

Reducing differences in the uptake of immunisations: Economic analysis 2

An exploration of the cost-effectiveness of interventions to reduce differences in the uptake of childhood immunisations in the UK using threshold analysis

National Collaborating Centre for Women's and Children's Health

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Introduction

This work was commissioned by the National Institute for Health and Clinical Excellence (NICE) to support the development of public health intervention guidance on reducing differences in the uptake of immunisations in children and young people aged under 19 years. The work draws on the results of a health economic model for the transmission of measles in a Western European country that was developed by Edmunds and Van Hoek (2008) [Economic analysis 1] for NICE's Public Health Interventions Advisory Committee (PHIAC), which is developing the guidance.

In England, although childhood immunisations are routinely offered through primary care services, persistent differences in uptake exist between different social groups and geographical locations. With coverage levels below those necessary to achieve elimination, there are potential gains to be achieved through increasing uptake above existing levels. However, any interventions implemented to increase coverage are likely to have a cost over and above that associated with delivery of the routine immunisation schedule. Therefore, from a policy maker's perspective it would be useful to know to what extent the additional resources needed to increase immunisation uptake represent a cost-effective use of public money.

In Part 1 of this report we briefly explore some of the equity-efficiency trade off which may exist (at least conceptually) for guidance which is concerned primarily with reducing differences in uptake but also considers the cost-effectiveness of the interventions designed to achieve this. Then, in Part 2,

the results of the model of Edmunds and Van Hoek (2008), which explores the impact of increasing vaccine coverage for measles in the UK on the distribution of disease are elaborated in more detail to show how small incremental changes in immunisation coverage affect the quality adjusted life years (QALYs) and costs associated with measles cases. Finally, in Part 3, we develop a simple model for a hypothetical intervention to reduce differences in uptake and explore the thresholds for immunisation coverage at which such an intervention would be considered cost-effective.

PART 1: A theoretical exploration of the efficiency-equity trade-off

The aim of the NICE public health intervention guidance that this work supports is to reduce differences in the uptake of immunisations between different population subgroups. Therefore, the guidance is quite likely to recommend interventions targeted at increasing uptake specifically in the relatively low coverage populations.

The model developed by Edmunds and Van Hoek (2008) suggested that in a population with uneven coverage, increasing coverage in either group had a similar effect on overall levels of disease. However, an intervention targeting low-uptake groups specifically would reduce inequalities in health and an intervention targeting the high-uptake group would increase health inequalities. Figure 1 (reproduced from Edmunds and van Hoek, 2008), which presents two separate graphs side by side, illustrates this result.

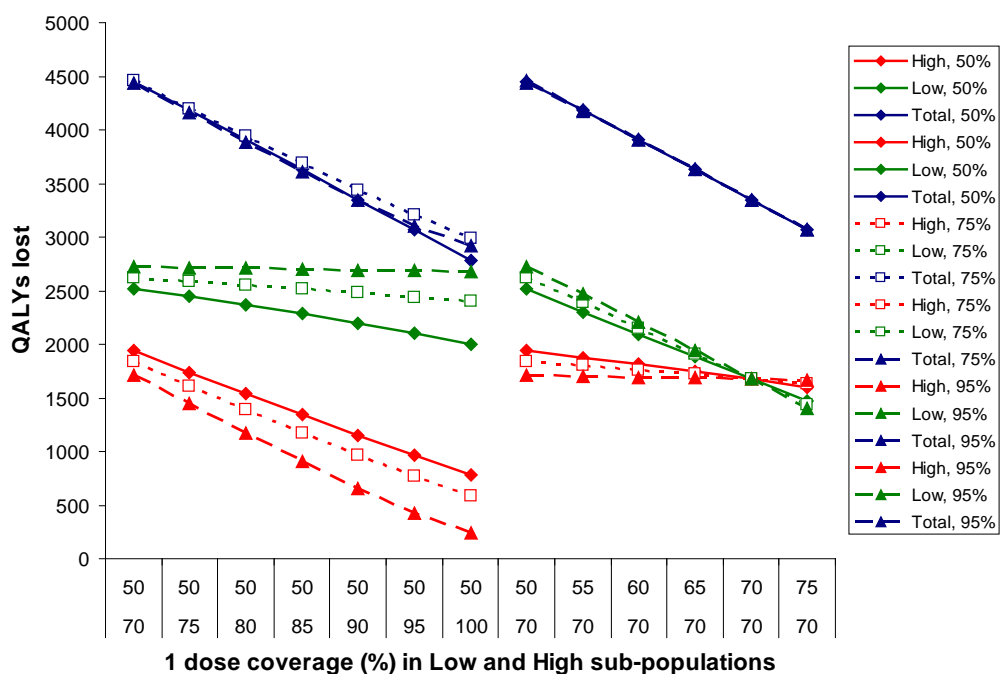
In the left hand graph, we see the effect on QALYs lost in both a low coverage group and a high coverage group of an intervention aimed at increasing the coverage in the population with high baseline coverage. The continuous red line at the bottom shows the number of QALYs estimated to be lost in the high coverage group as immunisation coverage in that group increases. The continuous green line in the middle shows the number of QALYs estimated to be lost by the low coverage group (by lower transmission of infection from the high coverage group to the low coverage group) as immunisation coverage in the high coverage group increases. As expected, this line dips rather more slowly. In the high coverage group, disease transmission is interrupted both

by directly making vaccinees non-susceptible (i.e. immune to infection) *and* by stopping the spread from vaccinees to non-vaccinees. In the low coverage group, the transmission is interrupted only by the second mechanism. This version of the model assumes that the people in the high and low coverage groups mix just as much between groups as within their own group. The equivalent dotted and dashed lines of the same colours assume that there is relatively less mixing between groups (and hence more mixing within groups). What is shown is, as expected, that when people mix mainly within their own group, the immunisation of one's own group has more effect within the group and less effect on the other group.

The graphs on the right swap high and low coverage groups: the intervention is targeted at the low coverage group, and the result is that the QALYs lost to the disease decline most among this group and least in the high coverage group.

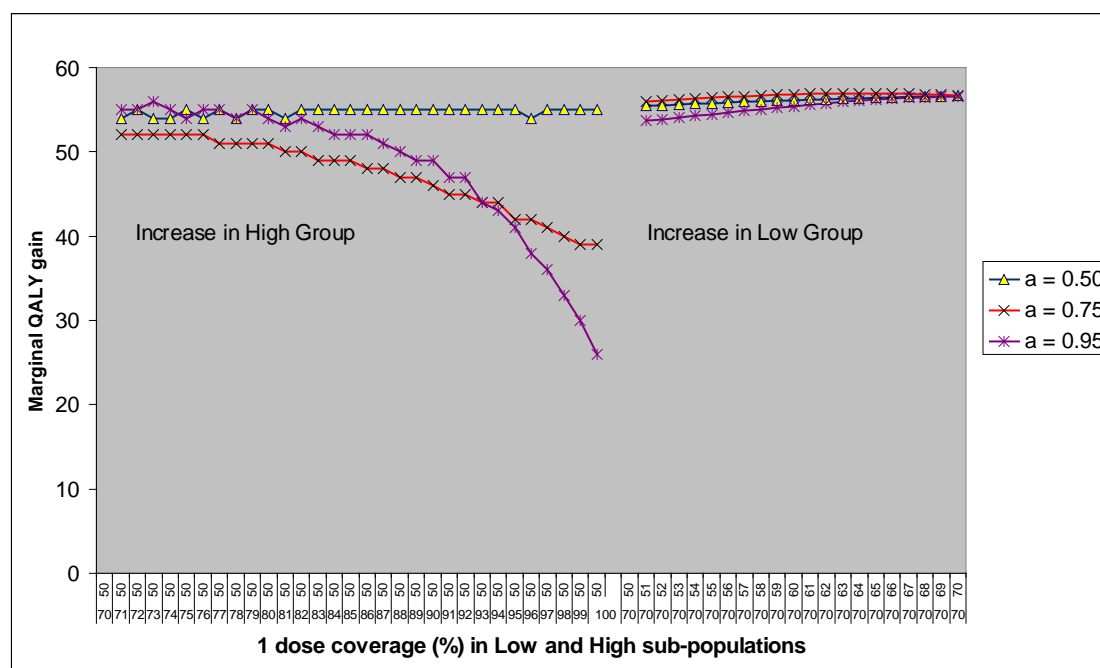
Although this result may seem intuitively obvious, the relationship between differences in health care utilisation and inequalities in health is more complicated for interventions addressing the control of infectious diseases.

Figure 1 – Estimated equilibrium impact (on QALYs lost) of increasing coverage in either a high-coverage area (left hand side) or a low coverage area (right hand side)



In Figure 2, the marginal QALY gain across both high and low coverage groups from a change in coverage at different levels of population mixing is shown. Effectively, this is a graph of the slopes of the blue lines in Figure 1.

Figure 2 – Marginal population QALY gain from increasing coverage in either high or low coverage group



Looking at the results in Figure 2 in more detail, the marginal QALY gain from increasing coverage in either group is almost identical for homogenous population mixing. Where there is relatively less mixing, a percentage point increase in coverage in the low coverage group, especially when coverage in the high coverage group exceeds 80%, produces a greater QALY gain than a percentage point increase in coverage in the high coverage group. Therefore, from the perspective of a decision maker with the objective of reducing differences in uptake an intervention targeted at the low coverage (uptake) group will unambiguously be preferred providing that the costs of achieving a given percentage point increase in coverage in the low coverage group are no greater than the cost of achieving an equivalent percentage point increase in coverage in the high coverage group and that the increase in coverage can be achieved at an acceptable cost per effect ratio, i.e. less than £20,000 per

QALY, which NICE often uses as an indicative willingness to pay threshold for cost-effectiveness.

Of course, the issue is less straightforward for decision makers if interventions, of a given cost, targeted at high coverage groups are more effective (i.e. more children are immunised) than interventions targeted at low coverage groups. In such a case there will be an efficiency-equity trade off to be made, in that there is an efficiency loss from choosing an intervention to reduce differences in uptake. In other words, because a given percentage point increase in coverage gives approximately the same QALY gain regardless of whether that gain occurs in the low or high coverage groups, then QALYs are not maximised by targeting low coverage groups if such interventions are less effective than interventions targeted at high coverage groups. Nevertheless, if the decision rule is simply to reduce differences in uptake, then the decision maker will trade-off efficiency for equity, again with the proviso that interventions targeted at low coverage groups achieve an acceptable cost per effect ratio.

Additionally, in the scenario where interventions targeted at high coverage groups are more effective, the decision is theoretically more complicated if the decision maker is concerned with the absolute health gain of the low coverage group as well as reducing difference in uptake. If, by increasing uptake in the high coverage group, it were possible to get a bigger absolute QALY gain in the low coverage group (via 'herd immunity') with an intervention targeted at high coverage groups for a given expenditure than it was with the same

expenditure targeted at low coverage groups then this might be the preferred solution for the decision maker on the grounds of 'Pareto superiority' (i.e. both high and low coverage groups would be better off). However, where there is little mixing between the groups ($\alpha=0.95$) then such a scenario would not arise as even increasing coverage to 100% in the high coverage group would not produce a QALY gain equivalent to a one percentage point increase in coverage in the low coverage group. Moreover, where there is either homogenous mixing ($\alpha=0.50$) or an intermediate level of mixing ($\alpha=0.75$) then there are coverage combinations which although less equitable in terms of the QALY distribution, nevertheless offer low uptake groups more QALYs. It should be noted though that no evidence has been identified to suggest that interventions targeted at high coverage groups would be more effective than those targeted at low coverage groups, let alone of the magnitude that would be necessary to achieve Pareto superiority (National Collaborating Centre for Women's and Children's Health, 2009).

This Pareto approach to decision making would be similar to a situation where the decision maker aimed to maximise the QALY gain in the low coverage group subject to a budget constraint. This would not inevitably favour interventions that reduced inequality, however. For example, where there is an intermediate level of mixing ($\alpha=0.75$) then the ratio of the QALY gains in low uptake coverage groups for an intervention targeted at low coverage groups compared to an intervention targeted at high coverage groups is approximately 7:1. In this case the decision maker would only favour an intervention that targeted high coverage groups and increased inequality, if

each percentage point increase in coverage from that intervention could be achieved at 1/7th of the cost.

Finally, the decision maker could make any equity-efficiency trade-off by pursuing a QALY maximisation approach but with an equity weight attached to QALYs gained in the low coverage group. This means that a QALY gained in the low-coverage group would be given a higher weight than a QALY gained in the high coverage group.

In conclusion it should be noted that any equity-efficiency trade-offs are contingent on the interventions that increase inequality (i.e. targeted at high coverage groups) being more efficacious than interventions that would reduce inequality (i.e. targeted at low coverage groups). If interventions targeting low coverage groups were equally or more effective than those targeting high coverage groups then there would be no equity-efficiency trade-off. No evidence on which to compare the effectiveness of different targeted interventions has been identified but quite plausibly interventions that promote equity will also be those that promote efficiency. In high coverage groups, an important reason for non-immunisation is an opposition to the measles/mumps/rubella (MMR) vaccine as a matter of principle (see National Collaborating Centre for Women's and Children's Health, 2009). Changing the mindset of such people via an intervention could be exceedingly difficult. In low coverage groups, whilst opposition to the MMR vaccine will be one of the reasons for non-immunisations there are likely to be other reasons relating to difficulties in accessing services etc. It seems likely that these barriers could

be more easily surmounted from a service provision perspective than those reflecting strongly held opinion.

PART 2: A detailed analysis of the incremental costs and effects of increasing measles immunisation coverage

This analysis uses the model for the transmission of measles in a Western European country which was developed by Edmunds and van Hoek (2008). A Microsoft Excel® macro was programmed to allow Edmunds and Van Hoek's model to cycle through 1,116 high- /low- coverage combinations between:

High 70%; Low 50% *and*

High 100%; Low 100%.

As shown by Edmunds and van Hoek (2008), there are wide geographical variations in MMR coverage in England. The effectiveness of interventions to increase uptake is not known but it is quite possible that pre-existing barriers to uptake may limit the scope for large increases in coverage. Therefore, it is potentially important to policy makers to have some idea of likely benefits if only relatively modest increases in uptake are achieved. This is especially important in an economic context when it would seem reasonable to assume that interventions to increase uptake in hard-to-reach groups would only be possible at marginal costs over and above those associated with the routine immunisation schedule. Furthermore, in the context of these wide geographical differences in coverage, it is interesting to explore to what extent there may be diminishing returns to increasing uptake as overall coverage rises. The existence of herd immunity makes diminishing returns a theoretical possibility but the situation is complicated by the fact that changes in the force of infection – the rate at which susceptible individual become infected by

infectious disease - can affect the time profile of cases, and the outcomes from them.

Three sets of analysis were undertaken, first for the case where mixing between high and low coverage groups occurs at random ($\alpha = 0.5$), and then for two assortative mixing scenarios ($\alpha=0.75$ and $\alpha = 0.95$). The model assumed that the high and low coverage groups were of equal size and the results presented are for a population of 200,000. For each analysis it was assumed that everybody who received a first dose of vaccine also received a second dose and that there was no catch-up for those who missed the first dose.

Results

Detailed results are presented in Appendix A. Here four graphs are presented for each of the three mixing assumptions ($\alpha = 0.5, 0.75$ and 0.95), to show the impact of increasing coverage in either group, while holding coverage in the other group constant.

i) $\alpha = 0.5$

Figure 3 – QALY gain¹ increasing uptake in low coverage group holding high coverage uptake constant at 80%

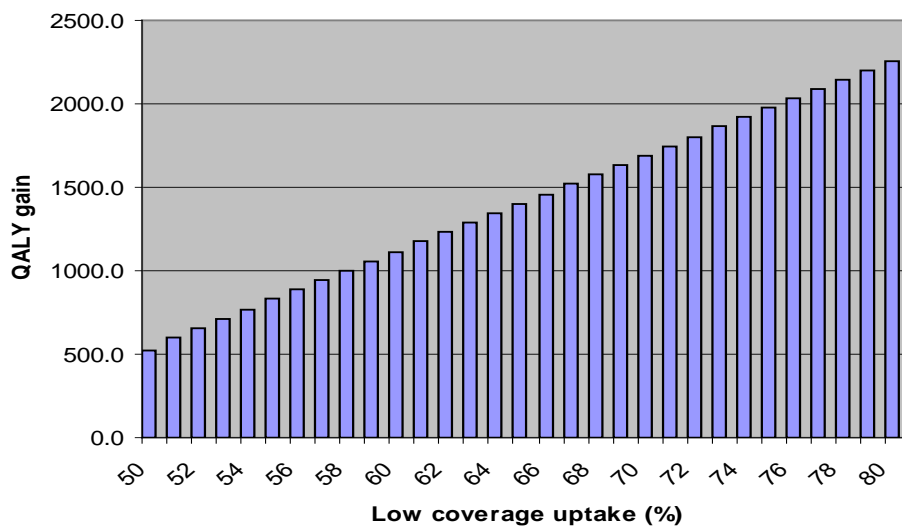
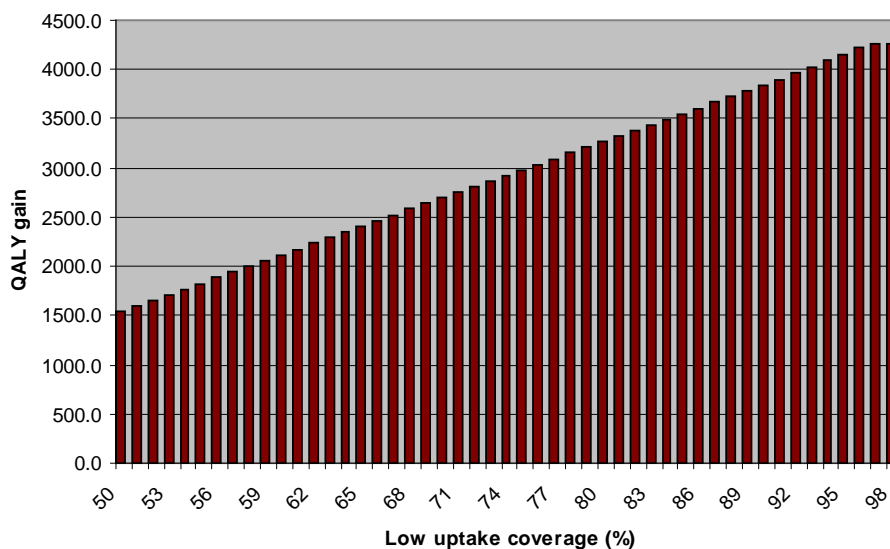


Figure 4 – QALY gain increasing uptake in low coverage group holding high coverage uptake constant at 98%



¹ QALY gain is aggregated across high and low coverage groups

Figure 5 – QALY gain increasing uptake in high coverage group holding low coverage uptake constant at 70%

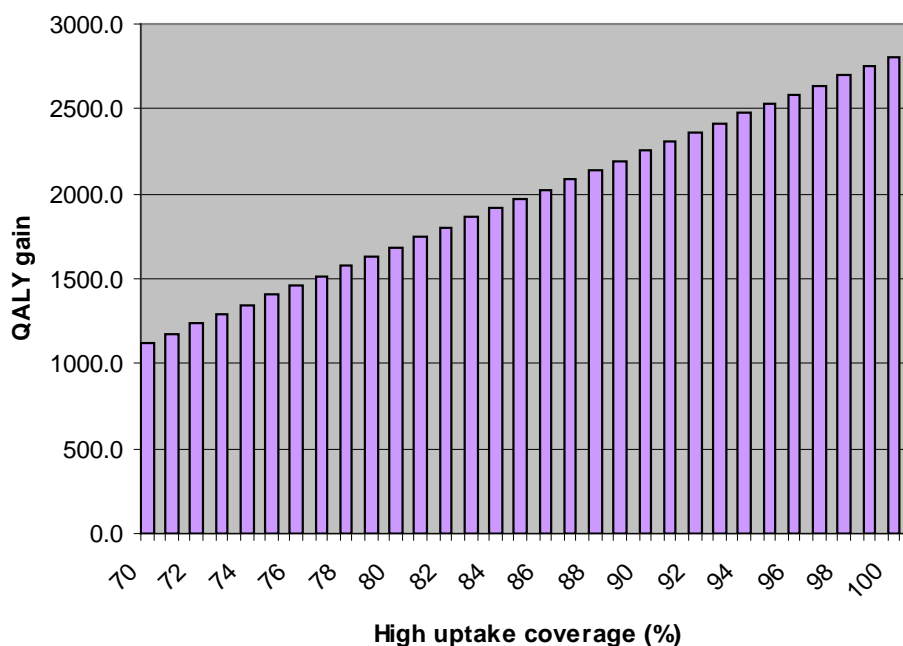
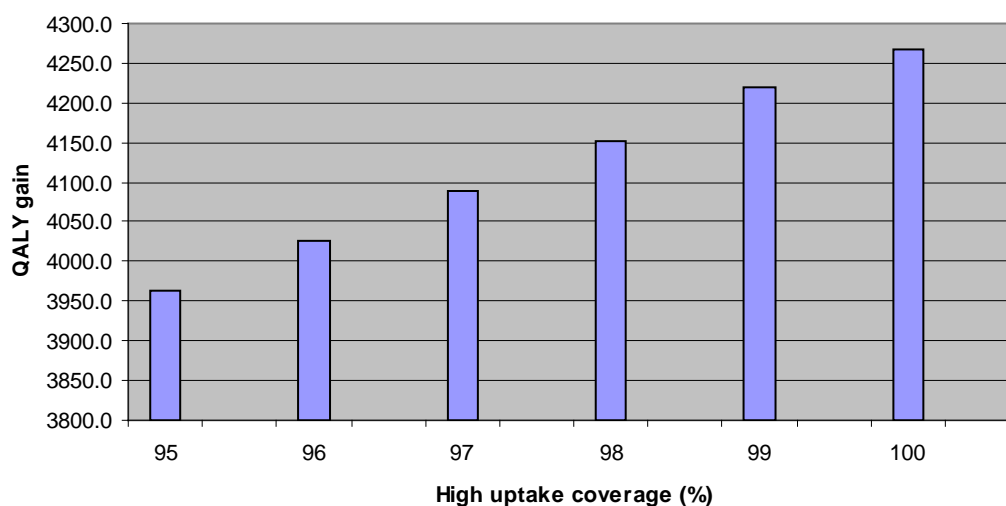


Figure 6 – QALY gain increasing uptake in high coverage group holding low coverage uptake constant at 95%



ii) $\alpha = 0.75$

Figure 7 – QALY gain increasing uptake in low coverage group holding high coverage uptake constant at 80%

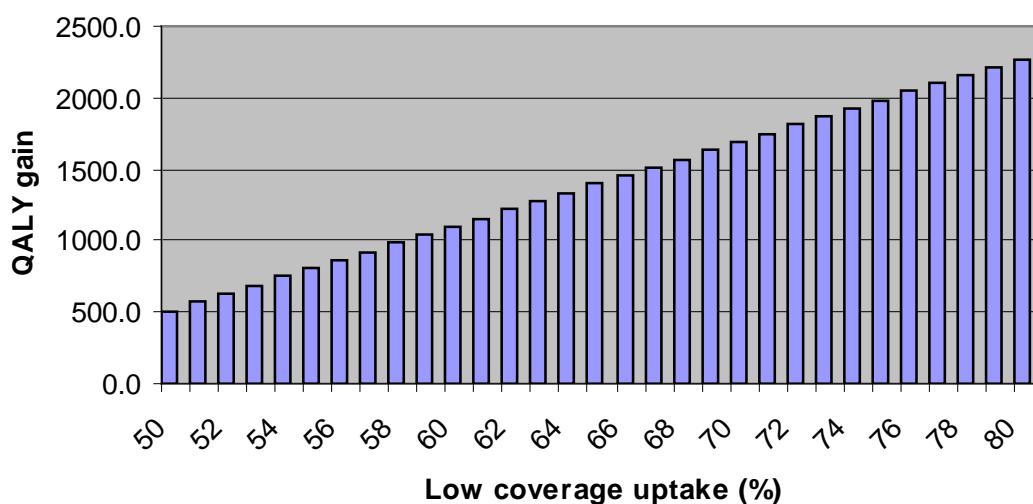


Figure 8 – QALY gain increasing coverage in low coverage groups holding high coverage uptake constant at 98%

Figure 9 – QALY gain increasing coverage in high coverage groups holding low coverage uptake constant at 70%

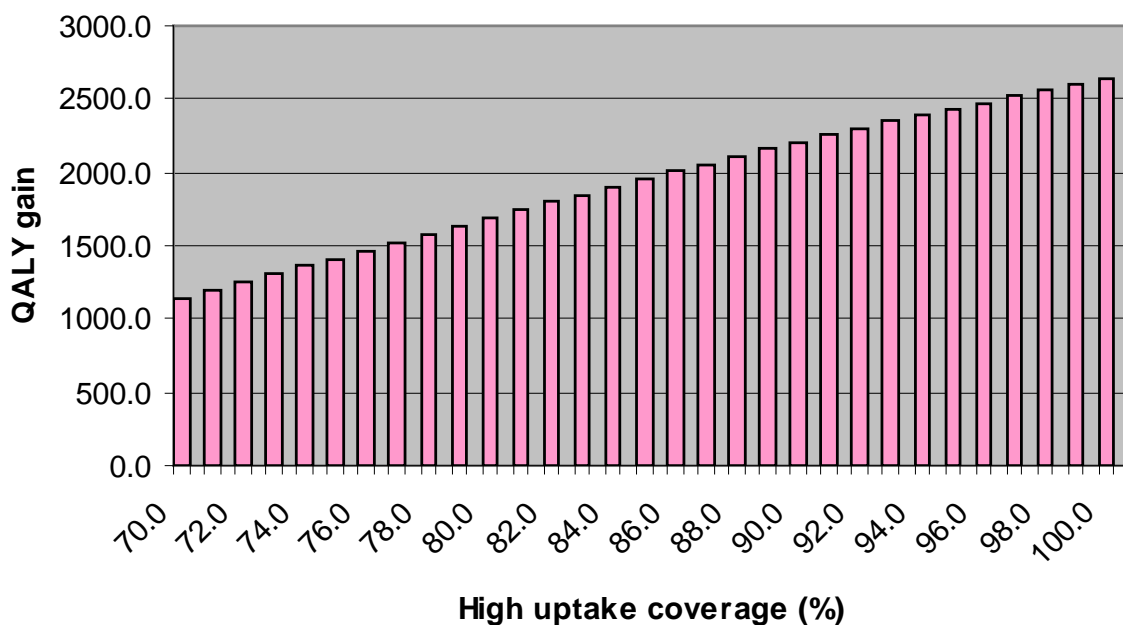
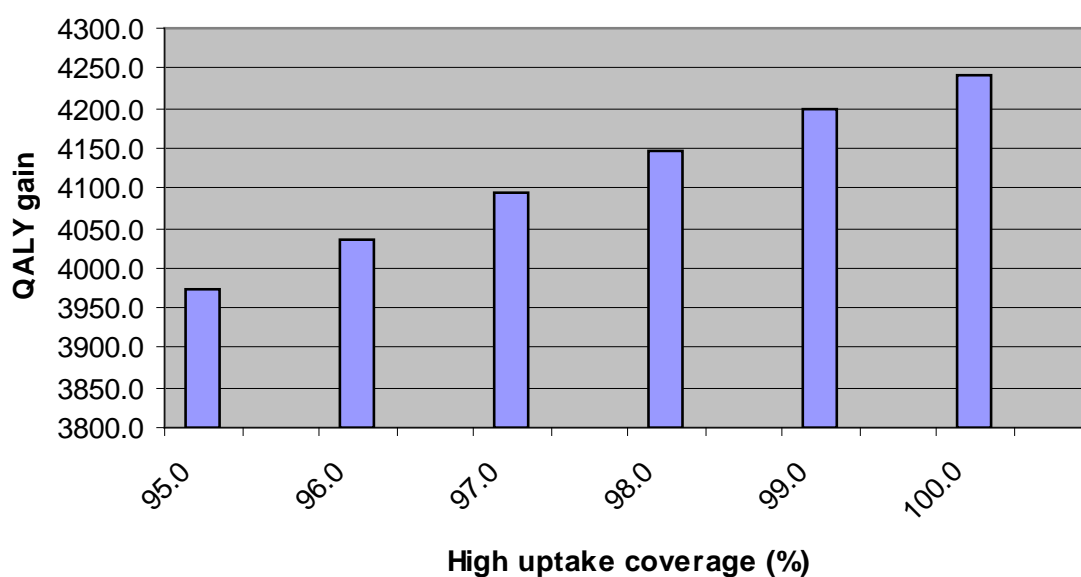


Figure 10 – QALY gain increasing coverage in high coverage groups holding low coverage uptake constant 95%



iii) $\alpha = 0.95$

Figure 11 – QALY gain increasing coverage in low coverage groups holding high coverage uptake constant at 80%

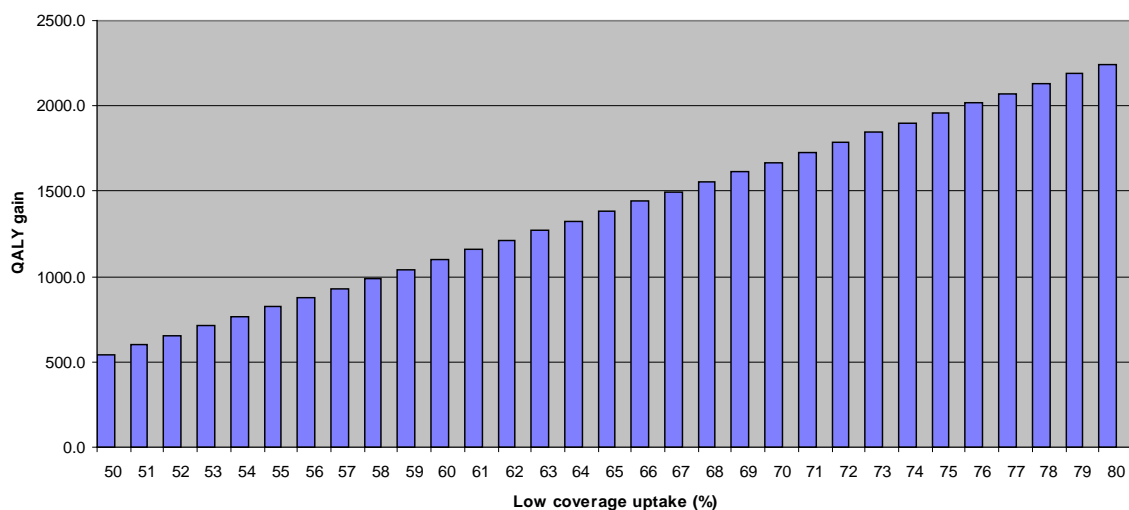


Figure 12 – QALY gain increasing coverage in low coverage groups holding high coverage uptake constant at 98%

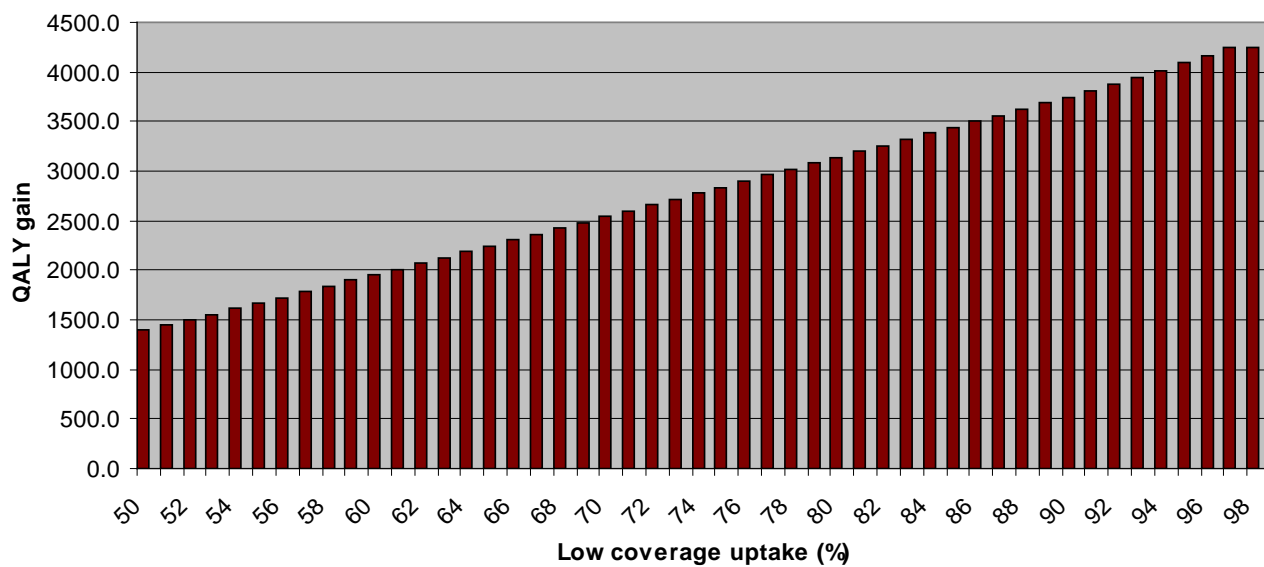


Figure 13 – QALY gain increasing coverage in high coverage groups holding low coverage uptake constant at 70%

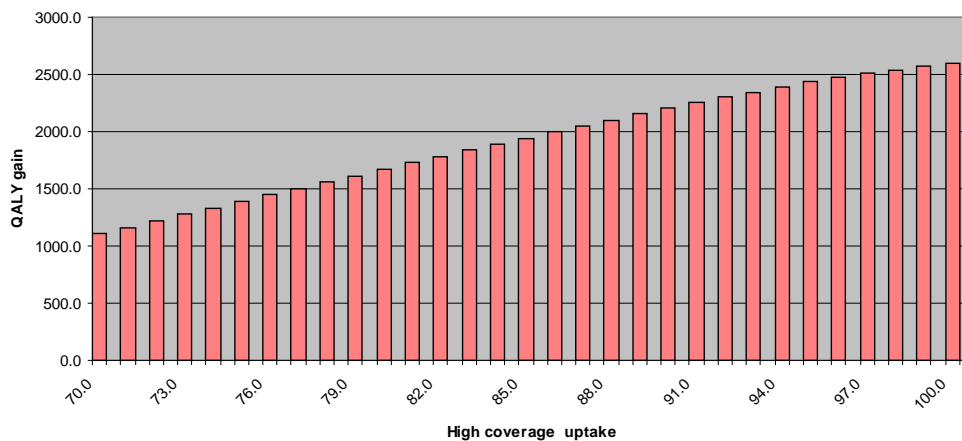
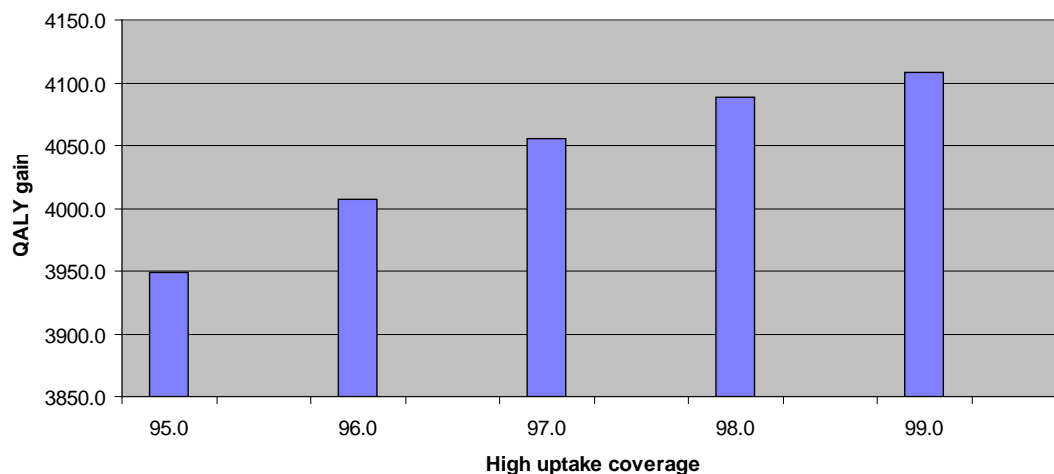


Figure 14 – QALY gain increasing coverage in high coverage groups holding low coverage uptake constant at 95%



Discussion

There may be considerable uncertainty as to the exact extent of population mixing and the model necessarily simplifies what is a complex relationship. However, at least for the assumption of two equally sized groups with different

coverage levels, the above results suggest that the overall QALY gain from increasing coverage is not sensitive to the degree of mixing between groups. As shown in Figure 1, the degree of mixing does affect the distribution of QALY gain between the two groups. So, for example, with homogenous mixing the low coverage group will benefit more from the herd immunity effects of increasing uptake in a high coverage group than they would in a situation where there was relatively little mixing between the two groups. For the policy maker the uncertainty about the exact mixing may not be important. The results show that increasing uptake more in the low coverage group relative to that in the high coverage group would reduce health inequalities with the degree of mixing only affecting the extent to which it does this – with a greater reduction in inequality occurring where there is less mixing between high and low coverage groups.

These results also reinforce the linearity of the results presented in Figure 1, even at much higher levels of immunisation coverage. It is only as immunisation coverage approaches 100% in both groups that significant diminishing returns set in, with this perhaps giving some indication as to the point where disease elimination could occur. Therefore, from these results there is little to support an intervention that would target only a few very low coverage population subgroups as increases in coverage in any low coverage group, however defined, will provide a similar level of benefit.

The results also show that in considering any intervention to increase uptake, it is important to realise that there are substantial ‘downstream’ savings to be

realised from averted measles cases resulting from an increase in immunisation coverage. If we take the current level of MMR vaccine coverage as being 87% then the model suggests that there are still lifetime disease related costs in the order of £7 million per 200,000 population, or £1.9 billion scaled up to a population of the size of England and Wales.

As noted by Edmunds and Van Hoek (2008), inferences about the likely cost-effectiveness of interventions to increase uptake based on these results need to be made with some caution. In particular, the results presented reflect a long-run equilibrium. Such an equilibrium may take a long time to achieve and the dynamic process of achieving that equilibrium could be important to the overall cost-effectiveness of an intervention designed to improve uptake. As such, the model has greater relevance where the changes in coverage level are small as the equilibrium state will be reached more quickly. However, in the real world, with the barriers to immunising 'hard-to-reach groups' the increases in coverage achieved by any intervention may actually be relatively small.

PART 3: A hypothetical public health intervention: modelling the cost-effectiveness of the provision of immunisation to Traveller children by a health visitor or other health care professional

Background

It has been estimated that there are approximately 250,000 Travellers in Great Britain². This community may represent a hard to reach population subgroup in terms of immunisation coverage as their lifestyle may make it more difficult for them to access primary care services and to receive concomitant reminders relating to the immunisation schedule. One hypothetical intervention might be to send health visitors to traveller communities and administer the MMR vaccine to non-immunised children. We assess below how we could evaluate the cost-effectiveness of such an intervention.

² <http://www.irishtraveller.org.uk/find-out-about-irish-travellers>

Model inputs

The data shown in Tables 1 to 3 were used to estimate the costs and effects of the hypothetical intervention.

Table 1 – Costs

Item	Unit cost	Source
Health visitor	£104 (per hour)	Curtis and Netten (2007)
MMR	£2.45	http://www.cks.library.nhs.uk/pre_conception_advice_and_management/management/quick_answers/scenario_advice_for_all_women/view_full_scenario
Willingness to pay for a QALY ³	£20,000	NICE guidelines manual (National Institute for Health and Clinical Excellence, 2007)

Table 2 – Demographic data

Variable	Value	Source ⁴
Population of England and Wales (approximate)	54 million	http://www.statistics.gov.uk/StatBase/Product.asp?vlnk=14238
Traveller population (approximate)	250,000	http://en.wikipedia.org/wiki/Irish_Traveller#cite_note-17
Proportion <19 years (approximate)	0.5	http://en.wikipedia.org/wiki/Irish_Traveller#cite_note-17

³ The willingness to pay (WTP) for a QALY can also give a monetary valuation of benefits in terms of health gain and measured in QALYs. This is simply the number of QALYs gained multiplied by the WTP

⁴ Websites accessed September 2008

Table 2: Single visit variables

Variable	Value
Duration of visit (hours)	4
Children covered per visit	20
Existing immunisation coverage	50%
Probability vaccination accepted if unimmunised	80%

Results

The costs associated with a single visit from a health visitor would be⁵:

staffing: $4 \times \text{£}104 = \text{£}416$

vaccine: $8 \times \text{£}2.45 = \text{£}19.60$

*Total costs of single visit: **£435.60***

It is then possible to scale up the intervention so that it is delivered across England.

Traveller children:	125,000
No. of visits to reach all Traveller children	$125,000 \div 20 = 6,250$
Total costs of visits	$6,250 \times \text{£}435.60 = \text{£}2,722,500$

⁵ This assumes that there is no joint production, with other primary health care services delivered on the same visit, including other immunisations. If other services were provided there would be additional benefits and costs

NICE often uses an indicative willingness to pay threshold for cost-effectiveness of £20,000 per QALY. Therefore, for the cost of an England-wide health visitor intervention to target increased immunisation uptake in traveller communities the minimum QALY gain needed for cost-effectiveness could in the simplest case, be calculated as $£2,722,500 \div £20,000 = 136$ QALYs. However, this calculation does not allow for any offsetting 'downstream' savings arising from averted measles cases. In Edmunds and van Hoek's (2008) model these result in a saving of approximately £5,000 for every QALY gain. Therefore, we need to solve the following equation:

$$(2,722,500 - 5,000Q) \div £20,000 = Q,$$

where Q is the threshold QALY gain needed for cost-effectiveness.

Rearranging the equation gives:

$$2,722,500 = 25,000Q,$$

from which $Q = 108.9$.

In other words, if the hypothetical intervention, with all the assumptions outlined above, delivered a gain of at least 108.9 QALYs it would be considered cost-effective.

With the assumptions made above we can estimate the number of additional children immunised as a result of the intervention:

number not immunised x probability immunisation accepted

$$125,000 \times 0.5 \times 0.8 = 50,000.$$

The results obtained using Edmunds and Van Hoek's (2008) model (see Appendix A) suggest that in a population with two equally sized groups, one with relatively high immunisation coverage compared to the other, that a one percentage point increase in the uptake of immunisation in the lower coverage population would lead to a QALY gain of the order of 50 QALYs for a population of 200,000. Scaled up to the entire population of England and Wales, this would represent a gain of approximately 13,500 QALYs.

If the intervention resulted in 50,000 additional immunisations, as calculated above, the estimated percentage point increase in the low coverage group would be:

$$((50,000 \div (54,000,000 \div 2)) = 0.18 \text{ percentage points.}$$

As the relationship between QALY gain and coverage is approximately linear, the estimated QALY gain from an additional 50,000 immunisations in the low coverage group would be the QALY gain from a one percentage point increase in the lower coverage population (13,500 QALYs from a previous calculation) multiplied by the actual percentage point increase arising from an additional 50,000 immunisations:

$$13,500 \times 0.18 = 2,500 \text{ QALYs.}$$

As noted above, the model estimates that each QALY gained will avert approximately £5,000 in measles related costs. In this case, as shown below,

the 'downstream saving' would more than offset the cost of the intervention, and the intervention would be said to 'dominate', meaning that it would be both cheaper and more effective than the no-intervention alternative. Such interventions are unambiguously cost-effective:

$$2,500 \times \text{£}5,000 > \text{£}2,722,500.$$

We can also use this approach to estimate the minimum effect an intervention costing £2.7 million could have and still be considered cost-effective according to the NICE threshold. It was noted earlier that a minimum QALY gain of 108.9 QALYs would be needed to justify an intervention costing this amount, just 4% of the QALY gain estimated in the hypothetical model. Therefore, the minimum number of traveller children that would need to be immunised for the intervention to be considered cost-effective would be 2,178.

Sensitivity analysis

Sensitivity analysis is used in health economics to explore the impact on the results of a change in model assumptions (with the model under the original assumptions being termed the 'base case'). This is particularly important where considerable uncertainty exists as to what the exact value of model inputs should be. It can also give insights into the key drivers of the results and suggest where further research may be most profitable in order to determine cost-effectiveness. Below we show a number of one-way sensitivity analyses, in which one input value is changed whilst holding all other values constant.

i) *Varying the QALY gain per percentage point increase in immunisation coverage per 200,000 population*

It was previously estimated that each percentage point increase in immunisation coverage in a lower coverage group would lead to a gain of approximately 50 QALYs and the base case suggested that such a gain would be dominant, producing cost savings. In this sensitivity analysis we explore the implications of a lower QALY gain (from 1 to 50) from each percentage point increase in immunisation coverage. The results of this analysis (including incremental cost effectiveness ratios [ICERs]) are shown in Figures 15 and 16.

Figure 15 – Impact on costs and QALYs of changing the QALY gain per percentage point increase in low coverage uptake groups

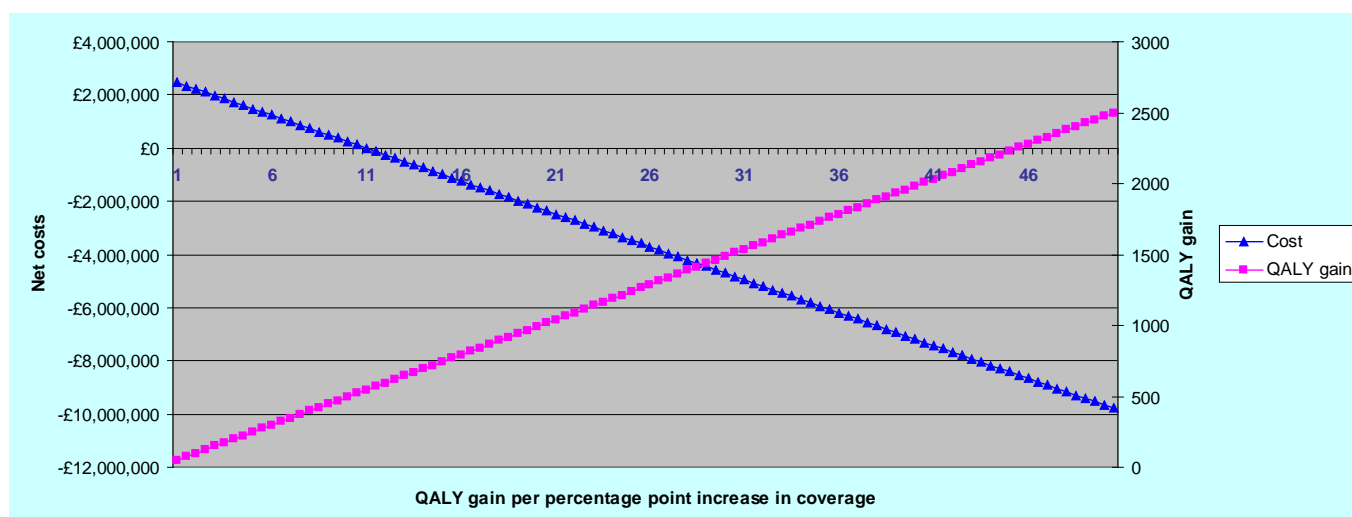


Figure 16 – ICER of intervention to increase uptake with different assumptions about the QALY gain per percentage point increase in coverage

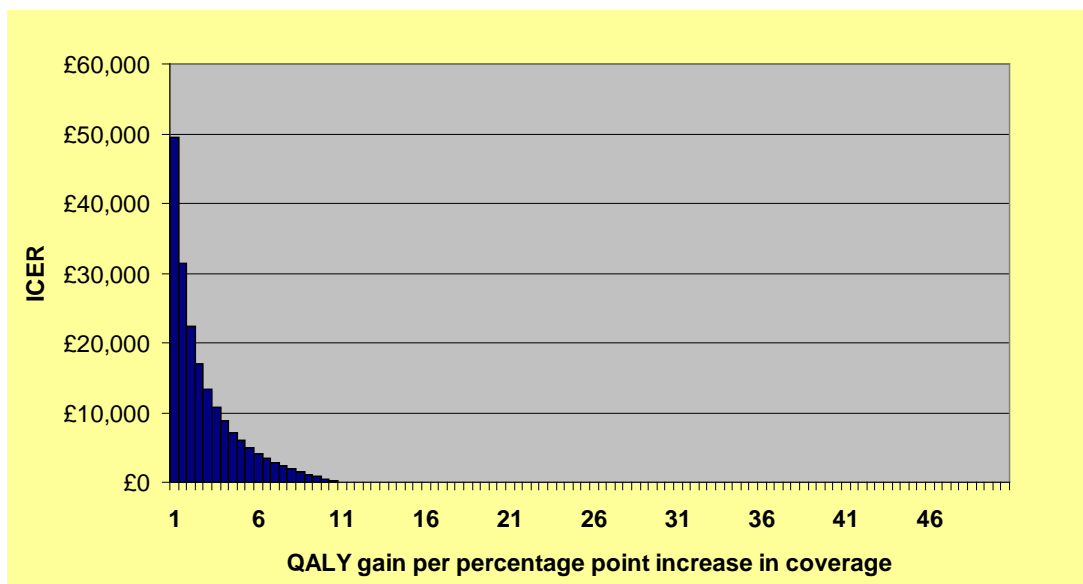


Figure 15 shows the inverse relationship between QALY gain and net costs. This is because it is assumed that each QALY gain generates savings of approximately £5,000 in measles related costs. The figure shows that the threshold QALY gain per percentage point immunisation coverage per 200,000 population for the intervention to generate net savings is 11 QALYs.

Figure 16 shows that once the QALY gain per percentage point increase in immunisation coverage per 200,000 population exceeds 2.3, the intervention would be considered cost-effective using a £20,000 willingness to pay for a QALY criterion. This is a much lower QALY gain than was used in the base case analysis.

ii) *Varying the probability immunisation accepted if unimmunised*

In the base case model, it was assumed that 80% of unimmunised children would accept vaccination. This sensitivity analysis explores the implications of lower acceptance rates (10% to 80%). The results are presented in Figures 17 and 18.

Figure 17 – Impact on costs and QALYs of changing vaccination acceptance rates

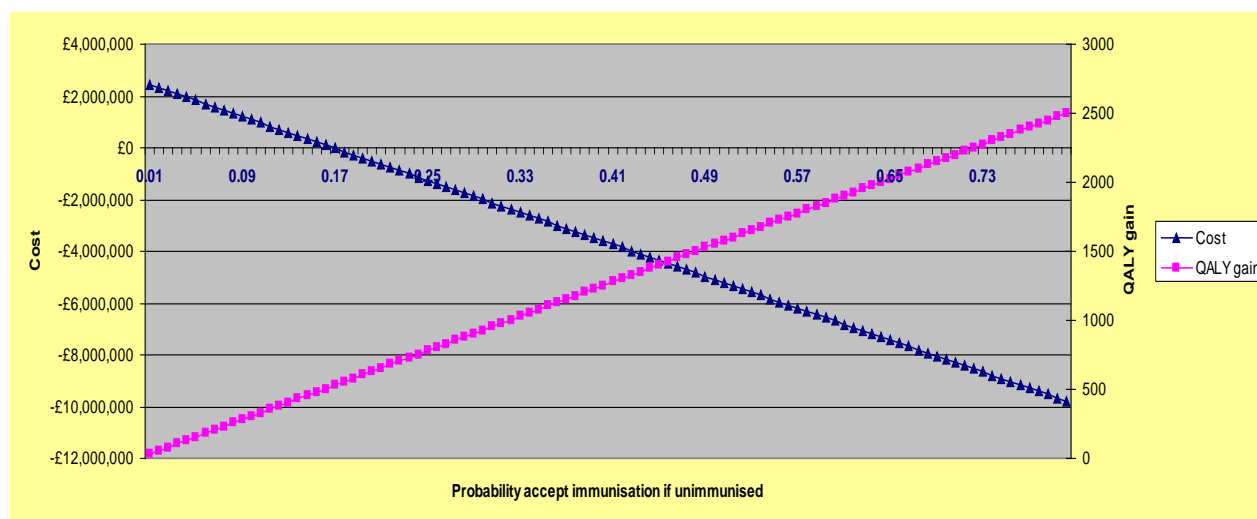
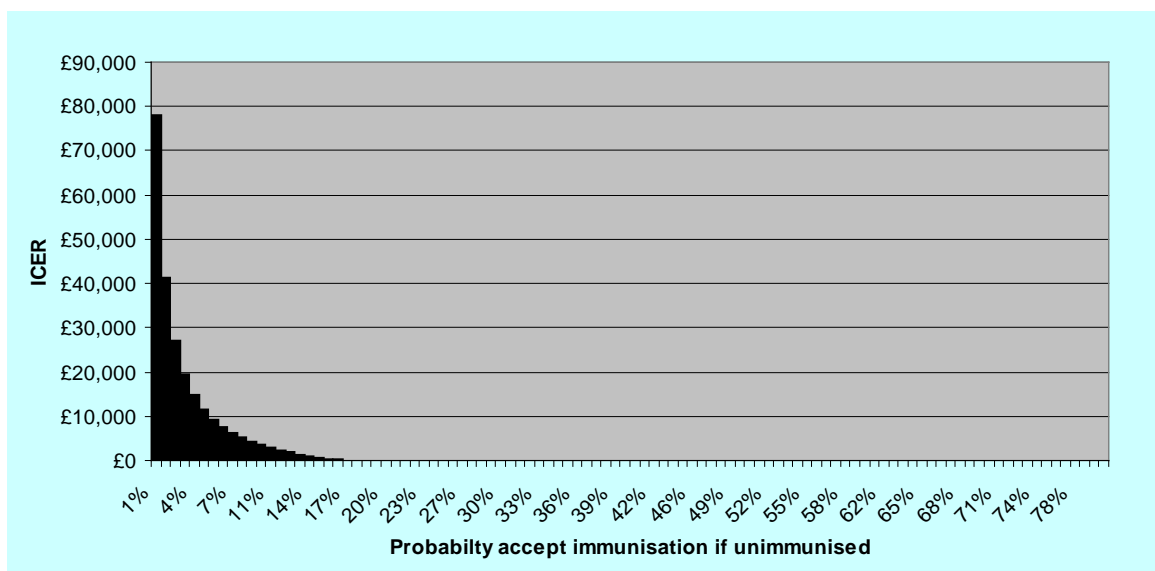


Figure 17 shows that once the acceptance rate is 17% or above the intervention generates net savings while holding all other base case input assumptions constant.

Figure 18 shows that the ICER is well under £20,000 per QALY even if only 10% of unimmunised children are vaccinated, with the threshold for cost-effectiveness being approximately 4%.

Figure 18 – ICER of intervention to increase uptake with different assumptions about the proportion of unimmunised traveller children accepting vaccination



iii) Varying the number of children for each site visit

In the base case analysis it was assumed that there would be 20 Traveller children at each site visited by the health visitor. In this sensitivity analysis we explore the implications of a smaller number of children per site (from 1 to 20) which implies that the intervention would require a higher number of site visits for a given traveller children population. The results for this sensitivity analysis are presented in Figures 19 and 20.

Figure 19 shows that the QALY gain is independent of the number of children per site, as this assumption simply changes the number of site visits that are required rather than the number of children who would be offered vaccine.

There is an economy of scale with the greater the number of children per site, as fewer visits are required, and therefore net costs fall as numbers increase.

The threshold at which the intervention becomes cost saving is reached when there are a minimum of 5 children per site.

Figure 19 – Impact of changing the number of traveller children per site on costs and QALYs

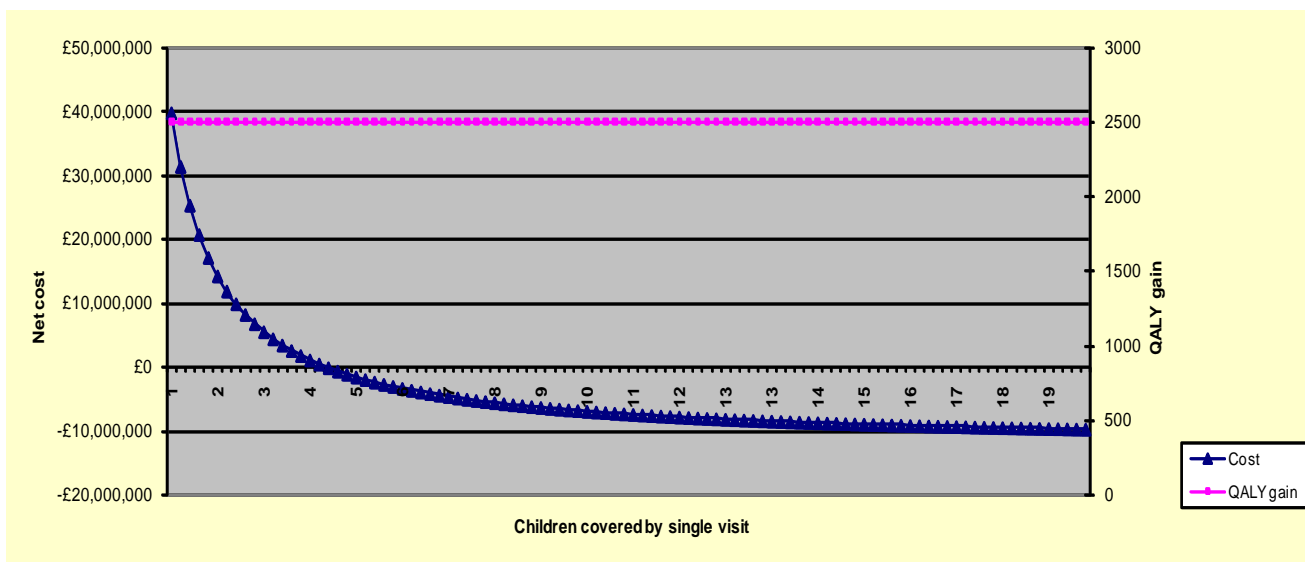


Figure 20 – ICER of intervention to increase uptake with different assumptions about the number of traveller children per site

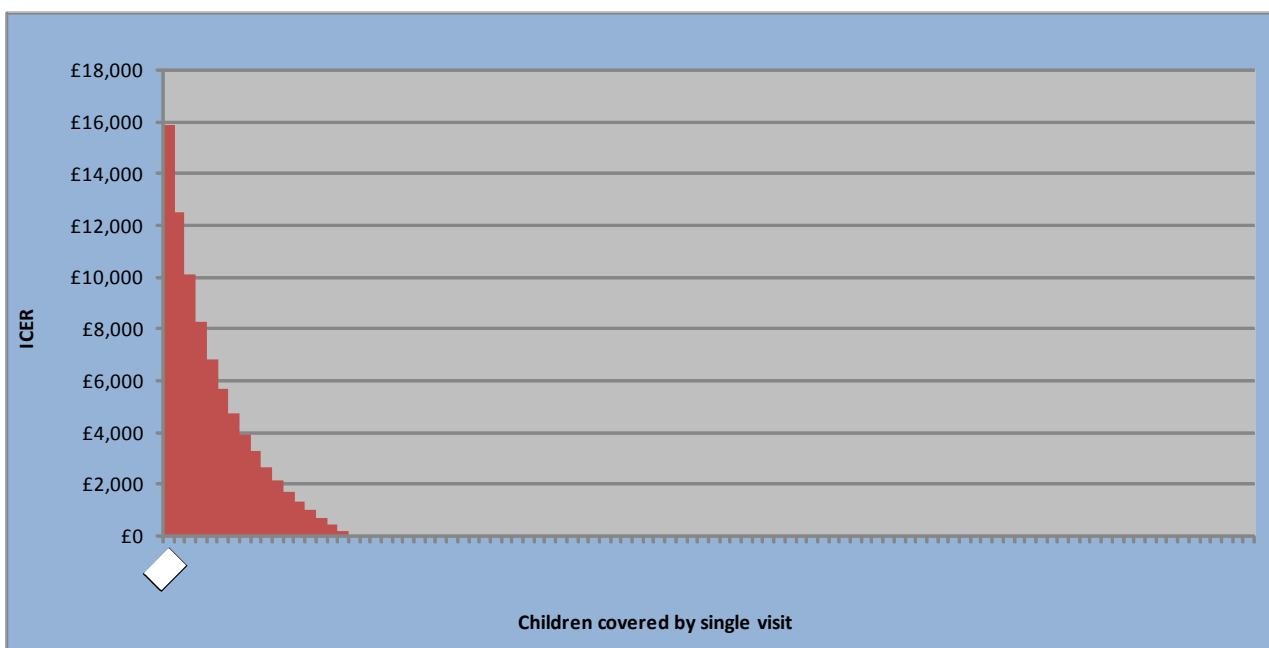


Figure 20 suggests that the cost-effectiveness of the intervention is not sensitive to the number of traveller children per site with other base case assumptions as the intervention is less than £20,000 per QALY even when there is only one child per site.

iv) Varying the existing immunisation coverage in traveller children

The sensitivity analysis suggests that cost-effectiveness is not sensitive to the existing immunisation coverage in traveller children. If 80% of unimmunised children would accept vaccination, then the intervention would still be cost saving even if the existing coverage was 85% as is illustrated in Figure 21.

Figure 21 – Impact of changing the existing immunisation coverage in traveller children

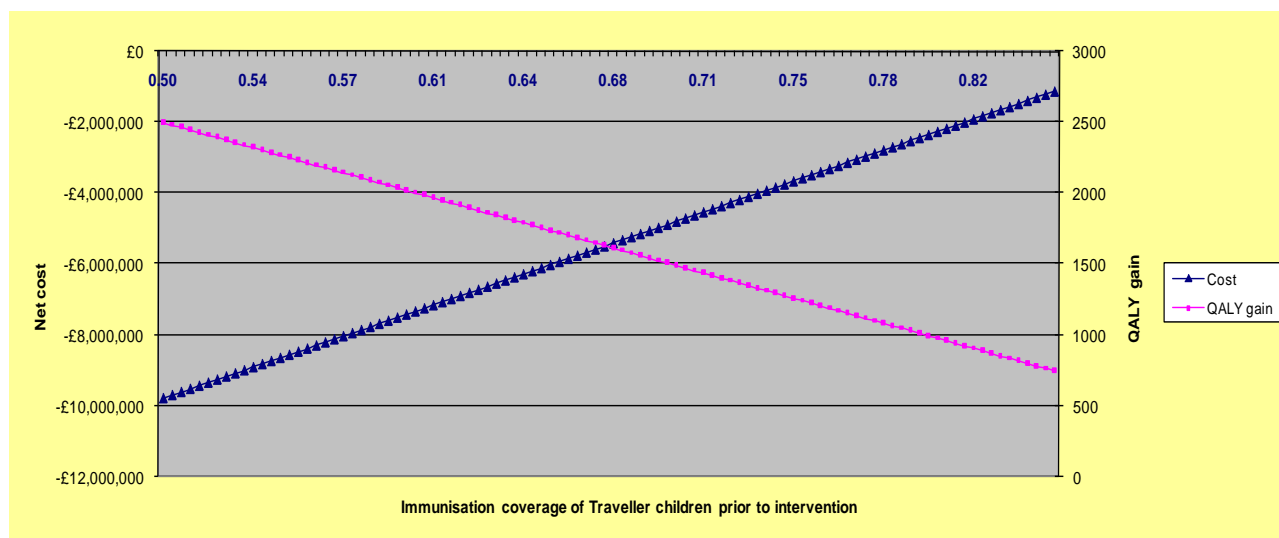


Figure 21 also shows, however, that the cost-effectiveness measured by net cost and QALY gain is greater the lower the existing coverage, or where the capacity to benefit is greater in absolute terms.

Discussion

It must be noted that most of the model inputs described in the analysis above are purely hypothetical. The assumptions can readily be modified to derive cost-effectiveness thresholds for such an intervention in different scenarios. The results presented above strongly suggest that an intervention which succeeded in increasing uptake could indeed be cost-effective. Nevertheless, it is also important to recognise that this hypothetical modelling reflects a lack of real-world evidence on the costs and, more importantly, effectiveness of any intervention of this type.

Finally, it should be remembered that in this model we have only considered the health related quality of life gains arising from averted measles cases. In the UK, immunisation against measles would be given through the MMR vaccine and therefore increasing uptake would also be expected to affect health outcomes relating to mumps and rubella, which would generate more gains than suggested in this analysis.

....A Natural Extension

The above analysis obviously has relevance for *any* programme of home visiting which is dedicated solely to deliver immunisation to targeted families and which has similar hourly costs. One such programme in a UK city spends

three mornings per week visiting an average of about 70 homes per month, potentially delivering about 90 immunisations. The programme has several stages, the first being to find out from GP records each month which children are not up-to-date with their immunisations. The parents/guardians of the children are contacted by phone where possible, or otherwise by post, and encouraged to take their child or children to their GP to be immunised. Home visiting only occurs after all else fails, and is tightly targeted.

On the basis of 60 immunisations (out of the 90 possible) per month, or an average of 5 per 4-hour session, the previous analysis for “Travellers” (which assumes an average of 8 immunisations per 4 hours) can easily be adapted.

Given the above assumptions, and assuming that immunisations for each disease have the same benefit, the cost per QALY gained will be $8/5 = 1.6$ times as high as the Traveller example, still well within a £20,000 per QALY threshold. The other difference between the two scenarios is that the Traveller example is for measles immunisation whereas the City Visiting example is for immunisation for more than one disease. The conclusions about whether the City Visiting programme is cost effective, however, will not alter unless the proportion of measles immunisations (out of the 60 injections given per month) is low.

Since home visiting will almost certainly be the most costly intervention per QALY gained in the City Visiting suite of programmes, it implies that the preceding steps in such a programme will all be cost effective.

Appendix A

i) $\alpha = 0.5$

Figure A.1 – QALY gain of various high and low uptake combinations relative to a high uptake coverage of 70% and a low coverage uptake of 50%

		High coverage (%)																		
		70	72	74	76	78	80	82	84	86	88	89	90	92	94	96	97	98	99	100
Low coverage (%)	50	0.0	108.4	216.9	325.8	419.4	525.2	630.4	734.8	873.4	983.2	1037.7	1093.1	1203.1	1312.4	1425.3	1480.5	1535.7	1590.7	1646.0
	52	111.0	219.9	329.1	438.6	548.2	658.1	768.1	878.2	988.5	1098.8	1154.0	1209.2	1319.5	1429.9	1540.1	1595.2	1650.2	1705.2	1760.1
	54	222.3	331.8	441.5	551.5	661.6	772.0	882.5	993.1	1103.7	1214.5	1269.8	1325.2	1435.9	1546.5	1657.0	1712.2	1767.3	1822.4	1877.4
	56	333.9	443.9	554.2	664.7	775.3	886.2	997.1	1108.1	1219.2	1330.3	1385.8	1441.3	1552.3	1663.2	1773.8	1829.1	1884.3	1939.4	1994.4
	58	445.8	556.4	667.2	778.1	889.3	1000.5	1111.9	1223.3	1334.7	1446.2	1501.8	1557.5	1668.7	1779.8	1890.6	1945.9	2001.1	2056.2	2111.3
	60	558.0	669.1	780.4	891.8	1003.4	1115.1	1226.8	1338.6	1450.4	1562.1	1617.9	1673.7	1785.1	1896.3	2007.2	2062.5	2117.7	2172.9	2227.9
	62	670.5	782.1	893.8	1005.7	1117.7	1229.8	1341.9	1454.0	1566.1	1678.0	1733.9	1789.7	1901.3	2012.6	2123.5	2178.8	2234.1	2289.2	2344.2
	64	783.2	895.2	1007.4	1119.8	1232.2	1344.6	1457.0	1569.4	1681.7	1793.8	1849.8	1905.7	2017.4	2128.7	2239.6	2294.9	2350.1	2405.2	2460.1
	66	896.1	1008.6	1121.2	1233.9	1346.7	1459.5	1572.2	1684.8	1797.3	1909.5	1965.6	2021.5	2133.2	2244.5	2355.3	2410.6	2465.7	2520.7	2575.6
	68	1009.2	1122.1	1235.1	1348.2	1461.3	1574.3	1687.3	1800.1	1912.7	2025.0	2081.1	2137.1	2248.7	2359.9	2470.7	2525.9	2580.9	2635.8	2690.6
	70	1122.4	1235.7	1349.1	1462.5	1575.8	1689.1	1802.3	1915.2	2027.9	2140.3	2196.3	2252.3	2363.9	2475.0	2585.6	2640.7	2695.7	2750.5	2805.2
	72		1349.4	1463.1	1576.8	1690.4	1803.8	1917.1	2030.1	2142.9	2255.2	2311.3	2367.2	2478.7	2589.6	2700.1	2755.1	2810.0	2864.8	2919.4
	74			1577.1	1691.0	1804.8	1918.4	2031.7	2144.8	2257.5	2369.8	2425.8	2481.6	2593.0	2703.8	2814.1	2869.1	2923.9	2978.6	3033.2
	76				1805.1	1919.0	2032.7	2146.1	2259.1	2371.8	2484.0	2539.9	2595.7	2706.9	2817.5	2927.7	2982.6	3037.4	3092.2	3146.9
	78					2033.0	2146.7	2260.1	2373.1	2485.6	2597.7	2653.5	2709.2	2820.3	2930.8	3041.0	3095.9	3150.8	3205.6	3260.4
	80						2260.5	2373.8	2486.6	2599.0	2710.9	2766.7	2822.3	2933.3	3043.8	3154.0	3209.0	3264.1	3319.1	3374.2
	82							2487.0	2599.7	2711.9	2823.7	2879.4	2935.0	3045.9	3156.5	3267.0	3322.2	3377.6	3433.0	3488.6
	84								2712.3	2824.4	2936.0	2991.7	3047.3	3158.3	3269.1	3380.2	3435.8	3491.6	3547.6	3603.9
	86									2936.4	3048.0	3103.7	3159.3	3270.6	3382.0	3493.9	3550.1	3606.6	3663.4	3720.6
	88										3159.7	3215.5	3271.3	3383.1	3495.4	3608.5	3665.6	3723.1	3780.9	3839.5
90											3383.5	3439.3	3551.7	3664.7	3778.2	3835.9	3894.7	3953.6	4013.5	
92												3610.1	3666.7	3780.1	3894.9	3953.6	4013.5	4073.4	4133.3	
94													3843.3	3900.7	4015.9	4075.6	4136.5	4197.4	4258.3	
96														4088.9	4148.9	4264.9	4325.8	4386.7	4447.6	
97															4221.3	4282.2	4343.1	4404.0	4464.9	
98																4266.5	4327.4	4388.3	4449.2	
99																	4266.5	4327.4	4388.3	
100																		4266.4	4327.3	

Figure A.2 – Measles related deaths at various high and low uptake combinations

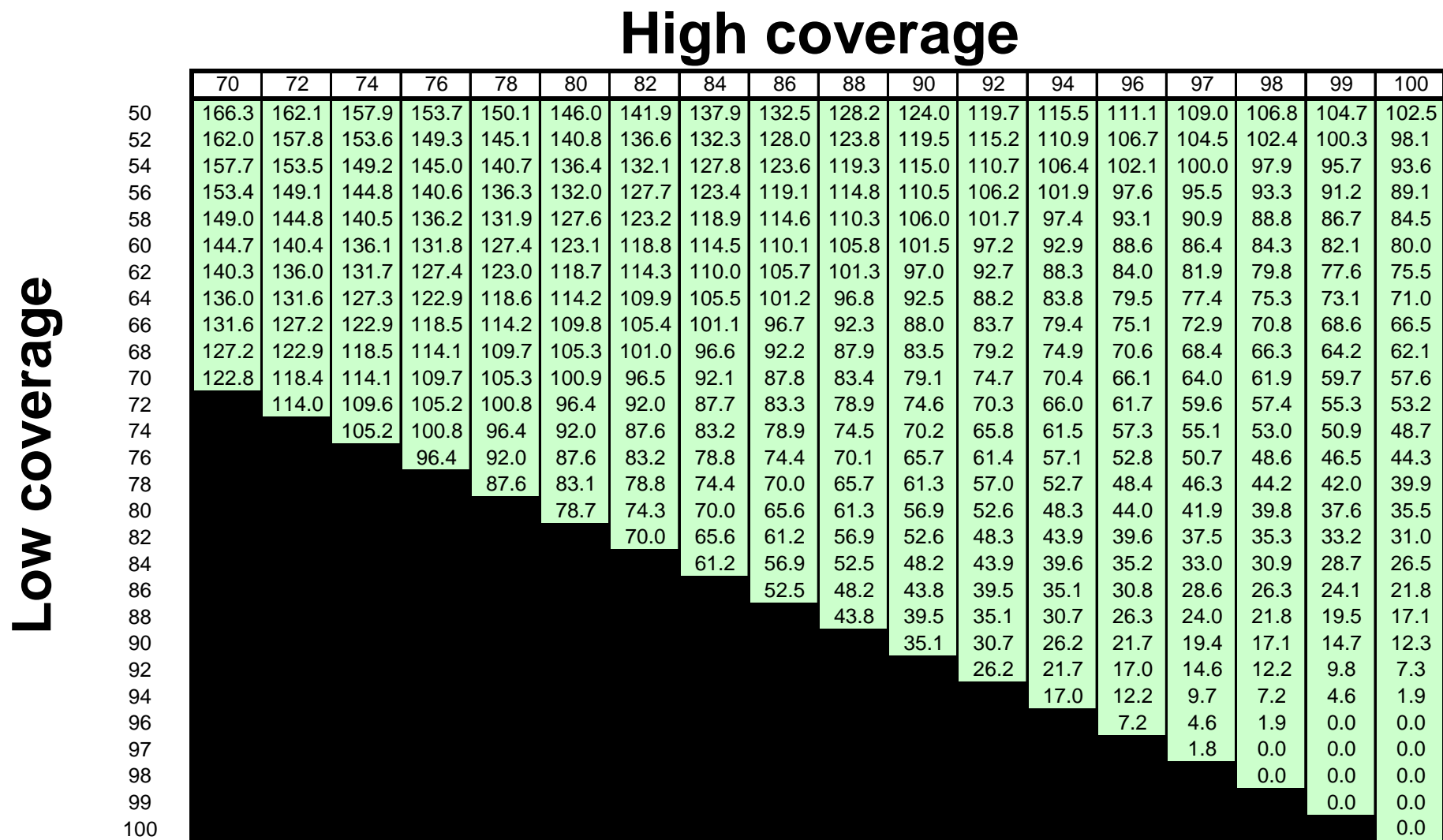


Figure A.3 – Cost of measles cases at various high and low uptake combinations (£)

		High coverage											
		70	74	78	82	86	90	94	96	97	98	99	100
Low coverage	50	22,411,104	21,324,832	20,292,298	19,224,226	18,030,066	16,922,788	15,813,450	15,246,237	14,966,408	14,686,646	14,407,090	14,126,074
	54	21,298,348	20,199,521	19,094,734	17,984,472	16,869,318	15,749,954	14,627,155	14,064,736	13,783,319	13,501,785	13,220,147	12,938,418
	58	20,177,970	19,066,977	17,950,150	16,828,061	15,701,387	14,570,892	13,437,424	12,869,853	12,585,910	12,301,874	12,017,761	11,733,584
	62	19,050,298	17,927,237	16,798,544	15,664,883	14,527,011	13,385,797	12,242,062	11,669,522	11,383,117	11,096,637	10,810,090	10,523,481
	66	17,915,760	16,780,814	15,640,518	14,495,629	13,346,994	12,195,434	11,041,722	10,464,261	10,175,350	9,886,373	9,597,301	9,308,132
	70	16,774,903	15,628,326	14,476,778	13,321,065	12,162,066	11,000,452	9,836,758	9,254,126	8,962,585	8,670,871	8,378,969	8,086,836
	74		14,470,497	13,308,110	12,141,977	10,972,910	9,801,224	8,626,822	8,038,276	7,743,559	7,448,498	7,153,015	6,857,052
	78			12,135,329	10,959,120	9,779,882	8,597,394	7,410,362	6,814,301	6,515,385	6,215,766	5,915,341	5,613,991
	82				9,772,761	8,582,672	7,387,465	6,183,939	5,577,364	5,272,457	4,966,272	4,658,637	4,349,368
	86					7,379,800	6,167,999	4,941,176	4,319,290	4,005,568	3,689,687	3,371,408	3,050,699
	90						4,932,838	3,672,013	3,027,662	2,701,734	2,371,659	2,038,258	1,700,458
	94							2,362,235	1,685,663	1,340,542	989,933	633,979	258,383
	96								987,236	628,287	260,442	3,717	2,524
	97									251,692	1,504	3,616	2,479
98										1,479	3,525	2,388	
99											3,464	2,328	
100												2,242	

ii) $\alpha = 0.75$

Figure A.4 – QALY gain of various high and low uptake combinations relative to a high coverage of 70% and a low coverage of 50%

		High coverage																	
		70.0	72.0	74.0	76.0	78.0	80.0	82.0	84.0	86.0	88.0	90.0	92.0	94.0	96.0	97.0	98.0	99.0	100.0
Low coverage	50	0.0	104.6	208.7	312.0	406.3	505.9	605.0	702.8	799.1	893.4	985.7	1075.8	1163.7	1260.1	1301.5	1342.5	1381.9	1420.2
	52	112.1	217.5	322.4	426.4	529.6	631.6	732.4	831.6	929.0	1024.5	1117.6	1208.2	1296.0	1380.5	1421.5	1461.6	1500.8	1539.0
	54	224.6	330.8	436.4	541.2	645.0	747.8	849.2	949.0	1047.0	1143.0	1236.5	1327.5	1415.5	1500.2	1541.2	1581.3	1620.4	1658.5
	56	337.5	444.5	550.8	656.4	761.0	864.5	966.5	1067.0	1165.6	1262.1	1356.1	1447.4	1535.6	1620.5	1661.5	1701.6	1740.7	1778.7
	58	450.8	558.6	665.7	772.1	877.4	981.6	1084.4	1185.5	1284.8	1381.8	1476.3	1568.0	1656.5	1741.4	1782.5	1822.5	1861.5	1899.4
	60	564.4	673.0	780.9	888.1	994.2	1099.2	1202.7	1304.5	1404.4	1502.0	1597.0	1689.1	1777.8	1862.9	1904.0	1944.0	1982.9	2020.7
	62	678.1	787.6	896.4	1004.4	1111.3	1217.1	1321.4	1423.9	1524.5	1622.7	1718.2	1810.7	1899.7	1984.9	2026.0	2066.0	2104.8	2142.5
	64	792.0	902.3	1012.0	1120.8	1228.7	1335.3	1440.3	1543.6	1644.9	1743.7	1839.7	1932.6	2022.0	2107.3	2148.4	2188.3	2227.1	2264.6
	66	905.9	1017.1	1127.6	1237.4	1346.1	1453.5	1559.4	1663.5	1765.5	1865.0	1961.6	2054.9	2144.6	2230.1	2271.1	2311.0	2349.6	2387.0
	68	1019.6	1131.7	1243.2	1353.8	1463.5	1571.8	1678.5	1783.5	1886.2	1986.4	2083.6	2177.4	2267.4	2353.0	2394.1	2433.9	2472.4	2509.5
	70	1133.1	1246.1	1358.5	1470.1	1580.6	1689.9	1797.5	1903.3	2006.8	2107.7	2205.6	2299.9	2390.3	2476.0	2517.1	2556.8	2595.2	2632.1
	72		1360.1	1473.4	1586.0	1697.5	1807.6	1916.2	2022.9	2127.3	2228.9	2327.5	2422.4	2513.1	2599.1	2640.1	2679.8	2718.0	2754.7
	74			1587.7	1701.3	1813.7	1924.9	2034.4	2142.0	2247.3	2349.8	2449.1	2544.7	2635.8	2722.0	2763.1	2802.7	2840.7	2877.2
	76				1815.8	1929.2	2041.4	2151.9	2260.5	2366.7	2470.2	2570.4	2666.6	2758.3	2844.8	2885.9	2925.4	2963.3	2999.6
	78					2043.7	2156.9	2268.5	2378.1	2485.6	2589.9	2691.0	2788.1	2880.5	2967.4	3008.5	3048.0	3085.8	3121.8
	80						2271.1	2383.8	2494.6	2603.0	2708.7	2810.9	2909.1	3002.4	3089.9	3131.2	3170.7	3208.4	3244.2
	82							2497.6	2609.6	2719.4	2826.4	2930.0	3029.5	3124.0	3212.3	3253.9	3293.6	3331.3	3366.9
	84								2723.0	2834.2	2942.8	3048.1	3149.4	3245.5	3335.1	3377.2	3417.2	3455.0	3490.5
	86									2947.1	3057.6	3165.1	3268.6	3367.0	3458.7	3501.5	3542.1	3580.2	3615.9
	88										3170.4	3280.6	3387.2	3488.9	3583.6	3627.7	3669.2	3708.1	3744.1
90											3394.2	3504.9	3611.1	3710.3	3756.5	3799.8	3840.0	3876.8	
92												3620.8	3733.3	3839.3	3888.7	3934.9	3977.5	4016.1	
94													3854.0	3970.0	4024.6	4075.6	4122.2	4163.8	
96														4099.6	4161.7	4221.3	4269.4	4273.8	
97															4231.1	4276.8	4269.4	4273.8	
98																4276.8	4276.6	4277.1	
99																	4276.6	4277.1	
100																		4277.1	

Figure A.5 – Measles related deaths at various high and low uptake combinations

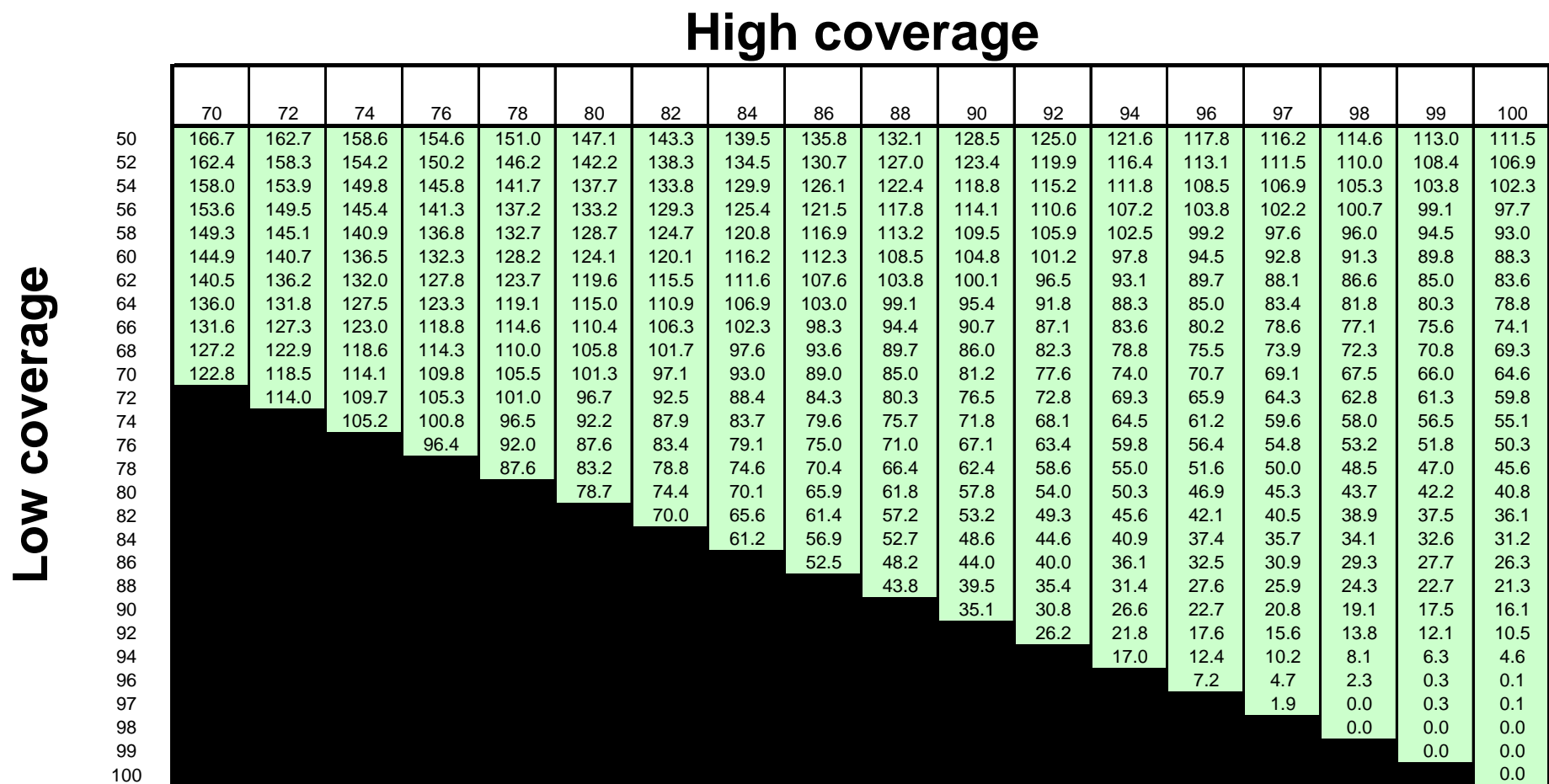


Figure A.6 – Cost of measles cases at various high and low uptake combinations (£)

		High coverage											
		70	74	78	82	86	90	94	96	97	98	99	100
Low coverage	50	22,439,459	21,380,144	20,359,161	19,337,144	18,334,193	17,363,958	16,432,936	15,940,732	15,723,332	15,509,107	15,301,587	15,100,114
	54	21,322,366	20,248,332	19,183,988	18,136,122	17,113,445	16,126,941	15,189,928	14,744,628	14,528,614	14,317,332	14,111,002	13,909,828
	58	20,195,341	19,106,171	18,026,607	16,963,860	15,927,299	14,928,906	13,983,383	13,535,605	13,318,885	13,107,282	12,901,034	12,700,360
	62	19,060,031	17,954,541	16,858,408	15,779,281	14,727,258	13,715,475	12,760,321	12,309,770	12,092,286	11,880,370	11,674,284	11,474,264
	66	17,918,790	16,795,704	15,681,495	14,584,227	13,514,789	12,487,662	11,521,312	11,067,539	10,849,182	10,636,934	10,431,084	10,231,889
	70	16,774,897	15,632,874	14,498,873	13,381,368	12,292,032	11,246,893	10,267,051	9,809,314	9,589,866	9,377,184	9,171,595	8,973,382
	74		14,470,504	13,314,817	12,174,511	11,061,965	9,994,922	8,997,880	8,534,828	8,313,829	8,100,423	7,894,992	7,697,851
	78			12,135,334	10,969,031	9,828,656	8,733,703	7,713,090	7,242,130	7,018,596	6,803,731	6,597,998	6,401,766
	82				9,772,763	8,597,991	7,465,384	6,409,625	5,925,518	5,697,261	5,479,164	5,271,781	5,075,727
	86					7,379,815	6,194,033	5,081,492	4,573,315	4,335,541	4,110,134	3,897,976	3,699,688
	90						4,932,819	3,724,458	3,169,063	2,910,848	2,668,421	2,443,443	2,237,008
	94							2,362,132	1,711,533	1,406,335	1,121,232	861,330	630,324
	96								986,855	641,539	310,827	44,572	20,220
	97									256,514	3,576	43,805	19,707
98										3,489	4,569	1,887	
99											4,475	1,851	
100												1,795	

iii) $\alpha = 0.95$

Figure A.7 – QALY gain of various high uptake and low uptake combinations relative to a high uptake coverage of 70% and a low uptake coverage of 50%

		High coverage																	
		70.0	72.0	74.0	76.0	78.0	80.0	82.0	84.0	86.0	88.0	90.0	92.0	94.0	96.0	97.0	98.0	99.0	100.0
Low coverage	50	0	110	220	330	429	537	655	758	868	967	1,065	1,150	1,225	1,325	1,360	1,393	1,410	1,442
	52	107	218	328	438	547	656	763	869	973	1,074	1,172	1,266	1,354	1,434	1,469	1,502	1,532	1,558
	54	216	326	437	547	657	766	873	979	1,083	1,185	1,284	1,378	1,466	1,545	1,581	1,614	1,643	1,670
	56	325	436	547	657	767	876	984	1,090	1,195	1,297	1,396	1,490	1,578	1,658	1,694	1,726	1,756	1,782
	58	435	546	657	768	878	988	1,096	1,202	1,307	1,409	1,509	1,603	1,692	1,772	1,808	1,840	1,869	1,895
	60	545	657	768	879	990	1,100	1,208	1,315	1,420	1,523	1,622	1,718	1,806	1,886	1,922	1,955	1,984	2,010
	62	657	768	880	992	1,103	1,213	1,322	1,429	1,534	1,637	1,737	1,833	1,922	2,002	2,038	2,070	2,099	2,125
	64	769	881	993	1,105	1,216	1,326	1,436	1,543	1,649	1,752	1,853	1,948	2,038	2,118	2,154	2,187	2,216	2,241
	66	881	994	1,106	1,218	1,330	1,441	1,550	1,658	1,764	1,868	1,969	2,065	2,155	2,236	2,272	2,304	2,333	2,358
	68	994	1,107	1,220	1,332	1,444	1,555	1,665	1,774	1,880	1,985	2,086	2,182	2,273	2,354	2,390	2,422	2,451	2,475
	70	1,107	1,220	1,334	1,447	1,559	1,670	1,781	1,890	1,997	2,102	2,203	2,300	2,392	2,473	2,509	2,541	2,569	2,594
	72		1,334	1,448	1,561	1,674	1,786	1,897	2,006	2,114	2,219	2,321	2,419	2,510	2,592	2,628	2,660	2,688	2,712
	74			1,562	1,675	1,789	1,901	2,012	2,122	2,231	2,336	2,439	2,538	2,630	2,712	2,748	2,780	2,808	2,832
	76				1,790	1,903	2,016	2,128	2,239	2,347	2,454	2,557	2,656	2,749	2,832	2,868	2,900	2,928	2,951
	78					2,018	2,131	2,243	2,354	2,464	2,571	2,675	2,775	2,869	2,952	2,988	3,020	3,047	3,071
	80						2,245	2,358	2,470	2,580	2,687	2,793	2,894	2,989	3,073	3,109	3,140	3,167	3,190
	82							2,472	2,584	2,695	2,803	2,909	3,012	3,108	3,193	3,229	3,261	3,287	3,309
	84								2,697	2,809	2,918	3,026	3,129	3,227	3,313	3,350	3,381	3,407	3,429
	86									2,921	3,032	3,141	3,246	3,346	3,434	3,471	3,502	3,528	3,548
	88										3,144	3,255	3,363	3,465	3,556	3,593	3,624	3,649	3,669
90											3,368	3,479	3,586	3,679	3,718	3,749	3,773	3,791	
92												3,595	3,707	3,807	3,847	3,878	3,901	3,917	
94													3,828	3,939	3,983	4,015	4,036	4,050	
96														4,074	4,132	4,167	4,186	4,184	
97															4,205	4,247	4,245	4,228	
98																4,248	4,246	4,249	
99																	4,251	4,251	
100																		4,251	

Figure A.8 – Measles related deaths at various high and low uptake combinations

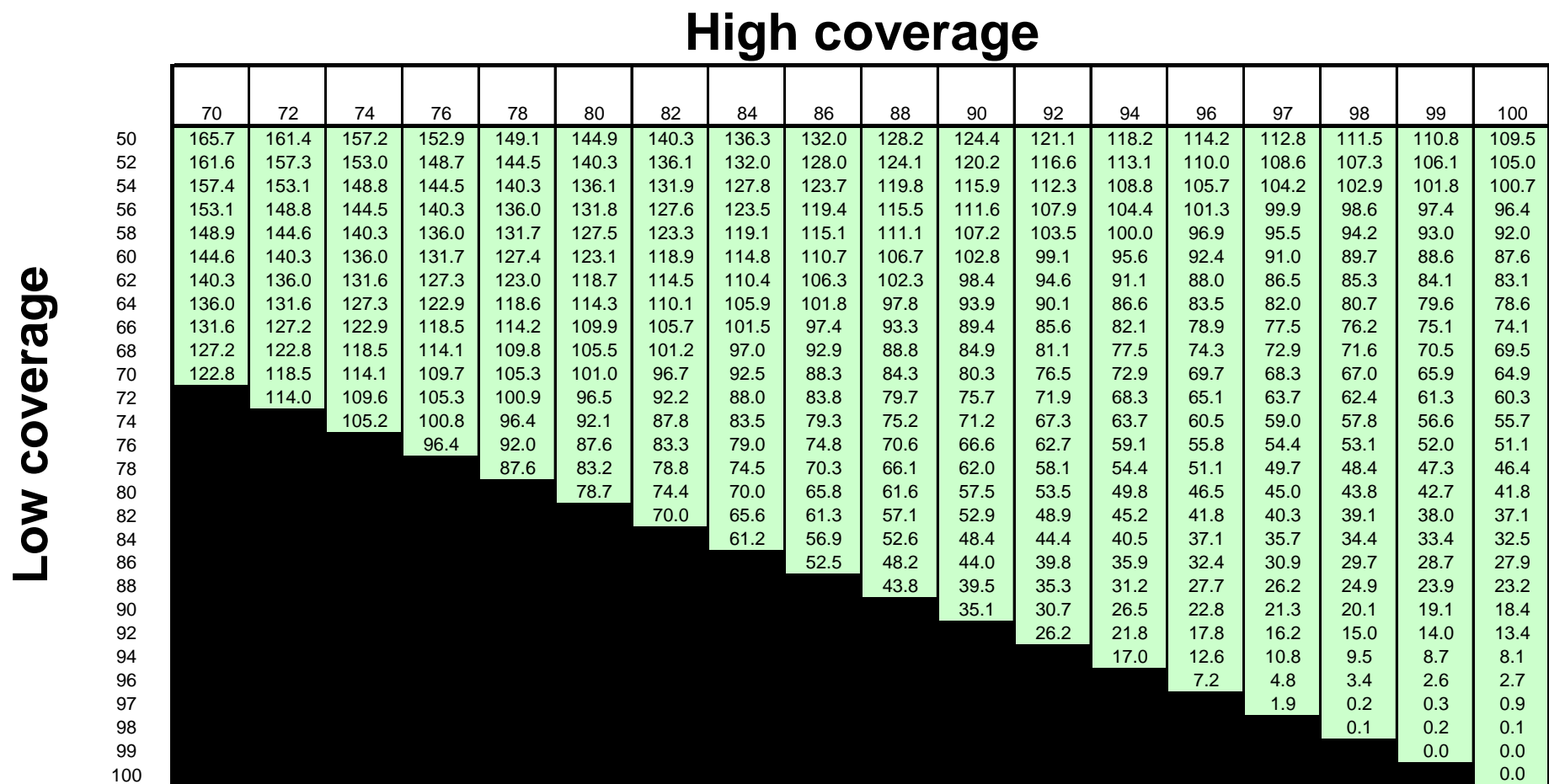


Figure A.9 – Cost of measles cases at various high uptake and low uptake combinations (£)

		High coverage											
		70	74	78	82	86	90	94	96	97	98	99	100
Low coverage	50	22,312,644	21,190,918	20,100,602	18,935,285	17,804,779	16,739,476	15,841,989	15,318,234	15,122,338	14,939,584	14,840,442	14,669,212
	54	21,237,424	20,110,889	18,979,747	17,850,603	16,733,763	15,650,741	14,652,047	14,214,661	14,018,284	13,838,905	13,677,368	13,533,720
	58	20,145,375	19,014,026	17,877,702	16,742,870	15,619,580	14,528,473	13,521,770	13,082,214	12,885,709	12,706,925	12,546,660	12,404,830
	62	19,036,847	17,900,106	16,757,937	15,616,684	14,486,587	13,387,722	12,372,541	11,930,078	11,732,992	11,554,414	11,395,196	11,255,205
	66	17,912,731	16,770,347	15,621,965	14,473,901	13,335,633	12,227,338	11,202,413	10,756,590	10,558,820	10,380,468	10,222,467	10,084,621
	70	16,774,945	15,626,280	14,471,012	13,315,183	12,167,697	11,048,338	10,009,798	9,559,990	9,361,809	9,184,280	9,028,220	8,893,285
	74		14,470,669	13,307,696	12,142,933	10,984,639	9,852,124	8,800,055	8,344,699	8,145,177	7,967,776	7,813,464	7,681,598
	78			12,135,356	10,960,551	9,789,896	8,640,830	7,569,772	7,107,716	6,906,735	6,729,636	6,577,612	6,449,855
	82				9,773,160	8,586,756	7,416,304	6,316,673	5,843,912	5,641,385	5,465,855	5,318,009	5,196,241
	86					7,379,929	6,179,568	5,038,504	4,548,697	4,342,709	4,168,306	4,025,825	3,912,404
	90						4,933,278	3,719,761	3,195,463	2,981,338	2,807,920	2,674,187	2,573,765
	94							2,361,773	1,737,861	1,492,258	1,314,723	1,198,123	1,123,270
	96								984,753	661,668	468,147	361,901	370,582
97									256,063	25,808	34,824	126,808	
98										18,898	29,320	13,752	
99											3,436	1,104	
100												1,073	

References

Curtis, L. & Netten, A. (2007) Unit Costs of Health and Social Care 2007, Personal Social Services Research Unit, University of Kent, Canterbury

Edmunds WJ & Van Hoek AJ. (2008) The impact of increasing vaccine coverage on the distribution of disease: measles in the UK. PHIAc 29.7a
Reducing differences in immunisation uptake: Economic Modelling Report 1.

National Collaborating Centre for Women's and Children's Health (2009).
Reducing differences in the uptake of immunisations (including targeted vaccines) in children and young people aged under 19 years: systematic review of effectiveness and cost effectiveness evidence. London: National Collaborating Centre for Women's and Children's Health

National Institute for Health and Clinical Excellence (2007). The guidelines manual. London: National Institute for Health and Clinical Excellence.

Available from: www.nice.org.uk

NHS Clinical Knowledge

Summaries http://www.cks.library.nhs.uk/pre_conception_advice_and_management/management/quick_answers/scenario_advice_for_all_women/view_full_scenario - (last accessed September 2008)

Office for National Statistics (2008)