreaks due to imported measles. [22] estimated the economic impact to public health departments in the US as the result of 16 outbreaks in 2011. The outbreaks lasted an average of 22 days and resulted in 107 confirmed cases; however, from these 107 cases, they estimated between approximately 8,900 and 17,500 contacts with confirmed cases, requiring between 42,600 and 83,100 personnel hours at a cost of between US$2.7 and 5.3 million. Overall, it was estimated that each contact required 4.7 personnel hours at a cost of US$298 per contact. [11] calculated the cost of containing a single case of measles that occurred in Iowa in 2004. They estimated that for the one week that the Iowa Department of Public Health (DPH) investigated the case, 2,525 hours were used to identify contacts, set up vaccination clinics, and institute and enforce quarantine orders for those who refused vaccination. In total, it was estimated the direct costs associated with three cases of measles was US$142,452, or nearly US$50,000 per case.

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

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

munologic screening tests for the parents' exposed to measles (US$240) for a total of US$23,816.

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

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

4.1 Methods

Costs were evaluated as either direct or indirect. Direct costs included physician consultations, hospitalisations, drugs, vaccination, long-term care for chronic sequelae, special education costs. Direct costs can be divided into medical and non-medical [28]. Direct medical costs include costs for diagnosis, treatment, continuing care, rehabilitation and terminal care. Personnel time (investigation and emergency response), materials (phone calls, vaccine), personnel (cost, wages and fringe benefits), overhead costs, public information, and mileage are estimated when calculating direct medical costs. Direct non-medical costs include transportation to and from health care providers.

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

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

Cost of the Auckland Regional Public Health Service (ARPHS) for measles response were obtained from the Ministry of Health. Data, for the period January 1 - March 9, 2014, reported salaries for people involved with the measles outbreak management medical team. The costs were reported as direct, additional (above normal budgeting) costs required to enable the management of measles. It includes a breakdown by individual performing the work and whether it was during the normal work schedule (Monday to Friday, M-F) or

weekends. Normal work was calculated as $1.2 \times$ full time equivalent (FTE) $\times$ number of days worked. Overtime was calculated as $1.6 \times$ FTE (M-F) and $2.0 \times$ FTE (weekend). A full day was considered as 8 hours worked. Salary (hourly) rates were calculated for the following: public health nurse (PHN, \$36), public health assistant (PHA, \$22), data support (\$26), data support (temporary) (\$33), management and programme supervisors (\$40), incident management team (IMT), which had the following work titles: incident controller (\$96), administrator (\$24), planning and intel (\$40), logistics (\$36), communications (\$45), informatics (\$40), operations (\$40), and safety/security officer (SSO) (\$26). In addition, measles operations personnel were calculated at a daily rate of \$600 and operations partners and IMT controller partners at \$729.

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

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

4.2   Results

Direct costs for measles management in New Zealand for the 10-week period, January 1 – March 9, 2014 are shown in Table 5. The reported direct medical costs do not appear to include hospital medical costs, which are reported separately in Table 6.

The total cost for the 192 publicly funded hospital discharges with a measles primary diagnosis was \$289,694 (Table 6). The mean cost per case was \$1,509. The mean cost per day of stay in the hospital was \$1,154.

From 16 December, 2013 through 19 June, 2014 there were 201 confirmed measles cases in New Zealand (note 14 of these occurred before Jan 2014, so 187 occurred from Jan 2013 – 19 June 2014). The number of cases by age group is shown in Table 7. 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 majority (191/192) of the measles cases stayed in the hospital from 0 to 7 days, with the exception of a male patient, who was discharged in 2011 at age 57, after a stay of 19 days and a cost of \$8,213. Eighty-three of the cases stayed for 0 days and the remaining cases stayed a mean of 2.30 (median 2) 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 2008–2013 appear in Table 8. The cost for these 192 hospitalisations was

Table 5: Estimated costs (NZ$) for measles management in New Zealand, January 1 – March 9, 2014 (see text for abbreviations)

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

Table 6: Number of cases, length of hospital day, cost, cost per case and cost per day for patients with measles as the primary diagnosis, 2008–2013

Year	Cases	Days	Cost	Per.case	Per.day
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
Total	192	251	289,694	1,509	1,154

Table 7: Frequency of measles cases and number and proportion admitted to hospital by age group, 16 December, 2013 – 19 June, 2014

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

Table 8: 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, 2008–2013

Year	Gender	Cost	Cases	Days	Per.case
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
Total		289,694	192	251	1,509

$289,964. Of the 292 cases, 87 were female and 105 were male. The number of days spent in the hospital was 251, making the mean daily cost $1,509. Of the 251 days, 114 were spent by females and 137 by males. The mean hospital stay per case was 1.31 and 1.30 days for females and males, respectively. The mean cost per case was $1,573 and $1,456 for females and males, respectively.

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 9). Results showed an increase of approximately $358 per day of hospitalisation, $139 for a female case, and $1 per year of case diagnosis. The cost was found to decrease by approximately $5 per year of case age.

Wages lost due to measles were calculated based on the assumption that 5 days of work were lost for each case; however, individuals under 15 years of age were not assumed to be employed and therefore did not suffer an income loss. If the case were less than 20 years of age, it was assumed there was an income loss of 5 days for the care giver, in addition to the wage loss of the case if 15–19 years of age. Total wage lost for the 192 cases and care givers was estimated to be $166,638. This consisted of $90,620 for the cases and $76,018 for the care

Table 9: Regression results ($R^2_{\mathsf{adj}} = 0.9$, p-value < 0.001) for measles hospitalisation cost based on length of stay (days), gender, case age and year of case ($n = 192$) in New Zealand, 2008 – 2013

Variable	Coefficient	P.value
Length of stay (days)	357.71	<0.001
Gender (0 = F, 1 = M)	−138.55	0.084
Case age (years)	−5.23	0.032
Year of case	0.60	<0.001

giver, but did not include wage losses for cases under 15 years of age.

This final figure brings an approximate estimate of \$786,479 for the current 2014 outbreak, which is comprised of earnings lost, case management and hospitalisation costs.

4.3 Cost analysis discussion

The results presented here are based on available data. While some of the data are complete and detailed, this is not true of all the data. In order to perform an accurate analysis of the current measles outbreak in New Zealand, more complete data are needed. For instance, age, gender, ethnicity, year of discharge, length of stay and estimated cost data are available for cases reported by publicly funded hospitals. In addition to this information, similar data would be needed for cases occurring outside the period 2011–2013 at publicly funded hospitals. In addition, similar data would be needed for non-publicly funded hospitals, e.g. private clinics. Other factors that we aim to investigate are whether or not a linear term for case age is appropriate, or what if any interaction 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. If detailed data, such as that provided for early 2014, are not available, aggregated data would be acceptable. However, it is 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. As other studies have demonstrated, direct costs required to manage measles are not linear.

In other outbreaks, the average cost per measles case was estimated to be US\$254, US\$276, and US\$307 for Canada, the Netherlands, and the UK, respectively (Carabin, et al., 2002). This and other findings will be compared and contrasted with New Zealand costs, once more complete New Zealand data are made available. The containment of a single case (also 2 secondary cases) of measles in 2004 in Iowa, USA was estimated to cost US\$142,542. In this outbreak, more than 2500 hours of personnel time were needed to investigate and

respond to the outbreak (Dayan et al., 2005). They estimated direct costs per case to be less than US$500. The annual cost for long-term care of people with moderate of severe mental retardation over a period of 50 years is estimated at US$31,059 and US$78,448, respectively [25]. In 2000 expenditures for care in large state mental retardation/developmental disabilities (MR/DD) facilities continued to increase and reached a national annual average of US$113,864 per person. In 2000 the average annual expenditures for care in large state MR/DD facilities were $113,864. The cost of a case of measles was estimated to range from $71 (no complications and no hospitalisation) to $29,556 (encephalitis and hospitalisation for 8.7 days). They estimated the annual cost of measles in the US with its vaccination program to be $1,234,083 (52.5% direct cost and 47.5% indirect cost) [38].

4.4   Cost analysis summary

- Our initial estimates suggest the ongoing 2014 measles outbreak has cost New Zealand over $750,000.

4.5   Future cost-benefit analyses

Using the results above we aim to:

- Estimate the costs and benefits for targeted vaccination, based either on the univariate analyses presented to date in the *Progress Towards Measles Elimination in New Zealand - Final* report or adjusted if any additional risk groups are identified in the multivariate analyses or modelling.

We also require additional clarifications of the data, regarding:

- What hospital costs refer to, such as if a hospital day were 0 does that mean the case stayed in the hospital but not overnight? Or, does it mean the case stayed for less than 24 hours?

Once more complete data are available, comparisons of these results will be made to other published studies, discussed above.

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 [27, 26, 32]. The results show that achieving coverage of greater than 90% at both vaccination opportunities is necessary if future epidemics of measles are to be prevented.

The original mathematical model for the dynamics of measles in New Zealand prepared in 1996 [32] successfully predicted the 1997 epidemic, which was curtailed by a mass vaccination campaign [21, 27]. Subsequent extension of this work in 1998 showed that the then current schedule of MMR1 at 15 months and

MMR2 at 11 years was insufficient to prevent further epidemics. The model developed by [27] supported the change in the immunisation schedule that took effect in January 2001, at which time MMR2 was changed from delivery at 11 years to delivery before the age of five. The schedule was changed in 2000 with MMR2 now being administered before 5 years [3] and later analyses suggested high levels of vaccination coverage (but less than 95%) could eliminate measles, but emphasised that it is necessary to maintaining high coverage rates in order to prevent future epidemics [26].

These results were comparable to others, for example: [5] suggested two-dose schedule for England and Wales, with the second vaccination given at age four; and [16] recommended a second vaccination at either 18 months or five years, to complement the first vaccination at 12 months in Canada. In addition, [1] found that vaccinating 85% of susceptible children aged one to seven years at five-yearly intervals would prevent epidemics in Israel. All agree that two vaccinations at no less than five years apart are necessary to prevent measles epidemics. [33] took existing policies in eight European countries and estimated the coverage rates required to reduce R_v below one. 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, 33] based on sets of nonlinear differential equation (ODE) models have reached similar conclusions. The differences in the models have been in the details of the representation of the infectious period, and in the ways in which the age and contact structures of the population have been specified. While analyses suggest that 85% coverage at MMR1 and MMR2 could be sufficient to prevent future measles epidemics, [17] in the Netherlands showed that high over-all levels of measles vaccination can obscure pockets of poor coverage, resulting in localised regions with increased risk of infection and effective immunisation is difficult to evaluate.

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

To understand the level of immunity in the population, the transmission dynamics of measles in the partially immune population and how likely an outbreak was of becoming endemic, we estimated R_v from all the outbreaks in New Zealand since 2009. To do this we estimated R_t, following an adaptation of
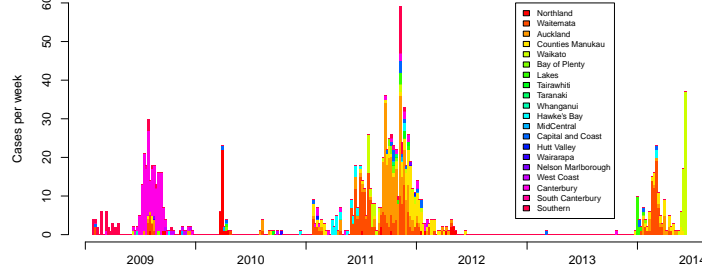
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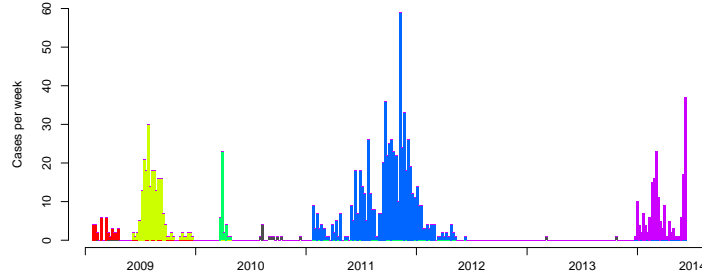Figure 8: Measles cases by district health board (DHB) from 2009 to 2014

Figure 9: Measles data classified as outbreaks for reproductive number of the infection (R_v) estimation

the methods in [23, 34]. We were required to compute the generation time for measles to do so. The generation time is the average time an index case infects others after becoming infected. We used a lognormal distribution with mean 12.0 and standard deviation (s.d.) 3.5 from [18]. We then estimated R_t from the incidence data for each outbreak, defining outbreaks in the dataset given their temporal and geographic correlations (Figure 8).The outbreaks we used in our analyses are shown in Figure 9.

The estimated R_v for each outbreak is shown in Figure 10. The probability density of the R_v estimates for each outbreak all include one. Of particular note is the ongoing outbreak, which has an R_v well above one and thus we may expect this outbreak to persist if conditions remain the same. An important caveat to this outbreak analysis is that because this 2013–2014 outbreak is an ongoing outbreak, and not in decline, R_0 is necessarily over one, and so the comparison with others must be cautious.

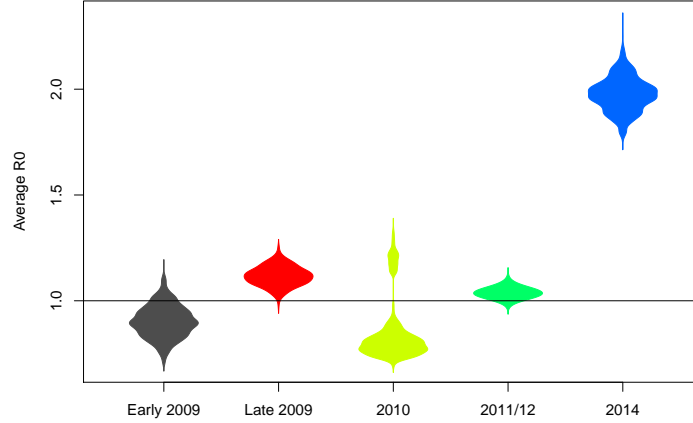These analyses also imply that the regular (approximately yearly) importa-

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Figure 10: Estimates of R_v (R_0) for the outbreaks each year, as classified in Figure 9 (page 20)

tion of measles is an ongoing process. Given the risk of importation of measles as highlighted in section 3.1 is likely to continue, these analyses suggest substantial efforts are required to maintain the level of immunisation to high enough levels that measles does not become endemic. The measles outbreak in 2011–2012 had an R_v of just greater than one, and yet it persisted for over 12 months. This implies that the current outbreak may persist within the population for a substantial period, given it's R_v is approximately twice that of the 2011-2012 outbreak. A caveat to this and other R_v estimates is that the 2013–2014 outbreak may include some sporadic cases and thus the true basic reproductive numbers may be lower than estimated. However, sub-clinical and underreporting may lower the estimate. The relative contributions of both to our estimates are currently unknown.

5.1 Summary of modelling

- Regular introductions of measles pose an ongoing threat to New Zealand's efforts to eliminate measles (also see section 3.1).

- The reproduction number for measles in a partially immune population is often close to one, suggesting increased population level immunity is required to prevent this measles persisting.

- The reproduction number, R_v, for measles in the current outbreak is well over one, suggesting that this outbreak has the potential to persist for

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prolonged periods, with the caveat that this estimate was made during the ongoing outbreak.

6 Future modelling

Future modelling we aim to perform are:

- An update of previous ODE models of measles in the overall population according the differing vaccine coverage scenarios [26].

- Model measles outbreaks with differing scenarios of measles importation into various population groups based on current introduction rates.

7 Summary of key findings

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

- The cost of the current measles outbreak is estimated to be at least \$750,000.

- Analyses of outbreak data suggest that measles R_v values often include 1 and in this year, 2014, are well above one. This analysis suggests improved vaccination is a requisite to prevent measles becoming endemic again.

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