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Flu Vaccination: Increasing Uptake

Final Report

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INVESTORS IN PEOPLE

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Abbreviations

ARI	Acute respiratory infection
A&E	Accident and emergency
BNF	British National Formulary
CHE	Centre for Health Economics
DoH	Department of Health
DSA	Deterministic sensitivity analysis
ES	Enhanced service
GP	General Practitioner
HCHS	Hospital and community health services
ICER	Incremental cost-effectiveness ratio
ILI	Influenza-like illness
JCVI	Joint Committee on Vaccination and Immunisation
LAIV	Live attenuated influenza vaccine
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
ONS	Office for National Statistics
PCA	Prescription Cost Analysis
PHAC	Public Health Advisory Committee
PHE	Public Health England
PSA	Probabilistic sensitivity analysis
PSS	Personal Social Services
PSSRU	Personal Social Services Research Unit
QALY	Quality-Adjusted Life Year
QOL	Quality of Life
ROI	Return-on-Investment
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Plain English Summary

The National Institute of Health and Care Excellence Public Health Advisory Committee (PHAC) is producing a guideline on the uptake of the flu vaccination (i.e. the number of people who receive the flu vaccination). A cost-effectiveness analysis was developed so that information could be combined to inform the Committee how different levels of uptake of the vaccination might impact health, as well as the impact that the intervention might have on the costs to the National Health Service (NHS), local authorities and to society as a whole. The PHAC is deciding whether or not to recommend different interventions (e.g. education and online campaigns) that aim to increase the number of people who receive the flu vaccine.

Flu is a virus that can cause individuals to be unwell, particularly over the winter months. It is easily spread amongst individuals but vaccination against the virus every winter can help to reduce the spread of the virus. Vaccination can also protect individuals who have a medical illness from flu as the flu can cause them to become more unwell.

The analysis has been done for four separate population groups:

(i) Children;
(ii) Clinical risk groups;
(iii) Carers;
(iv) Health and social care workers.

Children are known to be key spreaders of the flu virus because of the number of people they interact with. People in a clinical risk group have a medical illness (i.e. chronic heart disease) which puts them at increased risk of getting more severe complications if they get flu. Carers and health and social care workers often work closely with individuals who are in a clinical risk group and so vaccination could help to prevent them passing on the flu virus when they are providing care.

The flu virus can spread between individuals and it is important that this was included in the analysis. For the assessment of vaccination in children and clinical risk groups, a ‘dynamic’ model was used. This was based on a pre-existing model that has been used for previous economic assessments of flu vaccines. However, that model was not designed to assess the impact of vaccination for carers and health and social care workers. Because of this, a simpler ‘static’ model was used. This type of model does not normally include calculations for the spread of the virus. Instead, our analysis made a simple estimation of the extra number of people that would be affected each time that a carer or health and social care worker developed flu.

The health impact was calculated based on the likelihood of people developing flu, flu-related illness or dying, based on the uptake rate of the flu vaccine and if the vaccine prevents the individual getting flu. It also included any side effects from the vaccine itself. The likelihood of these events happening was taken from published evidence. We know the costs associated with people having these problems, such as going to the GP or into hospital, and so it was possible to calculate the overall costs for the whole of a flu season.

As well as estimating costs, we measured the health losses that people would have by becoming ill with flu. This was done by combining the decrease in life expectancy with decreases in patients' quality of life (if they had to go in to hospital, for example). This allowed us to calculate a measure known as the *quality-adjusted life year* loss for a person that could potentially be avoided if they did not get flu.

Different levels of vaccination were assessed compared against the current level of vaccination. The cost-effectiveness analysis asked questions such as: 'If an intervention increases vaccination levels by, say, 5%, what is the maximum cost for it to be cost-effective?' The Committee could then consider whether the maximum cost of the intervention for it to be deemed cost-effective is reasonable.

The results of the analysis showed that, for children, clinical risk groups, health and social care workers and a subgroup of carers, interventions that increase the uptake of the flu vaccination are likely to be cost-effective. This means that it would be beneficial to the NHS and to society as a whole to provide interventions that increase the level of vaccination, as long as the cost of the intervention is not too high. For example, if, compared to the current number of health and social care workers being vaccinated, the new intervention lead to every health and social care worker going to get their flu vaccination, the cost of the intervention could be no higher than £21.25 per health and social care worker if there is to be a benefit to the NHS and society. This maximum cost of the intervention changes depending on the group that is being analysed and the change in the number of people being vaccinated compared with current levels. For carers, however, the results for the carer population as a whole showed that it would not always be cost-effective to increase the level of flu vaccination. However, in some specific situations, (for example, where the carer looks after an individual who has complex needs and would require more expensive emergency care if their carer is off ill), it might be cost-effective to increase the level of vaccination.

As with any analysis of cost-effectiveness, there were some factors in our analysis that could be challenged or where alternative approaches could have been taken. The biggest example of this is that the spread of flu from carers and health and social care workers would have been better analysed if a dynamic model was used. This means that our results for carers and health and social care workers probably underestimated the real benefits of vaccination and therefore more money could probably be spent on interventions in these groups than reported here.

Executive Summary

1. BACKGROUND

This project will produce a guideline on increasing the uptake of influenza vaccination. This report details the economic modelling used to assess the cost-effectiveness of interventions that increase the uptake of influenza vaccination from the National Health Service (NHS) and Personal Social Services (PSS), local authority and societal perspective. The populations included in the model aligned with those given in the National Institute for Health and Care Excellence (NICE) scope for this project and are listed below:

- People aged from 6 months to 64 years in a clinical risk group including pregnant women and those who are morbidly obese (body mass index 40+);
- Children aged 2 to 17 years;
- People who are in receipt of carer's allowance or who are the main carer of a vulnerable person;
- Health and social care workers directly involved with people's care.

The specific questions and examples of the types of interventions considered for this guideline are given in the NICE scope.

2. METHODS

A dynamic model was used to evaluate outcomes in the children and clinical risk group populations. The dynamic model was originally developed by Public Health England (PHE) and was used to inform the Joint Committee on Vaccination and Immunisation (JCVI) recommendation to vaccinate children. In collaboration with PHE, the dynamic model was updated so that the outcomes of the model were the most representative and recent predictive estimates of influenza prevalence as required for this project. Influenza is an infectious disease, so a dynamic transmission model was considered as a framework for estimating the impact of vaccination on the spread of disease. Dynamic transmission models typically use a set of equations that represent the mechanisms of transmission, progression and treatment. In the children and clinical risk group models, the number of cases, ILI, ARI, hospitalisations, GP consultations and deaths were estimated by the dynamic transmission model. These were then included as input parameters in a separate model where the costs and consequences were applied and the results of the economic evaluation were calculated.

A static model was developed to evaluate outcomes in the carer and health and social care worker populations. It is important to note that carers and health and social care workers *who are also in a clinical risk group or carers who are elderly themselves* are not included in the assessments for carer and health care workers as they would be captured within the separate clinical risk groups model. The elderly are out with the scope of this guideline and so are not captured in the models described in this report. For this assessment, carers and health and social care workers are essentially healthy adults who are either in contact with those in a clinical risk group or in close contact with another person given their caring responsibilities. Those in a clinical risk group are more vulnerable to the negative impact of the influenza virus if they contract the virus. The models used a decision tree approach to estimate a number of influenza-related outcomes within the carer and health and social care worker populations associated with different levels of vaccine uptake, including the number of cases of influenza, ILI, acute respiratory infections (ARI) and deaths. The models also estimated the subsequent impact on resource use as a result of these outcomes, including the number of GP consultations, hospitalisations and need for replacement workers. Static models typically do not include transmission and, therefore, may underestimate the benefits of vaccination in populations where there is a higher degree of mixing and exposure to the disease in the population. To partially overcome the limitation of using a static model for carers and health and social care workers onward transmission was incorporated into the model by calculating the number of secondary cases of influenza-like illness (ILI) given the number of carers and health and social care workers with the virus. The average cost of treating an ILI for an individual in a clinical risk group was applied to the secondary cases of ILI.

Current vaccine coverage was informed by the series of reports produced annually by PHE on the Influenza Immunisation Intervention for England for the winter 2015-2016 season. Costs assigned to influenza-related and resource use were estimated from NHS Reference Costs and PSSRU. The mean vaccine injection cost was estimated as £5.96 in adults and £5.95 in children, but 90% of children between the age of 2 and 7 were assumed to receive the nasal spray vaccine costing £18. Additionally there was a service payment of £9.80 in certain subpopulations. QALY loss associated with influenza-related events was obtained from published literature. QALY loss associated with ILI, ARI and hospitalisation was modelled as 0.008, 0.001 and 0.018, respectively. The costs associated with hospitalisation and GP consultation (surgery visit or telephone consultation) were taken from national sources and were £1,029, £31 and £22, respectively. In the carer and health and social care worker models, a proportion of those with an ILI or non-ILI respiratory illness consulted a GP whilst a proportion of those with influenza required hospitalisation. The number of GP visits and hospitalisations required in the children and clinical risk group models was determined by the dynamic model.

Different levels of vaccination were assessed compared against the current level of vaccination for each of the population groups. The cost-effectiveness analysis asked questions such as: 'If an intervention increases vaccination levels by, say, 5%, what is the maximum willingness to pay per targeted person for it to be cost-effective?' The outcomes of the NICE evidence review reports were not directly included in the cost-effectiveness analysis due to concerns by the PHAC about the quality of the included studies and their suitability for addressing the questions in the scope, as well as heterogeneity between trials and differences in effect sizes. The results of the cost-effectiveness analysis can be used by the Committee when they are considering whether the maximum willingness to pay for the intervention for it to be deemed cost-effective is reasonable and whether they are able to make a decision on whether it can be recommended.

Extensive sensitivity analysis was conducted around the model parameters for each of the populations. Specifically for the carers model, the Committee were interested in conducting scenario analysis around some of the assumptions around the consequences of cases for carers. Two-way sensitivity analysis was conducted whereby the QALY loss to the cared for if a temporary replacement carer was required and the average cost of emergency care per episode was varied simultaneously. Three-way sensitivity analyses was also conducted whereby the average cost of emergency care per episode, vaccine efficacy for the carer population and onward transmission was varied simultaneously. All other inputs in the model base case remained unchanged.

3. RESULTS

The model results focus on the four populations, which were modelled separately: carers, health and social care workers, children and clinical risk groups.

The model incorporated a number of perspectives, including the NHS and PSS, local authority and societal. Outcomes were evaluated over a timeline of one influenza season (one year).

3.1 Carers

For carers, the maximum willingness to pay for the intervention per targeted person was never positive when uptake was increased from baseline levels in the model base case. From the NHS and PSS perspective, the maximum willingness to pay per carer for an intervention when uptake changes from baseline to 100% was -£5.19. This indicates that the results of the model suggest that vaccinating carers is not cost-effective and, as such, interventions aimed at increasing vaccination rates are not cost-effective. In the base case of the model, the average cost of emergency care was £50 based on 1% of cared for individuals requiring emergency hospitalisation at a cost of £4,995 per episode and the QALY loss to the person being cared for was assumed to be zero. Two-way sensitivity analysis was conducted whereby the QALY loss to the cared for if a temporary replacement carer was required and the average cost of emergency care per episode was varied simultaneously. When the average cost of emergency care per episode is £500 or higher, the maximum willingness to pay for the intervention was positive (i.e. there was a positive net benefit) irrespective of the value for the

QALY loss to the cared for individual. Specifically, the net benefit becomes £0 when the average cost of emergency care is £363. In a situation where a carer is caring for someone with more complex needs, the person being cared for may require emergency care that is more expensive than the average cost of emergency care used in the base case analysis if the carer is temporarily unable to care for them. In this subgroup of carers, where the average cost of emergency care (i.e. accounting for the fact that some patients might not require emergency care and would, therefore, not incur a cost) exceeds £363 per episode, vaccination is likely to be cost-effective from an NHS and PSS perspective. However, this assumes no cost for the intervention to promote uptake. In order for such an intervention to be cost-effective, the average cost of emergency care would need to be somewhat higher (depending on the cost of the intervention).

From a local authority perspective, increasing uptake from baseline to 100% results in cost savings of £338,643 as fewer individuals require provision of a replacement care when the carer was temporarily absent from their caring duties or permanently needed replacing due to death of the carer.

3.2 Health and Social Care Workers

At £20,000 per QALY, the maximum willingness to pay for the intervention per targeted health and social care worker, for a 5% increase in coverage is £2.15. The maximum willingness to pay per targeted health and social care worker is linear. That is, the maximum willingness to pay is not dependent on the uptake before the intervention is introduced and it is the same for a given increase in percentage points. The maximum willingness to pay for the intervention for an intervention to increase vaccination uptake is highest for the greatest increase in uptake. Any increase in vaccine uptake from baseline results in a positive net benefit.

From a local authority perspective increasing uptake from baseline to 100% results in cost savings of £735,515 as despite the overall cost of vaccination increasing as more people are vaccinated, there are cost savings generated as fewer health and social care workers are absent from work due to influenza-related illness.

3.1 Children

For children and clinical risk groups, scenario analysis was conducted whereby the uptake rate was varied from baseline by a certain percentage and the impact analysed, shown in Table 3.1. Given that the model used for these populations assumed that averting a case of influenza in one individual may avert cases of influenza in other individuals, the impact of increasing the uptake in these populations was determined for the whole population of England.

Table 3.5 presents the maximum willingness to pay per targeted person to get value from the intervention (willingness to pay) at a threshold of £20,000 per QALY gained, as coverage changes from one level to another for children. Coverage level is presented as relative to baseline coverage from the NHS and PSS perspective.

Table 3.5: Maximum willingness to pay for the intervention per targeted person: Children

		Coverage level with intervention				
		Baseline -5%	**Baseline**	**Baseline +10%**	**Baseline +25%**	**Baseline +35%**
Coverage level without intervention	**Baseline -5%**	No change	£2.12	£7.61	£13.60	£16.37
	Baseline	No benefit	No change	£5.50	£11.48	£14.25
	Baseline +10%	No benefit	No benefit	No change	£5.98	£8.76
	Baseline +25%	No benefit	No benefit	No benefit	No change	£2.77
	Baseline +35%	No benefit	No benefit	No benefit	No benefit	No change

Interventions are associated with a higher maximum willingness to pay for the intervention if the intervention is associated with a greater increase in uptake. For example, moving from -5% below baseline coverage to 35% above baseline coverage (an absolute change of 40% percentage points) is associated with the highest maximum willingness to pay per child, of £16.37. The maximum willingness to pay is not linear. That is, the maximum willingness to pay is also dependent on the uptake before the intervention is introduced (because of interaction / herd immunity). The results shown in Table 3.5 imply that increasing uptake at lower coverage rates is more cost-effective than increasing uptake at higher coverage rates, where the group approaches herd immunity (for example from baseline to baseline +10%, maximum willingness to pay is £5.50, whereas from baseline +25% to baseline +35%, maximum willingness to pay is £2.77).

Tables 3.6 to 3.8 present the maximum willingness to pay for the intervention at which an intervention is cost-effective at a threshold of £20,000 per QALY gained, as coverage changes from one level to another for the specified clinical risk group.

Table 3.6: Maximum willingness to pay for the intervention per targeted person: Adults in clinical risk groups

		Coverage level with intervention					
		40.7% (baseline -5%)	**45.7% (Baseline)**	**50.7% (baseline +5%)**	**60.7% (baseline +15%)**	**75.7% (baseline +30%)**	**85.7% (baseline +40%)**
Coverage level without intervention	**40.7% (baseline -5%)**	No change	£3.96	£7.92	£15.83	£27.20	£33.96
	45.7% (baseline)	No benefit	No change	£3.96	£11.87	£23.25	£30.01
	50.7% (baseline +5%)	No benefit	No benefit	No change	£7.91	£19.28	£26.05
	60.7% (baseline +15%)	No benefit	No benefit	No benefit	No change	£11.37	£18.14
	75.7% (baseline +30%)	No benefit	No benefit	No benefit	No benefit	No change	£6.76
	85.7% (baseline +40%)	No benefit	No benefit	No benefit	No benefit	No benefit	No change

In adults, the maximum willingness to pay follows a more linear trend, that is, the willingness to pay is similar for a given increase in percentage points, regardless of the uptake before the intervention is introduced, although there is a small association with higher uptake rates being associated with lower willingness to pay. This is likely due to the fact that while there is some onwards transmission in these groups, it is not as great as in the children group.

Table 3.7: Maximum willingness to pay for the intervention per targeted person: Pregnant women

		Coverage level with intervention					
		Baseline -5%	**Baseline**	**Baseline +5%**	**Baseline +15%**	**Baseline +25%**	**Baseline +35%**
Coverage level without intervention	**Baseline -5%**	No change	£4.47	£8.94	£17.88	£26.84	£35.78
	Baseline	No benefit	No change	£4.47	£13.41	£22.37	£31.32
	Baseline +5%	No benefit	No benefit	No change	£8.94	£17.89	£26.84
	Baseline +15%	No benefit	No benefit	No benefit	No change	£8.96	£17.91
	Baseline +25%	No benefit	No benefit	No benefit	No benefit	No change	£8.95
	Baseline +35%	No benefit	No benefit	No benefit	No benefit	No benefit	No change

A similar trend was observed in the pregnant women analysis to the adult in clinical risk group analysis (Table 3.6), whereby the maximum willingness to pay is similar for a given increase in percentage points, regardless of the uptake before the intervention is introduced, although there is a small association with higher uptake rates being associated with lower maximum willingness to pay.

Table 3.8: Maximum willingness to pay for the intervention per targeted person: Children in clinical risk groups

		Coverage level with intervention				
		Baseline -5%	**Baseline**	**Baseline +10%**	**Baseline +25%**	**Baseline +35%**
Coverage level without intervention	**Baseline -5%**	No change	£2.43	£7.27	£14.39	£19.02
	Baseline	No benefit	No change	£4.84	£11.96	£16.58
	Baseline +10%	No benefit	No benefit	No change	£7.12	£11.75
	Baseline +25%	No benefit	No benefit	No benefit	No change	£4.63
	Baseline +35%	No benefit	No benefit	No benefit	No benefit	No change

The trend in maximum willingness to pay in children in clinical risk groups is similar to that observed in the children group in Table 3.5. Children in clinical risk groups, however, are generally associated with higher maximum willingness to pay per person for the intervention compared with the whole children group.

5. LIMITATIONS

It is important to note that these model results must be treated with some caution, given the uncertainties in the model, all of which reduce the reliability of any conclusions which may be drawn.

The results of the analysis do not currently include any intervention costs. Data around intervention costs are scarce and the data that are available may not be applicable to other interventions of the same type. The Committee should consider not only the likely cost of an intervention, but the incremental cost over and above what is considered to be "current practice", since the NHS already has resources in place to promote and increase vaccination, such as posters in GP surgeries.

As with any economic model, there is some uncertainty, which impacts upon the reliability of the conclusions. However, extensive sensitivity analysis (both deterministic and probabilistic) were undertaken in order to determine to the extent of the reliability.

The full model report includes many sensitivity and scenario analyses to account for the uncertainty in the model. The number of ILI cases, influenza-related deaths, vaccine costs and QALY loss for ILI were among the parameters that had greatest impact on the results of the children and clinical risk group models. In the carer analyses, the parameters that had the greatest impact on the results were the proportion of cared for requiring emergency hospital admission, the proportion of individuals requiring hospitalisation due to respiratory illness and the proportion of infectious cases that are ILI. In the health and social care model, the parameters that had the greatest impact on the results were the average number of extra ILI cases per HSCW and the cost of secondary case of influenza.

There are a number of factors which may mean that the impact of vaccination is underestimated in certain groups. Firstly, in the carer and health and social group worker analysis a dynamic model was not used. Whilst onward transmission was included through calculating the number of secondary cases of ILI, this is a crude estimate and is a compromise given that a dynamic model was not available for these populations. Nonetheless, if the results of the model suggest that an intervention is cost-effective with the level of onward transmission included in the model, then incorporating the notion of herd protection may increase our certainty in this assessment.

Section 1: Introduction

1.1 BACKGROUND

As stated in the National Institute for Health and Care Excellence (NICE) final scope [1], influenza is the cause of hundreds of thousands of people visiting their general practitioner (GP) each winter, and tens of thousands of people being hospitalised [2]. Of those who are hospitalised, the death rate is estimated as 36 per 1,000 influenza hospital admissions for those not in a clinical risk group and 232 per 1,000 for those in a clinical risk group [3].

There is an increased risk of serious illness from influenza in certain populations; these are children under 6 months of age, elderly people, pregnant women and those with underlying health conditions [4]. The Joint Committee on Vaccination and Immunisation (JCVI) regularly reviews conditions that deem people at higher than average risk of flu-associated illness. These conditions are listed in Public Health England's (PHE) 'Green Book' [5] and include chronic respiratory disease, chronic heart, liver or kidney disease, chronic neurological disease and diabetes, amongst others. Pregnant women and those with morbid obesity (body mass index (BMI) ≥ 40) are also listed as a clinical risk group.

All children aged 2 to 4 years, and those in school year groups 1 to 2 (age 5 to 7) are currently eligible to receive the influenza vaccination. The JCVI recommend that all children aged 2 to less than 17 years receive the influenza vaccination [6] and this recommendation is on a phased roll-out in England. Therefore, older children are not currently vaccinated. However, some local authorities across the country are piloting vaccination schemes in older primary school children.

Generally, vaccine uptake among clinical risk groups and children is low. In England in 2014/15, the uptake of vaccination was 50% for all clinical risk groups and 44% for pregnant women. For all children aged 2, 3 and 4 years the vaccine uptake was 39%, 41% and 33% respectively in the winter of 2014 to 2015. Uptake in those aged 65 years or over was 73%, and for patients who are registered as a carer by their GP practice, the uptake of the influenza vaccination was 45% [7]. The 'Green Book' [5] also recommends that health and social care workers in direct contact with patients should also be vaccinated.

This guideline focusses on 4 distinct groups, as given in the NICE scope [1]:

- Clinical risk groups;
- Children aged 2 to 17 years;
- People who are in receipt of a carer's allowance and people who are the main carer of an older or disabled person whose welfare may be at risk if the carer falls ill (carers);
- Health and social care workers directly involved with people's care.

This project will produce a guideline on increasing the uptake of influenza vaccination. The guideline will be used to develop the NICE quality standard for influenza.

The aim of the economic modelling was to assess the cost-effectiveness of interventions that increase the uptake of influenza vaccination that have been identified during the effectiveness review and prioritised by the Public Health Advisory Committee (PHAC). The types of interventions that NICE are assessing the evidence for cover five areas and are given in Section 1.2 of this report. The outcomes from the economic model will help to inform the Committee's recommendations.

1.2 OBJECTIVES

The key questions from the NICE scope [1] and the interventions that they refer to are listed below. These questions refer to interventions that could be used to increase the uptake of the influenza vaccination.

Question 1. Are the interventions listed below effective and cost effective at increasing the acceptability and uptake of influenza vaccination among the target groups specified?

Interventions for Question 1 cover provision of information, and include:

- Campaigns (targeted, community-based including local radio campaigns, settings-based, online campaigns including social media and apps);
- Education (education tools, peer education carried out by a community member, lay education);
- Tailored information and advice (delivered during home visits, during consultation with health and social care workers, at support group meetings);
- Flu vaccination "champion" (practitioner or peer);
- Recommendations from a respected person (health or social care worker, carer, peer, volunteer, family member).

Question 2. Are the interventions listed below effective and cost effective at increasing the acceptability and uptake of influenza vaccination among the target groups specified?

Interventions for Question 2 cover improving access to vaccination, and include:

- Vaccination clinics in community settings (community pharmacies, antenatal clinics, specialist clinics, community venues e.g. libraries);
- Dedicated flu vaccination clinics;
- Mass vaccination clinics in community settings;
- Walk-in or open access immunisation clinics;
- Extended hours clinics (weekends, evenings, early mornings, 24 hour access);
- Out reach or mobile services (home visits, support group meetings, residential or care home visits, special schools visits, inpatient visits, immigration settings, mobile clinics);

- Parallel clinics (offer vaccination in parallel with regular appointments e.g. with midwives, clinics; coordinated timing of other interventions e.g. retinal screening for diabetic patients within flu season);
- Opportunistic vaccination (visits to GP, practice nurse or consultant for other medical conditions);
- Flu vaccination vouchers to enable eligible groups to receive vaccination from community providers.

Question 3. Are the interventions listed below effective and cost effective at increasing the acceptability and uptake of influenza vaccination among the target groups specified?

Interventions for Question 3 cover provider-based systems and processes, and include:

- Assigned lead for a flu intervention, local approach, practice approach;
- Interventions to modify standard searches of patient databases to identify eligible patients;
- Reminder and recall systems (for providers, clinical alerts and prompts);
- Personal invitation (GP, community pharmacy, health or social care worker);
- Booking systems (dedicated flu lines or online systems);
- Payment systems (fiscal arrangements);
- Reminders to eligible groups (text messages, emails, posters, telephone call);
- Approaches to follow-up (phoning patients);
- Personal health record (so eligible people can see if their vaccination is due);
- Sharing health records for providers (integration of primary and secondary care health records, centralised uptake record);
- Audit and feedback on uptake rates (weekly statistics, content and delivery of feedback, practical relevance, comparison data);
- Incentives for eligible groups (voucher schemes);
- Incentive schemes for providers (targets, quality and outcomes framework, voucher schemes).

Question 4. Are the interventions in listed below effective and cost effective in increasing the acceptability and uptake of influenza vaccination among health and social care workers?

Interventions for Question 4 cover education and intervention leadership for increasing uptake, and include:

- Assigned organisational lead to promote annual flu intervention to peers;
- Targeted and settings-based information campaigns;
- Education, for example, multidisciplinary, peer education, educational outreach, educational DVDs, myth busting and e-learning packages;
- Flu vaccination ‘champions’;
- Recommendations from a respected person, for example, a peer;
- Reminders and follow-up approaches (such as verbal reminders, text messages, emails, postcards and posters);
- Feedback on uptake rates;
- Incentive schemes, including targets for providers;

- Policies on conditions of employment (including the use of surgical masks, where applicable) and opt-out for health and social care workers;
- Signed statements from staff who decline a vaccine;
- Shared health record for providers of flu vaccination.

Question 5. Are the interventions listed below effective and cost effective in increasing uptake among health and social care workers?

Interventions for Question 5 cover improving access to flu vaccination, and include:

- On-site vaccination;
- Peer vaccination;
- Mobile flu vaccination clinics;
- Drop-in clinics for example, at staff events;
- Extended hours clinics, for example, 24-hour access to reflect different working patterns.

Section 2: Modelling Approach

2.1 MODEL OVERVIEW

2.1.1 Modelling Disease Transmission

Influenza is an infectious disease. Building a decision analytic model for influenza requires consideration into the use of a system that allows for the infectious and transmissible nature of the disease to be captured, such as with a dynamic transmission model [8]. Dynamic transmission models typically use a set of equations that represent the population and their interactions. The equations represent the mechanisms of transmission, progression and treatment [9]. The alternative modelling approach to dynamic modelling is to use a static model. Static models do not model disease transmission. The WHO guide for standardisation of economic evaluations of immunisation interventions [8] provides a flow chart to help determine when it is appropriate to use dynamic and static models. This highlighted that a dynamic model is not always necessary despite influenza being an infectious disease.

Table 2.1 outlines the key features of dynamic and static models.

Table 2.1: Features of static and dynamic models for infectious diseases

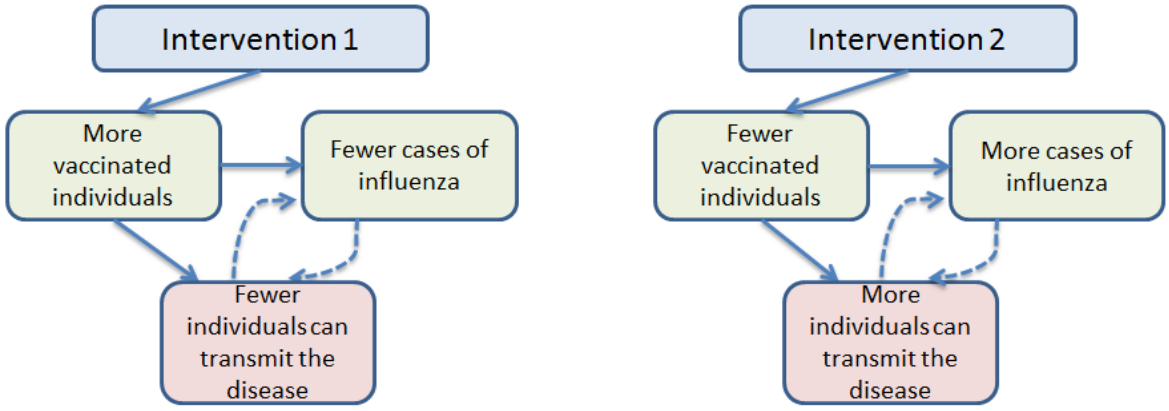
Dynamic models	Static models
Follow multiple cohorts over time	Typically follow an individual or single cohort over time
Model natural history of infection and disease	Model natural history of infection and disease
Describe transmission of the virus and resulting disease in a population	Do not include transmission
Capture direct and indirect "herd immunity" effects of vaccination	May underestimate the benefits of vaccination
Allow estimation of population-level variables over time	Allow estimation of cohort-specific variables
Potentially more realistic – allows interaction between individuals	Potentially less complex
May introduce additional uncertainty	

Adapted from: Snedecor *et al.* 2012

A dynamic model is able to capture the transmission among individuals taking into account the susceptibility of the individual, number of infected people in the population and the likelihood of contact between the infected and those susceptible [9]. The benefit of increasing uptake of the influenza vaccination is that there is a lower risk of disease transmission to other vaccinated or unvaccinated individuals.

Figure 2.1 shows the considerations that generate the results of the dynamic model [10]. The cost-effectiveness of Intervention 1 compared with Intervention 2 in Figure 2.1 is difficult to assess without accounting for the potential for onward transmission.

Figure 2.1: Dynamic model scenario



2.1.2 Disease Modelling in Patient Groups

York Health Economics Consortium (YHEC) and NICE have sought expert advice regarding the use of dynamic transmission models for the economic modelling to support the NICE guideline under consideration in this project. Each of the population groups included in the scope have individual requirements that must be considered when selecting the modelling approach to be taken.

Andrew Hayward and John Edmunds advised that using a static model would not be appropriate for clinical risk groups and children. John Edmunds had heavy involvement in the development of the dynamic transmission model that has previously been used to provide evidence to inform vaccine policy decisions, and recommended that YHEC collaborate with the developer of the PHE model, Marc Baguelin, to adapt and run the PHE dynamic transmission model (henceforth referred to as the PHE model) for the needs of this project.

The dynamic transmission model developed by PHE is an age- and risk-stratified transmission model that reproduces the strain specific behaviour over 14 seasons in England and Wales, accounting for the vaccination update during this period [11]. The model was used to estimate the reduction in infections and deaths achieved by different vaccination interventions before being used again for a cost-effectiveness study. Using data from England and Wales, the study showed that children are a major group of infection spreaders. The cost-effectiveness study evaluated the cost-effectiveness of extending the pre-2013 influenza vaccination intervention [12]. The study found that the influenza vaccination intervention that ran prior to 2013 which included risk groups and the elderly is likely to be cost-effective. The extensions to the vaccination intervention that were considered were for seven age groups of low-risk individuals. These were: 2 to 4 years, 50 to 64 years, 5 to 16 years, 2 to 4 years and 50 to 64 years, 2 to 64 years. The study found that vaccination of any of these groups is likely to be cost-effective but strategies that exclude school-aged children are less likely to be cost-effective.

The PHE model does not include carers or health and social care workers as distinct populations. Given the issues anticipated with disentangling the transmission between these groups and their contacts, as well as the evidence for transmission between health and social care workers and patients being unclear, as shown by numerous systematic reviews on the topic making different conclusions [13-17], it was determined that a static model could be used.

The major limitation of using a static model for influenza, an infectious disease, is that interactions among individuals are not accounted for. The static model does not account for the indirect benefits of the intervention such as herd immunity, and so the static model may not capture the full benefit (i.e. less disease reduction, quality-adjusted life years (QALYs) gained and disease costs) for the same amount of intervention costs. Therefore, the incremental cost-effectiveness ratio (ICER) of an intervention in a static model will likely be higher than the ICER for the same intervention in a dynamic model. To capture some of the likely cost savings and benefits associated with vaccinating carers and health and social care workers through the potential reduction of onward transmission in the model the secondary transmission was considered (see Section 0).

Table 2.2 summarises the modelling approach for each population group.

Table 2.2: Modelling approach for population groups

Static *De Novo* Model	**Dynamic Model & *De Novo* Model**
Healthcare workers	Clinical risk groups
Carers	Children

2.1.2.1 Children and clinical risk groups

YHEC collaborated with PHE to update the transmission model that was published in 2013 so that the outcomes of the model are the most recent and representative predictive estimates of influenza prevalence under different vaccination uptake scenarios. Data inputs that were updated in the PHE model included patient numbers (adapting to an England population only, and including the proportion who are in a clinical risk group) and baseline vaccine coverage. Details of the inputs and assumptions that have been updated in the transmission model are found in Section 2.3.2 and Section 2.3.3.

The PHE model was run for a pre-specified number of scenarios corresponding to different levels of vaccination uptake and coverage levels in different populations. The outcomes of the transmission model were then combined with a number of cost-effectiveness inputs. The cost-effectiveness inputs included in the models are described in Section 2.3 of this report.

2.1.2.2 Carers and health and social care workers

Given that the static modelling approach was used for carers and health and social care workers, the main considerations were the outcomes when a carer or health and social care worker falls ill. The carer model focused on capturing the cost, QALY loss of the carer getting influenza or influenza-related illness and the costs to provide a temporary replacement carer if the carer is ill or a permanent replacement if the carer dies due to an influenza-related cause. The model for health and social care workers captured the cost, QALY loss, and disruption to the National Health Service (NHS) and local authorities when a health and social care worker falls ill due to influenza or influenza-related illness. The associated productivity losses included in the models are described in Section 2.3.9.4.1.

The carer model includes the QALY loss to the cared for losing their carer given the likely familiarity of the carer to the cared for, as opposed to a more dynamic workforce for health and social care workers. In the base case this was assumed to be zero for both the temporary need for a replacement carer due to the carer having influenza and for the permanent replacement due to the carer dying due to influenza. The impact of this assumption has been explored using sensitivity analysis.

In the carer model, the number of secondary cases were susceptible household contacts who had ILI within 7 days from the onset of ILI or non-ILI respiratory illness symptoms in the index case. In the health and social care worker model, the dynamic nature of the contacts between the health and social care worker and patient meant that onward transmission was included as the average number of ILI cases per health and social care worker with the influenza virus.

2.1.3 Decision Problem

The economic models were designed to capture the incremental costs and QALYs associated with different interventions with the aim to increase uptake of vaccination in England among a number of target population groups. Table 2.3 gives the patient populations included in the analyses, their definitions were adapted from NICE scope [1].

Table 2.3: Patient populations

Population	Definition
Children	Those aged between 2 and 17 years
Clinical risk groups	People aged from 6 months to 64 years who are pregnant or have one of the following conditions: • Chronic respiratory disease such as severe asthma, chronic obstructive pulmonary disease or bronchitis; • Chronic heart disease; • Chronic kidney disease; • Chronic liver disease; • Chronic neurological disease such as Parkinson's disease or motor neurone disease, or a learning disability; • Diabetes; • A weakened immune system caused by disease (such as HIV/AIDS) or treatment (such as cancer treatment); • Asplenia or dysfunction of the spleen; • Morbid obesity (adults with a BMI greater than 40).
Carers	People who are the main carer of an older or disabled person whose welfare may be at risk if the carer falls ill, as described in the flu plan [18]. Carers who are under 65 years of age and not in a clinical risk group.
Health and Social Care Workers	Health and social care workers directly involved with people's care and who are not in a clinical risk group. This includes: • Social care workers employed by the NHS, local authority, independent providers and those who receive direct payments; • Health care workers including all doctors (including GPs), qualified nurses (including GP nurses), all other professionally qualified clinical staff, support to clinical and GP staff.

Interventions identified within this study were compared against interventions that are currently used to increase uptake of influenza vaccination given that interventions would have been in place to increase uptake when the baseline uptake rates were determined. There is difficulty in determining the definition of current practice at a national level given the heterogeneity in current practice between Clinical Commissioning Groups (CCG) and also between individual providers within these CCGs.

2.1.4 Model Settings

The economic models that were built to provide cost-effectiveness evidence for this guideline were developed in line with the NICE methods manual [19]. The model incorporated a number of perspectives, including the NHS and personal social services (PSS), local authority and societal.

Given that the impact of influenza is generally considered over the course of a season and that individuals must be vaccinated annually, the model assumed a time horizon of one year. The costs and health outcomes for all events of interest (apart from future QALYs lost due to premature death and the cost of permanent replacement care in the carer model) arise within this time period so discounting was not required. It was assumed that vaccination in a particular year does not provide protection in the following years, i.e. potential residual protection in the face of waning antibodies and drift of circulating viruses was not modelled.

Premature death may arise due to serious complications of influenza and influenza-related illness so the model accounted for the life years lost beyond the time horizon of the model and captured this impact across a lifetime time horizon. Discounting was applied to the QALYs lost due to premature death at a rate of 3.5%, as recommended by NICE [19].

The major outcome from the model was the ICER, expressed as the incremental cost per QALY, for the comparison between an intervention and current practice. The maximum willingness to pay for an intervention that gave the increase in uptake under analysis per targeted individual was also reported for each scenario. This was calculated based on a cost-effectiveness threshold of £20,000. Given that intervention costs were not included in the base case this value was equal to the net monetary benefit.

Sensitivity and scenario analyses were carried out. All uncertain parameters were varied in univariate (one-way) sensitivity analysis in order to identify the greatest causes of uncertainty in the model. Probabilistic sensitivity analysis (PSA) was conducted, whereby many iterations were run to generate the PSA results in order to provide a quantitative estimate of uncertainty.

2.1.5 Type of Analysis

The cost-effectiveness analysis took a threshold analysis approach for all populations. This involved running a range of scenarios based around different potential vaccine uptake rates rather than incorporating evidence on how specific interventions improve uptake. The analysis was designed in this manner so that the results of the models can be used to inform the PHAC discussions about the potential cost-effectiveness of a wide range of interventions.

Threshold analysis provides results that allows for questions such as 'If intervention A cost £X, how effective would it need to be at increasing uptake to be cost-effective?' or 'If intervention A increased uptake by X%, what is the maximum willingness to pay for the intervention per targeted person for it to deemed be cost-effective?' to be explored. Given that the data around intervention costs is scarce and the data that is available may not be applicable to all interventions, the results of the analysis can be used as guidance to allow the Committee to consider whether the maximum willingness to pay for the intervention per targeted person for it to be considered cost-effective is reasonable and whether they are able to make a decision on whether it can be recommended.

There are a number of benefits to taking this approach, including:

- Heterogeneity in both trial design and relative risk (RR) for similar interventions becomes less of a limiting factor in the analysis if these results are not used directly in the model; rather they are considered alongside the results of the model to provide guidance on whether a particular intervention may be considered cost-effective;
- The issue of only considering interventions with effectiveness data that is statistically significant is overcome, which would have been the case if specific interventions were to be modelled and the number of interventions in the analysis would be reduced (limiting the usefulness of the study);

- The analyses would be future-proofed in this regard as the findings can be applied to different interventions;
- Interpolation between different vaccine uptake rates allows for numerous interventions to be indirectly included in the analysis.

2.2 MODEL STRUCTURE

For each of the four populations, a *de novo* economic analysis was developed. These models were built within one Excel file given that the structure of the model and a large number of parameter inputs were common amongst the four populations, allowing for consistency across approaches. The models were run separately and the results for different populations are presented individually.

The *de novo* models used a decision analytic approach to estimate the incremental costs and health outcomes associated with each intervention compared with current practice. Given that the models for children and clinical risk groups required inputs from the PHE model and the models for carers and health and social care workers did not, the model structures are described separately under the sub-sections below.

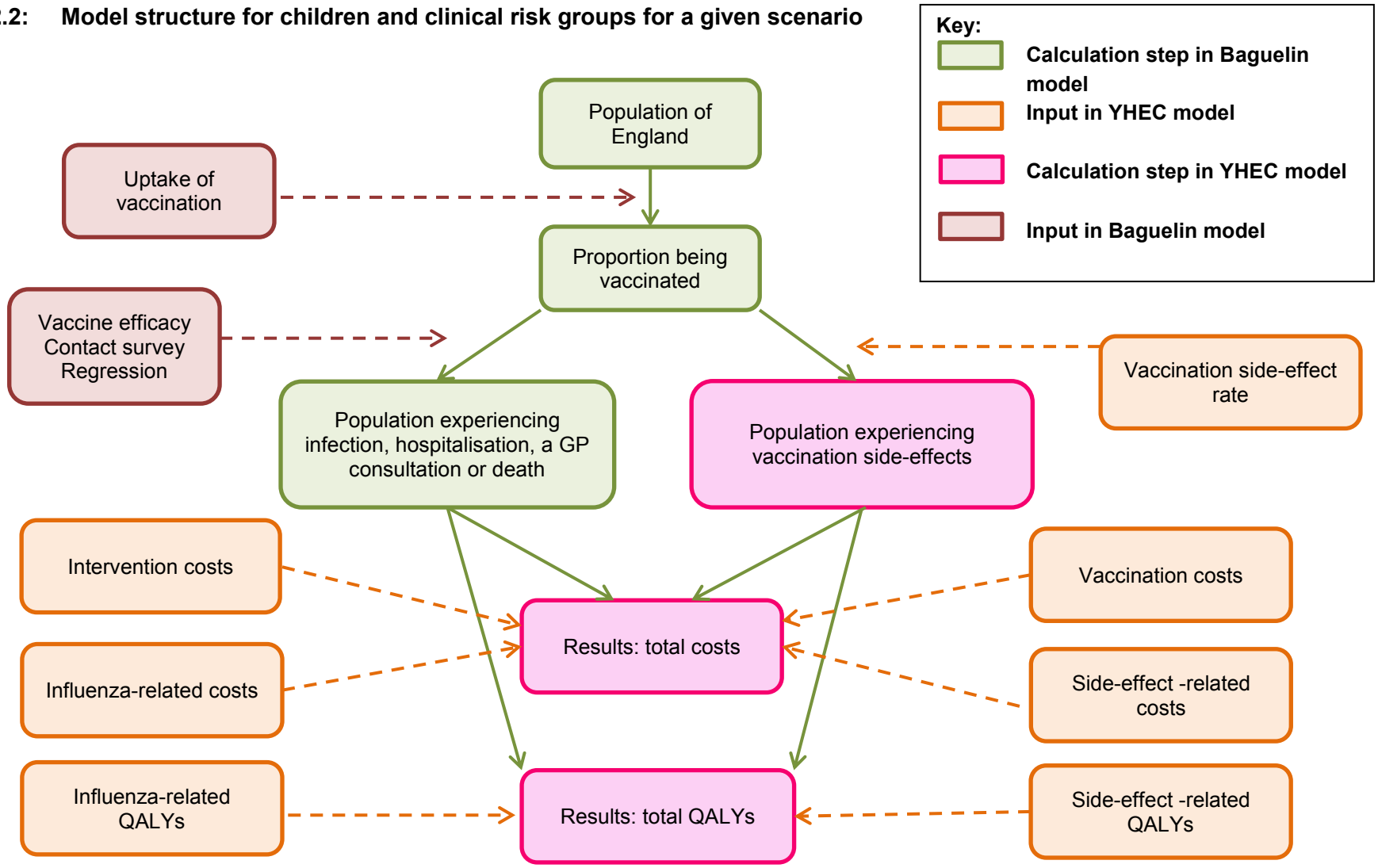
2.2.1 Children and Clinical Risk Groups

The structure of the model used to estimate outcomes in the children and clinical risk group analyses is presented in Figure 2.2. The model flow describes how costs and QALYs are estimated for a modelled scenario.

The model combines estimates from the PHE disease transmission model with a number of cost-effectiveness inputs. The flow of the model is as follows:

- Vaccination uptake rates were applied to the population of England to give the coverage rate;
- The PHE model provided estimates of the number of clinical cases of influenza, the number of hospitalisations, GP consultations and deaths by age-band, based on the expected vaccination coverage across the whole of England;
- Cost and QALY inputs were then applied to each of these events to estimate the impact of influenza events;
- Vaccine-associated side-effect rates were applied to those who are vaccinated;
- Cost and QALY inputs were then applied to each side-effect event;
- Vaccine costs were applied to those who are vaccinated;
- A intervention cost was applied that is reflective of whole target population in England (e.g. all high-risk children);
- Cost and QALY estimates from each modelled event (influenza, intervention, vaccine, vaccine side-effects) were then combined to provide estimates of the total costs and QALYs for the scenario.

Figure 2.2: Model structure for children and clinical risk groups for a given scenario



The transmission model for influenza used in this analysis was developed by PHE, and was introduced in Section 2.1.2 of this report. The transmission model estimated the prevalence of influenza-like illness (ILI), which includes true influenza as well as other illnesses which are clinically similar to influenza, such as acute respiratory infection (ARI). The costs and health outcomes of other ILI are included in the model as these are often indistinguishable from true influenza and may result in additional healthcare management costs as well as QALY losses.

The PHE model used the following process to estimate the prevalence of influenza and the number of deaths, hospitalisations and GP consultations associated with influenza in a given season:

- Demographic data were used to define the structure of the population in terms of age and risk groups;
- The structure of contacts between age groups was inferred from a contact survey;
- The outcomes of the model were fitted to time series of healthcare consultations complemented by virological surveillance and informed by vaccine uptake and match data;
- Links between infections and consultations were given priors using serology data.

Further details of the structure of the PHE dynamic transmission model can be found in a number of peer-reviewed publications [11, 12, 20, 21].

2.2.2 Carers and Health and Social Care Workers

The structure of the model used to estimate the cost-effectiveness of interventions in the carers and health and social care workers populations is presented in Figure 2.3. The decision tree structure for carers and health and social care workers is presented in Figure 2.4. Overall, the flow of the model is the same as described in Section 2.2.1. Points of difference are that the PHE model does not provide inputs for these analyses, the population is the target population (carers or health and social care workers) and the cost of replacing an individual who is absent from work is included. The model inputs are described in Section 2.3 of this report.

Figure 2.3: Model structure for carers and health and social care workers for a given scenario

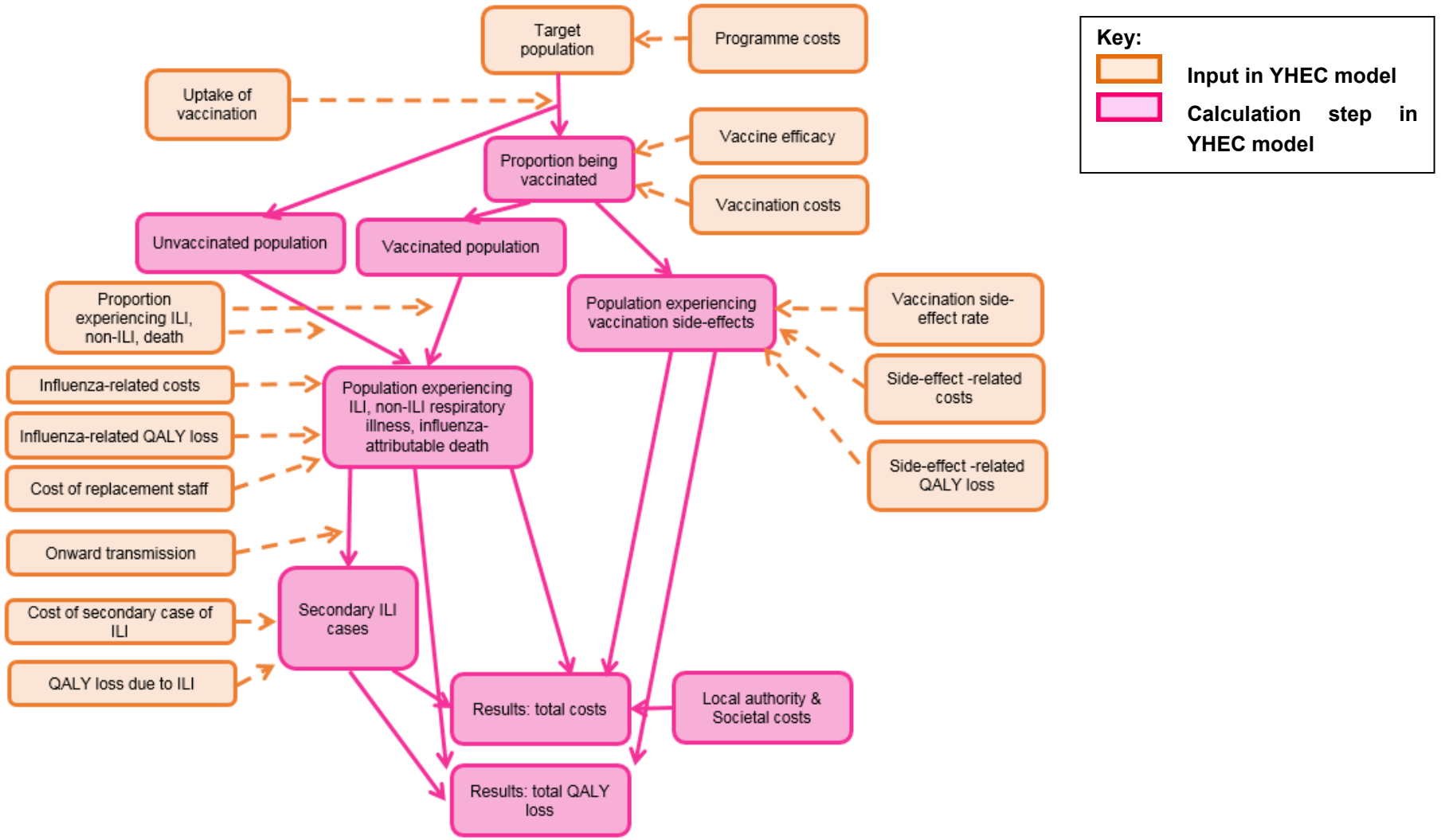
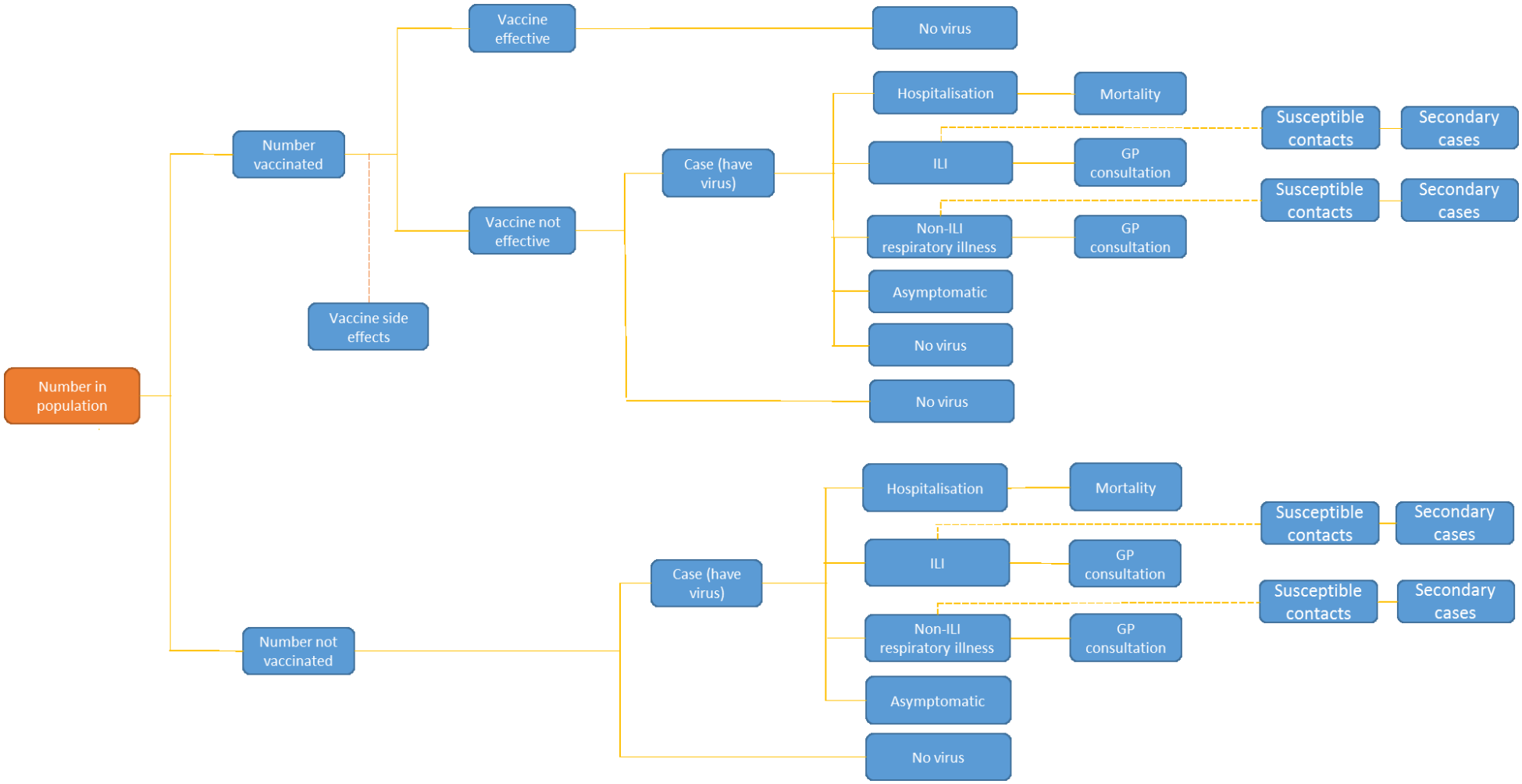


Figure 2.4: Decision tree diagram for carers and health and social care workers



2.3 MODEL INPUTS

This section outlines the model inputs that have been used to populate the economic models. Where model inputs differ between the different populations, the input for each population is described separately under the appropriate subsection. A table summarising all input values is provided in Appendix C.

2.3.1 Interventions and Effectiveness

The guideline is concerned with interventions that increase the uptake of influenza vaccination. The effectiveness of the intervention is the change in uptake of the vaccination.

The NICE evidence review team conducted a series of systematic literature reviews to identify appropriate evidence. The PHAC B Evidence Review Report SIGNPOST to effectiveness review report when available on NICE website, provides further details on the methods of the evidence review (inclusion and exclusion criteria), a quality assessment of each included study and a range of evidence statements for the possible effectiveness of each intervention type in each population. The outcomes of the studies from the effectiveness review were not directly included in the cost-effectiveness analyses since a threshold analysis was undertaken for all of the populations included in the analyses for this guideline (see Section 2.4.3 for details). However, the cost-effectiveness results for different effectiveness thresholds should be considered by the Committee alongside the effectiveness of the interventions from the reviews when determining whether an intervention might be considered cost-effective.

2.3.2 Population Numbers

The analysis assessed the impact of the introduction of interventions in England to improve vaccine uptake within the populations described in the scope.

The population numbers for children and clinical risk groups are used differently from the population numbers for carers and health and social care workers. This is due to the type of modelling that was used to determine the number of influenza cases, cases of illness and resource use.

For children and clinical risk groups the PHE dynamic model was used. This model calculates the outcomes (i.e. number of influenza cases) for total population of England based on a change of vaccine uptake in the population under analysis (i.e. children). The total population of England represents the susceptible population for the influenza virus. The size of the population under analysis is required because the intervention would be targeting only those in this population group and so the change in uptake is applied only to this group. The uptake of vaccination for the rest of the population in England remains at the current level.

In the carer and health and social worker models, given that a static model is used, other susceptible individuals in the population of England are excluded from the analysis (except for secondary cases as described below). Therefore, the population included in the model was the same as the number of people being targeted by the intervention. The population size was only used for calculating the total budget impact of introducing the intervention.

Other than the four patient groups listed in this section, the analysis did not break down the population into any further subgroups, for example by socioeconomic status. This may be of interest at a local level for targeting certain groups. However, the data are limited in these populations. The evidence review found only one low quality study that found no significant difference in uptake rate in those from lower socioeconomic backgrounds compared with the control group. Previous studies have also shown no relationship between socioeconomic status and vaccine uptake.

2.3.2.1 Children

The number of children in the analysis was obtained from ONS data for the whole of England [22]. Appendix B provides the total number in the population by age for 2016.

The, data on patient numbers fed into the PHE transmission model in order to determine the expected total number of infections in the population in the current scenario.

2.3.2.2 Clinical risk groups

The number of children and adults in the analysis was obtained from ONS data for the whole of England [22]. Appendix B provides the total number in the population by age for 2016.

Population groups for children and adults were further split between those who are pregnant, and between those who were in the high-risk groups and in the low-risk groups.

Individuals are considered at high risk if they have one of the following conditions as given in the scope for this project:

- Chronic respiratory disease;
- Heart disease;
- Renal disease;
- Diabetes;
- Immunosuppression due to disease or treatment;
- Morbid obesity (BMI ≥ 40).

It is likely that some patients have more than one of these conditions (i.e. these categories are likely to overlap) but this was not accounted for in the analysis as the clinical risk group population was assessed as a whole.

The proportion of patients in a clinical risk group for each age group was based on those used in the PHE model, which derived the proportion of individuals in a risk group by analysing data from the Royal College of General Practitioners (RCGP) Weekly Returns Service over a period of 5 years (2003 to 2008). The proportion in each risk group by age and pregnancy status is given in Table 2.4. Rates were adjusted to reflect the new JCVI recommendation of vaccinating those with morbid obesity.

Table 2.4: Proportion in each risk group by age and pregnancy status

Age Group	High risk (%)	Low risk (%)
< 2	5.2%	94.8%
2	8.6%	91.4%
3	8.6%	91.4%
4	8.6%	91.4%
5	12.9%	87.1%
6	12.9%	87.1%
7	12.9%	87.1%
8	12.9%	87.1%
9	12.9%	87.1%
10	12.9%	87.1%
11 to 15	12.9%	87.1%
16 to 65	15.8%	84.2%
> 65	48.1%	51.9%
Pregnant 15 to 24	11.0%	89.0%
Pregnant 25 to 44	11.0%	89.0%

In the cost-effectiveness analysis for clinical risk groups, data on patient numbers fed into the PHE transmission model in order to determine the expected total number of infections in the population in the current scenario.

Pregnant women

The annual influenza surveillance report PHE acknowledges the difficulty in estimating the total number of pregnant women in a population [23]. This is due to a number of factors, including the dynamic nature of the group with women continually entering and leaving the risk group, the number and variable use of READ codes that can be used to identify pregnant women and the delay in updating the individual's electronic GP clinical record following birth or loss of pregnancy.

As such, the number of pregnant women in England was estimated by applying an annual age-specific conception rate to the number of women in the population between the ages of 15 and 44. The age-specific conception rate was estimated from ONS data presented in Table 2.5 [24]. The number of conceptions was adjusted by the proportion not resulting in a termination (since it was assumed that these women would not be vaccinated). The conception rates were then re-estimated for the wider age bands used in this model (15 to 24, and 25 to 44) by inferring the estimated number of women in the two age bands and calculating the conception rate (0.044 between the ages of 15 and 24, and 0.07 between the ages of 25 and 44).

Table 2.5: Conception rates by age group

Age at conception	Number of conceptions	Percentage of conceptions leading to abortion	Adjusted number of conceptions	Conception rate per 1,000 women in age-group	Estimated total women in age group	Estimated conception rate (per 1,000)
15 to 19	59,433	45.0%	32,688	37.8	1,572,302	-
20 to 24	164,226	30.2%	114,6230	92.8	1,769,677	-
15 to 24	-	-	147,318	-	147,318	44.08
25 to 29	235,212	17.8%	193,344	126.6	1,857,915	-
30 to 34	229,855	13.3%	199,284	123.4	1,862,682	-
35 to 39	113,417	16.6%	94,590	66.7	1,700,405	-
40 to 44	27,547	28.0%	19,834	14.7	187,346	-
24 to 44	-	-	507,052	-	507,052	69.51

Obese patients

The PHE model did not include obese patients (BMI ≥ 40) within the category of high risk. The rates used in the PHE model were adjusted within this study to include these patients in order to incorporate into the present analysis. The PHE model assumed that the proportion of people in a risk group in a particular age group was constant over the period of the study.

Many patients in this group will already be eligible for vaccinations due to complications of obesity that place them in another risk category, and so the increase in the risk group was adjusted so that only obese patients with no other risk factors were added.

The report published annually by PHE on vaccine uptake in GP patient groups has estimated the change in the population size of the risk group category since the JCVI recommended that morbid obesity was included as a risk group in 2014. The total at-risk denominator for six months to 65 year olds has increased overall by approximately 13.2% (an increase of 795,825). It was estimated that 15 to 20% (~186,000) of the increase is down to morbid obesity with no other risk factors [25]. This is equivalent to around a 3.1% increase across all age groups, and this was assumed to be constant across age groups given the lack of age-specific data.

2.3.2.3 Carers

The number of carers used in the model was 586,351. The number of carers reported in the Influenza Immunisation Intervention for England, GP patient group survey for 2015 to 2016 [7] was 369,401 and this has been adjusted to account for a proportion of carers who are not registered with a GP.

Carers and health and social care workers who are in a clinical risk group are not included in this population number as they would be captured within the clinical risk group model. Carers and health and social care workers are essentially healthy adults who are in contact with those in a clinical risk group and so more vulnerable to the negative impact of the influenza virus if they contract the virus.

The Influenza Immunisation Intervention for England, GP patient group survey [25], reports the number of carers for the season 2015 to 2016. The survey states that 'The survey collects data on carers who fit the criteria set out in the annual flu letter, who are under 65 years of age, who are not pregnant and who do not fall into a clinical risk group' and who fit the definition of a carer given as 'those who are in receipt of a carer's allowance, or those who are the main carer or the carer of an elderly or disabled person whose welfare may be at risk if the carer falls ill' which is in line with the NICE scope [1] for this guideline. In communication with the project Resource Impact Lead at NICE the number of carers reported in the GP patient group survey was uplifted to account for carers who are not registered with a GP. The number of carers not registered with a GP is not known but a crude calculation was carried out based on evidence from Citizens Advice [26] that states that 37% of individuals who are entitled to Carer's Allowance do not claim it. It was estimated that the number of registered carers may be 63% of the total number of carers and this was applied to uplift the figure reported in the GP patient group survey.

2.3.2.4 Health and social care workers

The number of health and social care workers in England used in the model was estimated as 2,137,503. This number was generated based on evidence from a Public Health England survey [27] and a report produced by Skills for Care [28]. It was adjusted to exclude health and social care workers who are in a clinical risk group.

This population size was estimated using figures reported separately for health care workers and social care workers, given that a combined figure was not available. Public Health England report the number of health care workers in England in their survey of the Seasonal influenza vaccine uptake amongst frontline healthcare workers (HCWs) survey [29]. The survey includes data by staff grouping including: doctors (excluding GPs), GPs, qualified nurses (excluding GP practice nurses), qualified GP practice nurses, all other professionally qualified clinical staff, clinical support staff and support to GP staff. The number of frontline health care workers directly involved in patient care reported in the PHE survey was 991,323 [29]. This number marginally underestimates the total number of frontline health care workers because one trust did not provide the necessary data for the survey.

Skills for Care report [28] the estimated number of adult social care jobs in 2015 by employer type in England. NICE contacted Skills for Care and determined that there was a total of 1,296,000 social care jobs directly involved in patient care. The employer types were also included in the report. These were the NHS, local authority, independent and direct payments. The proportion of patient facing health and social care workers employed by each sector was calculated. The NHS employed 44% of health and social care workers, 47% were employed by the independent sector, 5% by local authorities and 5% were paid through direct payments.

In communication with the project Resource Impact Lead at NICE the number of health and social care workers was adjusted to exclude health and social care workers who have diabetes as these individuals would be in a clinical risk group and so would be eligible for vaccination through their GP. The prevalence of diabetes within the health and care workers population was assumed to be in line with the prevalence in England, 6.55% [30]. It was assumed that diabetes is the only condition listed in the clinical risk group criteria that would not prevent an individual with the condition working as a health and social care worker. The total number of health and social care workers directly involved in patient care, 2,287,323, was adjusted to exclude 6.55% of health and social care workers as they are deemed likely to be in a clinical risk group.

2.3.3 Baseline Coverage

Baseline coverage in the models was informed by the Influenza Immunisation Intervention for England reports published by PHE for the winter 2015 to 2016 season [23, 29, 31]. In addition to providing information on the vaccine coverage levels for the season, the reports also provide a commentary for how coverage has varied over the most recent seasons, in particular with relation to the change in policy regarding eligibility for vaccination. Limitations associated with the data are also discussed within the reports. Further information on how these data were collected is provided in the individual PHE reports.

2.3.3.1 Children

Coverage is reported by age and by risk group status (while the interventions assessed within this scenario aim to increase vaccination in children and do not distinguish between risk groups, it was necessary to incorporate rates in this manner since interventions in other scenarios in this analysis targeted only high-risk children). These rates are provided in Table 2.6.

Table 2.6: Vaccine coverage by age and risk group

Age group	Low risk	High risk
< 2	0.0%	18.6%
2	35.0%	48.3%
3	37.1%	52.3%
4	29.1%	47.3%
5	54.4%	39.2%
6	52.9%	39.2%
7	57.2%	39.2%
8	56.2%	39.2%
9	56.0%	39.2%
10	54.7%	39.2%
11 to 15	0.0%	39.2%
16 to 65	1.5%	45.7%
> 65	71.0%	71.0%
Pregnant 15 to 24	40.6%	55.9%
Pregnant 25 to 44	40.6%	55.9%

Vaccine uptake in children was estimated from two sources: the Influenza Immunisation Intervention for England reports on children of primary school age and on GP patient groups [25, 31].

Coverage rates for high-risk children between the ages of 6 months and 16 years were provided by the GP patient groups report.

Coverage rates for low-risk children between the ages of 2 and 4 years were provided by the GP patient groups PHE report.

Coverage rates for all children were provided by the children of primary school age PHE report. At the time of the report, all children in school Years 1 and 2 (aged 5 to 7) were eligible for vaccination through schools or an alternative scheme such as community pharmacies and general practices. An extension to the childhood vaccine intervention was piloted in five areas, where children 4 to 11 years of age (reception to school Year 6 age) were targeted. Coverage in the pilot areas for Year 1 and Year 2 children was slightly higher than the national average (62.6% vs. 54.4% in Year 1 children, and 62.7% vs. 52.9% in Year 2 children). In this analysis, it was assumed that should the intervention be available nationwide, there would be similar levels of coverage in Year 3 to 6, given a lack of data to inform these rates on a national level.

It was assumed that coverage in children under the age of 2 and between the ages of 11 to 15 at low risk of complications was 0%, since these children are not eligible for vaccination through schools or through the NHS under the current intervention.

In the cost-effectiveness analysis for children, baseline vaccine coverage data fed into the PHE transmission model in order to determine the expected number of infections in the population in the current scenario.

2.3.3.2 Clinical risk groups

In the cost-effectiveness analysis for patients in clinical risk groups, baseline vaccine coverage data fed into the PHE transmission model in order to determine the expected number of infections in the current scenario.

Vaccine uptake in children was estimated from the Influenza Immunisation Intervention for England reports on GP patient groups [25]. Coverage was reported by age and by risk group status, and by pregnancy status for adult women.

Coverage for adults over the age of 65 is not disaggregated by patient risk, and so the same rate was applied to both groups. This approach was also taken in the PHE model. While high risk patients are associated with a higher rate of hospitalisation and GP consultation (Section 2.3.9) and death (Section 2.3.10), this approach is expected to have a minimal impact on the outcome of the analysis, since this patient group was not targeted by the interventions in the analysis.

The PHE vaccine uptake report noted some limitations with the estimation of coverage rates, specifically regarding the fact that there may be delays in the coding of certain vaccinations, meaning that the total number of vaccinations may not be recorded correctly (underestimated). Firstly, GP practices may have delays in updating records to reflect coding of pregnant women and/or changes in pregnancy outcomes following birth or loss of pregnancy. Secondly, there is likely to be a lag in data being fed back into the GP record where patients aged 18 to 65 in a clinical risk group have received vaccination in community pharmacies.

2.3.3.3 Carers

The vaccine uptake used in the model was 37.4% for the carer population. This input was taken from the PHE document, Influenza Immunisation Intervention for England, GP patient group survey for the season 2015 to 2016 [25].

2.3.3.4 Health and social care workers

The vaccine uptake by frontline health care workers and social care workers with direct patient care used in the model was 50.6% [29].

Public Health England report the vaccine uptake rate by frontline health care workers in England in their survey of the Seasonal influenza vaccine uptake amongst frontline healthcare workers (HCWs) [29]. The survey did not include social care workers and this was acknowledged in the discussion of the survey report. For this project, it was assumed that the uptake rate for social care workers is consistent with the uptake rate for health care workers.

Scenario analysis has been conducted whereby the uptake rate from the 2016/17 season has been used, given that this information is available for health and social care workers. Vaccine uptake was 61.8% in 2016/17 [32]. This uptake rate has not used in the base case as data from the 2016/17 season is not available for all of the populations covered by this guideline and so for consistency the base case used uptake rates from the 2015/16 season.

2.3.4 Disease Transmission

Disease transmission is an important factor when modelling infectious diseases, since preventing a case of influenza benefits not only the individual but also for those who may be indirectly protected. This was captured differently for different populations within the analyses for this project.

2.3.4.1 Children and clinical risk groups

Transmission of influenza in the analyses for children (identified as the main spreaders of influenza infection), and those in clinical risk groups were estimated within the PHE model, which was used to predict the total number of influenza cases in the population.

A contact survey [33] was used in the PHE model to predict structure of contacts between individuals. Data for the UK arm from the survey was used in the transmission model: the survey dataset consisted of 1,012 participants aged 0 to 79 years of age who recorded 11,876 contacts in total. Participants were asked to complete diaries recording information such as with whom they had contacts during a day, the age of the contact, the nature of the contact (conversational or physical contact) and the nature of the day (weekday, weekend, or holiday).

A number of other parameters are included in the transmission model, including the activity of acute respiratory infections (ARI) in general practices, respiratory Virus RCGP surveillance data and serology for previous seasons. Further details on these parameters are provided in the publication for the model [11].

2.3.4.2 Carers

In the carer model a secondary attack rate of 19% was used in the model. This was taken from a Spanish study that reported the household transmission of influenza in the pandemic and post-pandemic seasons [34]. The authors calculated the secondary attack rate as the number of secondary cases divided by the number of susceptible household contacts with the secondary cases being susceptible household contacts who had ILI within 7 days from the onset of symptoms in the index case.

In the model the number of susceptible contacts was calculated based on the number of carers with ILI or non-ILI respiratory illness, vaccine efficacy (as described in Section 2.3.5) and the proportion of unvaccinated people infected by the influenza virus.

Vaccine efficacy differs depending on the age of the individual being vaccinated. In the model base case 30% of secondary cases were under 65 years of age and the remaining 70% were aged 65 years and over. This was based on a published report by the King's Fund reporting the age of care recipients in the year 2000 [35].

In the model 18% of unvaccinated people are infected by the influenza virus. This figure was taken from a published Flu Watch cohort study [36] that reported that each winter season, based on rates per 100 person seasons, influenza infected 18% of the unvaccinated population.

2.3.4.3 Health and social care workers

In the health and social care model the average number of extra ILI cases per health and social care worker with the influenza virus was 0.7. This was calculated based on the reported influenza vaccination uptake rates by staff in care homes and cases of ILI in the cared for population (care home residents) as published by Hayward *et al*. [37].

Hayward *et al.* reported the vaccine uptake rate for two seasons (2003-04 and 2004-05) by care home staff and the number of cases of ILI amongst care home residents for care homes where staff were not vaccinated and care homes were there was some uptake of the influenza vaccination. The number of care home staff with influenza was determined using the *de novo* model which accounts for the vaccine efficacy (as described in Section 2.3.5) and the proportion of unvaccinated people infected by the influenza virus (described in Section 2.3.4.2). The ratio of cases of influenza amongst the care home staff and the number of cases of ILI from the published study was calculated as 0.7. This was used in the base case of the model but with the understanding that this was likely to be an upper bound. Sensitivity analysis was conducted around this input.

2.3.5 Vaccine Efficacy

2.3.5.1 Children and clinical risk groups

Vaccine efficacy was a parameter informing the estimation of the number of influenza cases within the PHE transmission model. In the dynamic model (children and clinical risk groups) this was a static input (i.e. no variation in efficacy rate is incorporated into the model base case or sensitivity analysis).

Vaccine efficacy in this analysis was based on the rates used in the PHE transmission model and has not been updated for this analysis. Efficacy was differentiated by age group (above and below 65) and whether the vaccine is well-matched to the strain that year, as shown in Table 2.7.

Table 2.7: Vaccine efficacy

Age	Poorly-matched year	Well-matched year
Under 65	42%	70%
Over 65	28%	46%

The Baguelin *et al.* study [11] discussed the applicability of two sources for vaccine efficacy for the PHE model. A Cochrane review [38] suggested that efficacy was 73% in years in which the vaccine was well-matched to the circulating strain, and 44% in years when there was a poor match. All studies in the Cochrane review enrolled healthy young adults. Another analysis found that efficacy was lower in the elderly (46%) compared to younger adults (70%). The PHE model, therefore, assumed that vaccine efficacy was 70% and 46% in those under or over 65 years of age respectively in a well-matched year, and 42% and 28% in those under or over 65 years respectively in poorly matching years, as shown in Table 2.7. The analysis also assumed that the efficacy of the live attenuated influenza vaccine (LAIV) in children would produce similar protection to the current vaccine in adults.

While vaccination interventions are designed with a long-term perspective, vaccine efficacy was demonstrated to vary from one season to another. In order to be able to derive estimates of the vaccine efficacy for each strain and season, Baguelin *et al.* used data from the Health Protection Agency to establish the match between the circulating and vaccine strains, given in Table 2.8. This allows for the predictions of the model to be applicable to an average season (including potential future seasons), rather than for just a single, specific season.

Table 2.8: Match of vaccine strains to the circulating seasonal strains

Season	Strain of influenza		
	A/H3N2	A/H1N1	B
1995/1996	U	M	U
1996/1997	M	U	U
1997/1998	U	M	U
1998/1999	M	U	U
1999/2000	M	U	U
2000/2001	U	M	U
2001/2002	M	M	U
2002/2003	M	M	U
2003/2004	U	M	U
2004/2005	U	M	U
2005/2006	M	M	U
2006/2007	M	M	U
2007/2008	M	M	U
2008/2009	M	M	U

U = unmatched, M = matched.

2.3.5.2 Carers and health and social care workers

Vaccine efficacy was included in the static models for carers and health and social care workers. Vaccine efficacy was 64% for those under 65 years of age and 42% for those who were 65 years or over in the model base case.

To account for the annual variation in virus strain, the probability of the vaccine matching the circulating strain has been included as an input. In the base case this was 79% based on the likelihood of Influenza A/H1N1 being the predominant strain and data from the Health Protection Agency, Table 2.8, showing that the vaccine matched this strain for eleven of the fourteen seasons where data was available. Influenza A/H1N1 was the predominant circulating strain during the 2015/16 season [39]. The vaccine efficacy input was then calculated as a weighted average based on the probability of the season being a well-matched year as opposed to a poorly matched year. The vaccine efficacy for a well and poorly-matched year used in this calculation are given in Table 2.7, above, where the values for <65 years are appropriate for the carer and health and social care worker populations.

The vaccine efficacy for individuals aged 65 and over was included in the carer model when the number of susceptible carer contacts was calculated as described in Section 2.3.4.2.

2.3.6 Vaccine Side Effects and Associated Impact

2.3.6.1 Rates of vaccine-associated side effects

Injection side-effects

Minor adverse vaccine events such as local reactions (sore arm, swelling, itching, redness *etc*.) and systemic reactions (feverish, ILI, tiredness, headaches *etc*.) have been demonstrated to be associated with the administration of the influenza vaccine. In the models this was estimated as being 2% of those vaccinated with the injection form of the vaccine. This parameter was varied in the sensitivity analysis.

This adverse event rate was applied in the analysis which encompassed all types of minor reactions. This was based on the approach taken in TA158 that covers the use of different influenza prophylaxis treatments [40].

The TA158 used adverse event estimates from a HTA evaluation of the prevention and treatment of influenza, who in turn estimated the rates of adverse events from a RCT evaluating side effects associated with influenza vaccination in healthy working adults. In this study, the probability of adverse events from vaccination was estimated at 2%, based on the observation of a two-day work absence per 100 healthy adults in the week following influenza vaccination [41]. Each day of work absence was assumed to be equivalent to a single day with influenza symptoms. The HTA report states that this same figure would be applicable to the paediatric and high-risk populations, so the rate was applied to all those receiving the vaccine.

Other economic analyses have included injection site reactions, systemic reactions (defined as fever within 2 to 7 days of vaccination), and anaphylaxis, occurring at similar rates to that assumed in this analysis (range from 1% to 5%) [27, 42-44].

Nasal spray side-effects

The rate of adverse event in children receiving the LAIV nasal spray vaccine was estimated as being 3.1% in the base case and varied in sensitivity analysis. A Cochrane study [38] reviewed the impact of influenza vaccines in healthy children. One primary study identified in the review reported a significant difference in the rate of bronchitis, which was included in the economic analysis.

The study authors were unable to pool the data in the review due to differences in how each study defined adverse events. Other adverse events that were identified in the study included temperature rise, nasal congestion and headache, all of which were considered to have negligible impact on quality of life or resource use, and so were excluded from the economic analysis. Upper respiratory tract infections were also reported, but the primary study stated that there was no evidence to suggest that this outcome was linked to vaccine administration.

Other side-effects

No serious adverse events associated with the vaccine have been included in the analysis due to a lack of evidence for association. A Cochrane review published in 2014 [45] evaluated the effect of vaccines and determined whether exposure to vaccines is associated with serious or severe harms. The review found that found that vaccine use is not associated with a number of serious conditions including multiple sclerosis, optic neuritis (inflammation of the optic nerve of the eye) or immune thrombocytopaenic purpura (a disease that affects blood platelets). The review also found that the administration of pandemic monovalent H1N1 inactivated vaccine is not associated with Guillain-Barre syndrome (a disease that affects the nerves of the limbs and body). The administration of vaccines during pregnancy were demonstrated to have no significant effect on abortion or neonatal death. This is reasserted in the Green Book for influenza [5], where it is stated that no study to date has demonstrated an increased risk of either maternal complications or adverse foetal outcomes.

2.3.6.2 Impact of side effects on quality of life

Previous studies have taken a range of approaches in modelling the impact on quality of life associated with vaccine side-effects. One study includes a QALY loss of 0.0015 (0.55 quality-adjusted life days) [43], equivalent to one day with influenza symptoms. In this study, this value was used in the base case analysis, and applied to side-effects experienced both with the injection and the nasal spray vaccines. This value was varied in sensitivity analysis.

Many previous economic analyses that model vaccine-related adverse events have not incorporated an impact on quality of life, since the events have an insignificant impact to the patient and are transient. In the TA158 the assumption was made that adverse events due to vaccination had no impact upon health-related quality of life. Given the uncertainty in the value of this parameter, it was explored in a sensitivity analysis, where the range of values in the analysis included no impact in order to reflect the assumptions made in these other studies.

2.3.6.3 Cost of treating side effects

All patients experiencing adverse events due to vaccination were assumed to consult their GP for advice, and so the cost of a GP visit was incurred for these patients. This was applied to side-effects experienced both with the injection and the nasal spray vaccines

No published evidence was identified that provides the proportion of patients who have vaccine-related side effects who visit a GP. Therefore, an assumption was made that 100% of patients with side-effects would consult their GP about vaccine side effects, based on expert opinion within the Committee. The impact of this assumption was explored in a sensitivity analysis by varying the proportion of patients who consult their GP.

Previous studies have taken a range of approaches in modelling the cost associated with treating minor vaccine side-effects. A number of analyses applied the cost of a physician visit to all minor adverse events [27, 42-44, 46].

2.3.7 Influenza-Associated Mortality

Patients who experience a case of influenza have an associated risk of death. Given the short time horizon of the analysis, all-cause mortality was not considered in the model.

To predict influenza-associated mortality, the probability of the model-derived infections resulting in death was based on a regression analysis for children and clinical risk groups (specifically an age-specific, and strain and risk specific when available, negative binomial regression model with identity link and intercept) [3]. The study authors analysed weekly laboratory reports for influenza from a number of national databases for the eight years immediately preceding the A(H1N1) pandemic (2000/1 to 2007/8). In the regression, deaths were defined as deaths following hospitalisations. This provides a more conservative estimate than regressing against all-cause mortality. Table 2.9 presents the expected number of influenza-related deaths per 1,000 hospitalisations.

Table 2.9: Mean estimated annual incidence of influenza-attributable deaths (per 1,000 hospitalisations)

Age	Low risk group	High risk group
0 to 14y	0.43	17
15 to 64y	6.1	40
65+ y	185	428

These incidence rates were applied only to the carer and health and social care worker populations given that the dynamic model estimated mortality in the children and clinical risk group models.

2.3.8 Quality of Life

Patients in the model will experience an impact to their health related quality of life (QoL) due to three different events; a case of flu, influenza-related illness and side effects of the vaccine.

The key outcome measure of this study is the QALY. This measure accounts for the impact to an individual's quality of life and length of life. QALY loss for each event was sourced from the published literature. The model included QALY loss for the following events:

- Non-fatal influenza cases:
  - ILI;
  - ARI,
  - Hospitalisation.
- Fatal cases of flu;
- Side-effect of the vaccine (see section 2.3.6.2).

The values included in the model for non-fatal QALY loss (given in Section 2.3.8.1) are the same for all populations in the model.

The carer model also included the QALY loss to the cared for individual when their care is provided by a temporary carer due to their regular carer being absent from their caring duties due to influenza or when their carer dies from influenza.

More information on each of the QALY loss parameters is provided below.

2.3.8.1 Non-fatal influenza cases

The average QALY loss for the three non-fatal influenza case types included in the model, ILI, ARI and hospitalisation, were taken from the Baguelin *et al.* (2015) cost-effectiveness model [12]. Data specific to each different patient groups were not available, and so all ages and groups were assumed to have the same average QoL weight. Table 2.10 presents the QALY loss per case for each case type.

Baguelin *et al*. [12] derived the value for hospitalisation by taking the QALY loss for ILI cases not requiring hospital treatment from their previously published study [47] and adapted it for hospitalised cases. Their study, Van Hoek *et al.*, reported the QALY loss for ILI cases not requiring hospitalisation as 0.008. The authors then assumed that the QALY loss described for hospitalised cases was 2.17 times greater than the QALY loss for non-hospitalisation cases. This assumption was based on a ratio of QALY loss between hospitalised and uncomplicated influenza cases used in a previous economic evaluation of interventions during the influenza pandemic. This provided a QALY loss of hospitalisation of 0.018.

Table 2.10: QALY loss for non-fatal cases of flu

Event	QALY loss (per case)
Influenza-like illness	0.008 [48]
Acute-respiratory infection	0.00101 [49]
Hospitalisation	0.018

It was noted at the PHAC 3 meeting that a non-fatal case of influenza may result in deterioration in condition of people in a clinical risk group. However, this impact has not been quantified and therefore has not been included within the model. The QALY losses in the base case scenarios were therefore conservative values in this respect. This parameter was therefore included in a sensitivity analysis.

In the carers and health and social care worker models the QALY loss that was applied to secondary cases of ILI was consistent with the QALY loss due to ILI given in Table 2.10. Therefore the assumption that all ages and groups have the same average QoL weight also applies.

2.3.8.2 Fatal influenza cases

Fatal cases of influenza were associated with an average age-specific QALY loss. QALY losses were estimated for a number of discrete age bands and were calculated based on the average life expectancy in the UK and quality of life over the average lifetime. In this analysis, the influenza-related mortality was higher for individuals in a clinical risk group (shown in Section 2.3.7). Therefore, in effect, QALY loss was higher for those in a clinical risk group.

General population utility was obtained from a Department of Health (DoH)-funded Measurement and Valuation of Health survey conducted by the Centre for Health Economics (CHE) in 1993 [50], who estimated quality of life using the generic EQ-5D instrument. This is the most recent UK-based population study, based on 3,395 adult respondents. For those under 18 years of age in the model, it was assumed that the utility for was equivalent to the youngest age band in the CHE study.

Table 2.11: General population utility weights

Age band	Utility weight
Under 18	0.94
18 - 25	0.94
25 to 34	0.93
35 to 44	0.91
45 to 54	0.85
55 to 64	0.80
65 to 74	0.78
75+	0.73

The utility weights in Table 2.11 were combined with the average survival of the population as set out by UK Life Tables (ONS, 2015) [51] in order to estimate the average QALY loss at each age. Example calculations are provided in Appendix A of this report.

As with non-fatal cases of influenza, quality of life and life expectancy specific for each risk group were not available, and so both low and high risk groups were assumed to have the same average QoL weight.

Lost QALYs as a result of death from influenza was discounted to its present value at a rate of 3.5 % per year, as recommended by NICE [19].

2.3.8.3 QALY loss by cared for individuals (carer model only)

In the base case of the model the QALY loss to the cared for individual when their care is provided by a temporary carer given the absence of their regular carer due to influenza or influenza-related illness or when their carer dies from influenza was assumed to be zero. There was limited published literature available and consideration was given to the issue that by definition only the loss of quality of life related to one's health should be included within the economic model. The impact of this assumption was explored in sensitivity analysis.

2.3.9 Costs and Resource Use

The model includes analysis from multiple perspectives including the NHS and PSS, local authority and the whole of society.

The costs that are considered in the analysis for each of the four populations include:

- Vaccine costs;
- Cost to the NHS of treating vaccine side effects;
- Cost to the NHS of treating cases of flu, ILI and non-respiratory ILI and secondary cases of ILI in the carer and health and social care worker models, including hospitalisation and GP consultations;
- Cost of the intervention to increase vaccination uptake;
- Wider societal costs.

Intervention costs were not included specifically in the threshold analyses due to a lack of a "standard" cost per person for a given intervention. The heterogeneity in trial design of the studies included in the effectiveness review also limited the generalisability of a single cost per intervention. Further detail is provided in Section 2.3.8.5.

The cost to temporarily replace carers and health care workers absent due to influenza or influenza-related illness was included in the carers and health and social care workers models.

Unit costs were obtained from the published literature and from nationally published databases. A summary is provided in Table 2.12. Further detail on each of these costs is provided in the sections below.

Table 2.12: Summary of cost parameters and perspectives

		Perspective		
Cost input	**Cost (base case)**	**NHS and PSS**	**Local Authority**	**Societal**
Vaccine	Adults: £5.96 Children (injection): £5.95 Children (nasal spray): £18	For all children, clinical risk groups, over 65 year olds, carers and health and social care workers employed by the NHS.	Health and social care workers employed by the local authority.	Health and social care workers employed by the private sector or who receive direct payments.
Service payment	£9.80 per vaccine	For over 65 year olds, pregnant women, patients between 6 months and 64 years who are in a clinical risk group and carers.	N/A	N/A
Cost of treating vaccine side-effect	£31	All individuals who experience side-effects	N/A	N/A
Intensive care	£1,113	Included in the calculation of the cost of a secondary case of ILI	N/A	N/A
Hospitalisation	£1,029	All hospitalised cases (children and clinical risk groups) and a proportion of influenza cases (carers and health and social care workers)	N/A	N/A

		Perspective		
Cost input	**Cost (base case)**	**NHS and PSS**	**Local Authority**	**Societal**
GP cost	At surgery: £31 At home: £98 Telephone £22	All GP consultation cases (children and clinical risk groups) and a proportion of ILI and ARI cases (carers and health and social care workers). Also included in the calculation of the cost of a secondary case of ILI	N/A	N/A
Secondary cases of ILI (clinical risk group)	Carer model: £343 Health and social care worker model:£289	All secondary cases of ILI (carers and health and social care workers)	N/A	N/A
Temporary replacement carer	Residential care:£199 per day Hospitalisation: £4,995 per episode	Hospitalisation may be required if provision of care is not available by other means	Local authority provide residential care	N/A
Permanent replacement carer	£16.70 per hour	N/A	Local authority may provide or arrange for provision of Homecare services. Applied when carer dies [52].	N/A
Carer's Allowance	£62.10 per week	N/A	N/A	Applied as a cost saving when carer dies whilst accounting for only 63% of carers being in receipt of Carer's Allowance [26].
Temporary replacement of health and social care worker	£26 per hour	Applied to cases of ILI and non-ILI respiratory illness, 43% employed by NHS	Applied to cases of ILI and non-ILI respiratory illness, 10% provided by /paid for by the local authority	Applied to cases of ILI and non-ILI respiratory illness employed by independent sector
Average lifetime earnings	£660,927	N/A	N/A	Applied as a loss if a child dies from flu
Travel cost to GP	£7.94 per visit	N/A	N/A	Cost applied to GP consultations in the surgery
Travel cost to hospital	£10.03 per visit	N/A	N/A	Cost applied to hospitalisations

		Perspective		
Cost input	**Cost (base case)**	**NHS and PSS**	**Local Authority**	**Societal**
Over the counter medications	£5.09 per episode	N/A	N/A	Cost applied to cases of ILI
Median gross weekly earnings – full-time employment	£539	N/A	N/A	Cost applied to mean time that an adult in full-time work (not carer or HSCW) is absent from work with ILI, and to the mean time that a child is absent from school with ILI (assumes parents take time off work for childcare). Included in the calculation of the average weekly wage for an adult, accounting for employment status
Median gross weekly earnings – part-time employment	£177	N/A	N/A	As above but for part-time employment
Median gross weekly earnings – carer	£110	N/A	N/A	Cost applied to mean time that a carer is absent from work with ILI Included in the calculation of the average weekly wage for carer, accounting for if in part-time employment or unemployed

2.3.9.1 Vaccine costs

Unit costs for a number of vaccines were obtained from the British National Formulary (BNF) [53]. Given that there are a number of different vaccines available, each with a different associated cost and that the recommended vaccine varies between influenza seasons, a weighted average was calculated based on average vaccine usage in the UK. Vaccine usage was estimated from Prescription Cost Analysis (PCA) (where figures were available) [54]. Unit costs and details of each vaccine are provided in Table 2.13.

Adults

Adults are advised to be immunized using the inactivated vaccine administered via intramuscular or intradermal injection. The mean cost of this was estimated as £5.96 per dose (Table 2.13) [53, 54].

There were no PCA data available on the Split Virion and Surface Antigen vaccines (vaccines 1 to 3 in Table 2.13) to allow for an overall weighted average to be calculated, so it was assumed that each of these vaccines was used in equal proportions (i.e. a crude average was taken across the three items).

Children

Children can either receive the vaccine administered via intranasal spray or injection, depending on their age. A weighted average cost of vaccine for children was used in the model calculated based on 90% of children aged 2 to 7 years receiving the nasal spray at a cost of £18 per vaccination and 10% receiving the vaccination by injection at a cost of £5.95 per vaccination.

The cost of an intranasal vaccine was applied to children between the ages of 2 and 7. In the base case of the model, it was assumed that 90% of children in this age group would receive the nasal spray form of the vaccination, based on expert advice from the Committee. This vaccine has an associated cost of £18 per dose. The Enhanced Service (ES) specification [55] recommends that a LAIV is recommended for patients between two years and 18 years (without a valid contra-indication, when an inactivated vaccine would be used). Children under the age of 2, over the age of 7, and a proportion of children between the ages of 2 and 7 were assumed to receive the injection form of the vaccine. The weighted average cost of the injection form of the vaccine was estimated as being £5.95.

A source of uncertainty in the mean cost of vaccination for children is the proportion who will receive the injection form of the vaccine and which will receive the nasal spray. In the base case, it was assumed to be 90%. At-risk children contraindicated for LAIV vaccination were largely referred to their GP for vaccination with quadrivalent inactivated influenza vaccine [31]. Since there is no information on the proportion of children who receive vaccination in each form, this input was varied in a sensitivity analysis (injections are substantially lower in cost, with the intranasal vaccine approximately three times the cost of an injection).

The guidelines for vaccinating children state that the dose should be repeated after at least four weeks in high risk children aged 2 to 9 who are vaccine naïve. The proportion of children who are vaccine-naïve is not known so this has not been explicitly included in the calculations for the estimation of average dose cost. As such, the model will underestimate the vaccine cost, but it is expected that this will have minimal impact since the number in this age range who is in the high risk group is low. The JCVI [56] also acknowledge that a two-dose schedule is likely to make the intervention more complex and challenging to implement and that compliance with the schedule may be poor, and so this was excluded from the base case analysis.

Table 2.13: Vaccine costs

Vaccine	Dose	Units used (1,000s)	Target population	Net price
Inactivated Influenza Vaccine (Split Virion)	Injection (0.25mL prefilled syringe)	NR	Adults, children 9 to 18	£6.29
Inactivated Influenza Vaccine (Split Virion)	Injection (0.5mL prefilled syringe)	NR	Adults, children 9 to 18	£6.59
Inactivated Influenza Vaccine (Surface Antigen)	0.5mL prefilled syringe	NR	Adults, children 9 to 18	£4.15
Agrippal	0.5mL prefilled syringe	83.116	Adults, children 9 to 18	£5.85
Enzira	0.5mL prefilled syringe	244.332	Adults, children 9 to 18	£5.25
Fluvirin	0.5mL prefilled syringe	15.068	Adults, children 9 to 18	£5.55
Imuvac	0.5mL prefilled syringe	1,619.13	Adults, children 9 to 18	£6.59
Influvac Desu	0.5mL prefilled syringe	0.28	Adults, children 9 to 18	£5.22
Optaflu	0.5mL prefilled syringe	9.407	Adults, children 9 to 18	£6.59
Fluarix Tetra	Injection (0.5mL syringe)	237.545	Adults, children 9 to 18	£9.94
Intanza	Injection (9 micrograms, 0.1mL syringe) for intradermal use	1.354	Adults	£9.05
Intanza	Injection (15 micrograms, 0.1mL syringe) for intradermal use	55.985	Adults	£9.05
Fluenz Tetra	Nasal spray (0.2mL nasal applicator)	NR	Children 2 to 9	£18.00

Service payment

Each vaccine (with some exceptions) had an additional service payment of £9.80 per dose. This payment is available to participating general practitioner (GP) practices under the ES Specification for 2016/17.

The ES specification covers patients aged 65 and over, pregnant women, patients between 6 months and 64 years who are in a clinical risk group and carers. Children aged 2, 3 and 4 and those receiving vaccination through their school are not included in the ES specification as these patients are covered by the childhood seasonal influenza vaccination intervention [57].

The cost vaccine delivery (i.e. a GP visit) was not included in the economic analysis, to be consistent with the PHE model used to inform the recommendations made by the JVCI.

2.3.9.2 Direct costs of influenza

2.3.9.2.1 Hospitalisation

Hospitalisation may be required by individuals with more serious complications related to influenza. The unit cost for Lobar, Atypical or Viral Pneumonia, without Interventions, with CC Score 0 to 3, code DZ11V, was used as a proxy for the hospitalisation cost for influenza and other ILI. This was £1,029 [58]. NHS reference costs do not include influenza specifically. This hospitalisation cost was applied to the number of hospitalisations in the model.

The assessment group for a previously published NICE technology assessment report, TA158, [40] used this unit cost in this way to proxy the cost of hospitalisation. The unit costs listed in NHS reference costs give the full cost of the service delivered to the average patient requiring hospitalisation for the given condition. The cost then includes hospital length of stay. To use the proxy cost in the model it was assumed that the length of stay for patients with lobal, atypical or viral pneumonia was equal to that for influenza or influenza-like illness. To capture the uncertainty around this assumption, this input was varied in the sensitivity analysis.

Accident and Emergency (A&E) resource use and associated costs were included in the NICE appraisal document [40]. In the model for this guideline A&E attendance was not explicitly included. Given that NHS reference costs report the average cost for the episode of hospital stay, the A&E costs would be captured in the hospitalisation cost. It was assumed that only those who were hospitalised used hospital-based services.

To determine the resource use, the probability of the model-derived infections resulting in hospitalisation was based on a regression analysis for children and clinical risk groups (specifically an age-specific, and strain and risk specific when available, negative binomial regression model with identity link and intercept) [3]. The study authors analysed weekly laboratory reports for influenza from a number of national databases for the eight years immediately preceding the A(H1N1) pandemic (2000/1 to 2007/8). Table 2.14 presents the expected number of influenza-related hospitalisations per 1,000 infectious cases.

Table 2.14: Mean estimated annual incidence of influenza-attributable hospital admissions (per 1,000)

Age	Low risk group	High risk group
< 6m	3.33	2.27
6m to 4y	1.76	1.53
5 to 14y	0.10	0.56
15 to 44y	0.09	0.42
45 to 64y	0.16	0.74
65+ y	0.46	0.84

To account for uncertainty in the estimated number of the different health outcomes attributable to influenza per year, the estimates from Cromer *et al.* [3] were sampled in the PHE model, using the resulting normal distributions from the regression study rather the mean estimates.

Table 2.15 presents the presents the expected number of influenza-related GP consultations per 1,000 infectious cases as used in the PHE model.

Table 2.15: Mean estimated annual incidence of influenza-attributable GP consultations (per 1,000)

Age	Rate per 1,000
< 6m	73.61
6m to 4y	60.90
5 to 14y	38.75
15 to 44y	18.78
45 to 64y	18.29
65+ y	5.82

For carers and health and social care workers it was estimated that 0.82% of influenza cases would require hospitalisation. This was calculated using data from a Flu Watch cohort study [36]. The midpoint between the maximum estimated hospitalisation rate for PCR-confirmed cases of influenza and maximum estimated hospitalisation rate for those with serological infection was used.

2.3.9.2.2 GP costs

Unit costs for GP consultations were derived from the Personal Social Services Research Unit (PSSRU), Unit costs of Health and Social Care. The cost per patient contact lasting 9.22 minutes in the surgery was £31 without qualification costs [59]. The cost per out of surgery visit lasting 23.4 minutes was given as £95 in 2013, without qualification costs [60]. Given that a more recent cost was not available, this cost from 2013 was inflated to reflect the cost in 2016 using the hospital and community health services (HCHS) index. A cost of £98 was used in the model.

This cost of a GP visit was applied to the number of GP consultations in the model.

In TA158 it was assumed that patients with symptomatic ILI see a GP or attend A&E. In line with TA158, in the model 7% of those with symptomatic ILI were assumed to require a home visit from the GP for all model population. The fraction of GP consultations for ILI attributed by risk group in the PHE model (and so children and clinical risk groups) was based on the risk group prevalence and the relative risk of an ILI consultation in those in any risk group compared to the low-risk population in an internet-based cohort (FluSurvey) [61]. The relative risk for consulting a GP if in a clinical risk group was estimated by Baguelin *et al.* as 1.51 (SD 0.18, normally distributed). GP consultation data were not available by risk group status.

For the carer and health and social care populations the proportion of cases requiring a GP consultation was based on results from the Flu Watch Cohort study [36]. The study gave the proportion of people with ILIs and non-ILI respiratory illnesses resulting in at least one GP consultation for 16 to 44 year olds and 45 to 64 year olds. The reported figures were used to calculate the proportion of 16 to 64 year olds requiring a GP consultation for ILI and non-ILI respiratory illness. These were 20% and 15%, respectively. It was assumed that only one GP visit was required by those requiring a GP consultation.

The figure used for the proportion of people with symptomatic ILI requiring a GP consultation at home may be considered an overestimation as it is reported for adults aged below 75 years whilst the carers and health and social care workers would likely be below retirement age.

2.3.9.2.3 Temporary replacement care and staffing costs

Given the type of work that carers and health and social care workers do, it is likely that when a carer or health and social care worker is absent from their caring duties or work, respectively, they are replaced so that patient care continues.

The FluSurvey reports that those reporting any flu-like symptoms were absent from work for 2.5 days [62] and so this duration of absence was applied in the calculations for the cost of the temporary replacement of a carer or health and social care worker.

2.3.9.2.3.1 Temporary replacement of carers

Following discussion at the committee meeting it was established that provision of emergency residential care or hospitalisation may be required for an individual who usually receives care from a carer. In the base case, it was assumed that 1% of the cared for individuals would require residential care provided by the local authorities and 1% of individuals would require hospitalisation.

In the model, the cost of a temporary replacement carer dependent on the type of care received. The cost of residential care for adults requiring physical support is given in the PSSRU as £834 per week [59] and is provided by the local authorities. The cost of hospital admission for emergency care for a person with Alzheimer's was used in the model base case for the cared for individuals requiring hospitalisation in the absence of their carer. This was £4,995 as given in the NHS reference costs [58].

It is important to note that the perspective which was taken for the analysis impacts on the costs that are included in the results. The cost of temporary care provided by through hospitalisation of the individual was included under the NHS and PSS and societal perspectives. The cost of temporary care within a residential facility was included under the Local Authority and societal perspectives.

2.3.9.2.3.2 Temporary replacement of health and social care workers

The cost of temporarily replacing a health and social care worker was included in the model as the weighted average hourly pay rate by job role for a health and social care worker. This was calculated as £26 per hour. It was assumed that health and social care workers work 7.5 hours per day. This cost was applied for the duration of the health and social care workers absence from work, 2.5 days or 18.75 hours, as detailed in Section 2.3.9.4.1.

The cost of temporarily replacing a health and social care worker was calculated using the hourly pay rate for each job role included in the population being considered (given in Table 2.3). The hourly cost for health care workers was taken from the PSSRU [63] and for social care workers from a report by Skills for Care [64]. However, given the possibility that agency staff may be used to replace absent staff or that absent staff are not replaced at all, sensitivity analysis was conducted around this input.

This cost was applied in each perspective based on the proportion of health and social care workers employed by each sector, as detailed in Section 2.3.2.4.

2.3.9.2.4 Permanent replacement carer costs

The cost of replacing a carer who dies from influenza or influenza-related illness was included in the model given the requirement for an extended duration of care and the likelihood of this needing to become a formal arrangement. This was included in the analysis taken from a Local Authority and societal perspective given that the permanent care would be provided by the Local Authorities. The cost of permanent replacement care was included as the cost of Homecare, costing £16.70 per hour. It was assumed that the carers provide 35 hours of care per week given that this is the minimum number of hours of care that must be provided for the carer to receive Carer's Allowance [65]. It was assumed that a permanent replacement carer would be required for the duration of 10 years in the base case. The cost of permanent replacement care was discounted at an annual rate of 3.5%.

The United Kingdom Homecare Association report that the minimum price for homecare services is £16.70 per hour if carers are paid minimum wage or national living wage and that whilst homecare is provided by the independent and voluntary sector, their services are purchased by primarily local authorities [66]. In the model this cost was applied to the number of hours of care provided. To receive Carer's Allowance the carer must provide a minimum of 35 hours caring for someone and this figure was used in the base case analysis [65]. Given that Carer's Allowance (£62.10) would no longer be paid to carers who had died, this was accounted for in the model.

2.3.9.3 Cost per secondary case of ILI (carers and health and social care workers models)

The cost of a secondary case of ILI was £343 in the carers model and £289 in the health and social care workers model. It was assumed that all secondary cases were in a clinical risk group. This cost was applied to all secondary cases of ILI.

In the base case 30% of those who are cared for are under 65 years and the remainder are over 65 years of age. A report published by the King's Fund reported that, in 2000, 30% of care recipients were under 65 years of age and 70% were 65 years and over [35]. In the health and social care worker model it was assumed that half of the secondary cases were under 65 yeas whilst the remainder were over 65 years old. These assumptions were explored in sensitivity analyses.

The cost per secondary case of ILI was calculated using data on individuals who are in a clinical risk group. These values were taken from an economic evaluation by Baguelin *et al*. [20] who report in their economic evaluation the proportion of ILI cases in a clinical risk group that require contact with a GP, hospitalisation or admission in an intensive care unit. Table 2.16 gives the values reported by Baguelin *et al.* and the calculated gross average that was used in the model. The cost of each outcome was taken from national sources (given in Table 2.12) [20, 26, 67].

Table 2.16: Resource use and costs elements used to calculate the cost of a secondary case of ILI

	Proportion of ILI cases in a clinical risk group	
	Adults <65 years old	**65+ years old**
GP visit	13%	21%
GP phone consultation	36%	22%
Hospitalisation	6%	32%
Intensive care	7%	

2.3.9.4 Societal costs

To conduct the analysis from the societal perspective, the costs of managing influenza included productivity loss as absenteeism costs related to influenza and influenza-related complications for adults aged 16 to 64 years and absenteeism of parents whose child is sick in addition to the costs to the NHS and PSS and the Local Authorities. Lifetime future earnings in case of premature mortality, over-the-counter medication costs and transportation costs related to travel to the GP and hospital were also included. Each is described separately in the following sub-sections.

2.3.9.4.1 Productivity loss

The cost of lost productivity was included in the models for working-age adults who have absence from work due to suffering from influenza or complications associated with influenza and for parents who have had absence from work due to their child suffering from influenza or related complications. The cost of absenteeism from work was calculated by multiplying the average daily wage by the number of days lost. Productivity loss due to premature death was also partially accounted for in the models. Productivity losses were included in the analyses conducted from a societal perspective only.

In the model the average wage for adults was £420. The Office for National Statistics (ONS) reported that in April 2016 the median gross weekly earnings was £539 for full-time employees and £177 for part-time employees. The ONS also report the number of adults in full-time, part-time and no employment. This was used to determine the proportion of those within each type of employment, 70% full-time, 26% part-time and 5% unemployed. These employment rates were then used to calculate the average wage.

In the model the average wage for carers was £72.90. This was based on 66% of carers being in paid employment which was assumed to be part-time with a weekly earning of £110.

The weekly earnings of carers was assumed to be £110 as this is the maximum that a carer can earn whilst also receiving Carer's allowance [65]. This average wage for carer's was applied to all carers who required time off their caring duties and so also assumed to require absence from paid employment. However, not all carers receive Carer's Allowance and so this assumption may not fully represent the productivity loss in the total carer population. Furthermore, given that some carers may have been absent from their caring duties but not from their paid employment, this would mean that the productivity loss would be lower than estimated. It was assumed that carers who are employed are in part-time employment. This is because there is an earning's cap within the eligibility criteria for the Carer's Allowance. The 2001 census reported that 66% of carers of working age were in paid employment.

As health and social care workers were assumed to be replaced when they were temporarily absent from work due to influenza-related event (described in Section 2.3.9.2.3.2) the productivity loss to society was zero.

The results from the FluSurvey for the 2015 to 2016 season reported that, on average, those reporting any flu-like symptoms were absent from work for 2.5 days [62]. A study investigating the social and economic impacts of school influenza outbreaks reported that the mean school absence for a child reporting ILI was 3.7 days [68]. In the model, where a child with ILI is absent from school it is assumed that their parent would be off work for the full duration of their child's absence and so the productivity loss is calculated for 3.7 days. However, when an adult had ILI, their productivity loss was calculated based on an absence from work for 2.5 days. The number of days of absence for both children and adults was explored in sensitivity analyses. It was also assumed that people aged over the age of 65 did not incur any productivity losses.

The complications of influenza can result in premature death. The dynamic model did not report the number of hospitalisations, and therefore deaths (number of deaths was dependent of those hospitalised), by age group. Therefore, in the children and clinical risk group models the productivity loss for the premature death of employed adults was not included in the analyses. This would result in an underestimation of the productivity loss in the model results from a societal perspective.

In the model for children and children in a clinical risk group productivity loss of child who had a premature death was included in the model as loss of a future earnings. A report produced by the Department for Business Innovation and Skills [69] reported discounted future earnings in 2013. The NPV of life time earnings with varying employment over the lifecycle and including dropouts was £575,000 for non-graduate males and £774,000 for graduate males. For females, these figures were £450,000 and £727,000, respectively. The gross average was calculated and used in the model. The average lifetime earnings at net present value was £631,500 (2013 £). This estimate was inflated to 2016 values using the Consumer Pricing Index (£660,927).

In the carer model the productivity loss for the premature death of employed carers was not included in the analyses. This would result in an underestimation of the productivity loss in the model results from a societal perspective.

2.3.9.4.2 Travel costs

Individuals who attend a GP appointment or require hospitalisation due to influenza or influenza-like illness had the cost of travel applied as an out-of-pocket expense.

A recently published study investigating the cost-utility of influenza vaccination in Germany reported the transportation costs of medical advice visits and hospitalisation [70]. These were provided as 9.07 Euros and 11.47 Euros respectively for all ages and risk groups, reported as 2014 prices. These costs have been converted to British pounds [71] and inflated to 2016 prices using the UK consumer price index [72, 73]. In the models, transportation costs related to GP visits was given as £7.94 and transportation costs related to hospitalisation are £10.03 for all ages and risk groups.

It was assumed that these costs were for a return journey and these costs were applied to the number of GP consultations requiring travel to the GP surgery (i.e. excluding home visits) and the number of hospitalisations.

2.3.9.4.3 Over-the-counter medications

The recently published cost-utility study from Germany (introduced in Section 2.3.8.3.2) also reported the average over-the-counter medication costs. This was stated as 5.74 Euros (2014 price). For the model, this cost was converted to British Pounds [71] and inflated to 2016 price using the UK Consumer Price Index [72, 73]. The cost for over-the-counter medications used in the model is £5.09 for all ages and risk groups.

The cost of over-the-counter medications was applied to 100% of ILI cases in the base case analyses.

2.3.9.5 Vaccine side effects

The cost of a GP visit was applied to a proportion of those experiencing a vaccine-related adverse event. Section 2.3.5 provides further details on this assumption.

2.3.9.6 Intervention costs

Intervention costs were not explicitly included in the models for children and clinical risk groups. This was due to the data around intervention costs being scarce and the data that is available may not be applicable to all interventions. Threshold analysis was conducted so that the results of the analysis can be used as guidance to allow the Committee to consider whether the maximum additional cost of the intervention for it to be considered cost-effective is reasonable.

Table 2.17 provides details on the cost of some relevant public health interventions. These may be useful in guiding the Committee's discussion around possible intervention costs appropriate for increasing influenza vaccination uptake. Discussion by the Committee at the PHAC 3 meeting highlighted that some interventions would be zero cost, for example, a GP may have a higher propensity to promote influenza vaccination when an individual is attending a non-influenza related GP appointment but subsequently receives the influenza vaccination.

A systematic review published by Cochrane [74] searched for intervention costs within their evidence review for interventions aimed at improving immunization rates. The review found fifteen studies that reported basic cost data, but noted that costs varied widely across studies and that the cost information would be of limited use. This was due to a number of factors, including variability in methods of calculating costs and items included in analyses, different study time periods and different levels of intensity of interventions (from single postcard reminders to repeated reminders plus home visits). Telephone reminders were found to be more costly than letter or postcard reminders (no specific costs were reported in the study but the limitations associated with the evidence were considered to be noteworthy for inclusion in this report).

The PHAC were asked to provide any relevant unpublished data containing cost information which they were aware of. This has been included in Table 2.17 below.

Table 2.17: Intervention costs

Intervention	Total cost	Notes	Source
A ten-minute opportunistic brief advice session	£36 for a GP £8 for a practice nurse	This cost was for smoking cessation but may be considered applicable to interventions delivered in primary care (e.g. education, promotion)	Public health interventions. PSSRU, 2016 [59]
SMS	Text messaging system configuration programming $7,000. $270 per week of messaging ongoing cost. Messaging costs for the entire study were an estimated $165.	Cost-effectiveness analysis of a text messaging intervention implemented in the US during the 2010 to 2011 influenza season Configuration was 160 hours. An additional 6 hours per week were used for preparation and monitoring.	Stockwell *et al.* 2012 [75]
Mass media campaigns	Between £0.30 and £2.06 per person.	The cost was provided for a smoking cessation campaign but may also be applicable to the promotion of vaccination. Estimates of cost are higher when the unit receiving the intervention is defined as those potentially exposed to the campaign (£26-£49).	PSSRU, 2016. Table 7.4 [59]
Community pharmacy-based vaccination intervention	A pharmacy-administered influenza vaccine dose costs the NHS up to £2.35 less than a dose administered at a GP	The cost to implement the pharmacy system (Sonar) was associated with a cost of £0.29 per dose (£0.11 for development and £0.18 for service fees). In pharmacies, the cost of the vaccine was lower and had no associated dispensing fees.	Atkins *et al.* 2015 [76]
Text messaging and mass media	Cost of tailored messages: £4.67 per person Cost of mass media intervention: £0.09 Cost of text messaging £0.045* per text based on bulk text messaging price (does not include cost of writing message, intervention to send message, or cost of setting up the database)	The study focused on interventions to improve exposure to sunlight, but the costs may be applicable to the promotion of vaccination.	Clinical guideline for sunlight NG34 [77]
Clinical reminders	Physician sees and resolves clinical reminder $0.71 ($0.5 to 0.89) Nurse sees and resolves clinical reminder $0.28 ($0.21 to 0.35)	The study assessed the costs of a reminder system for HIV testing in the US, but the costs may be applicable to the promotion of vaccination. Data was collected from 2004 to 2011.	Chan *et al.* 2014 [78]

Intervention	Total cost	Notes	Source
Funds to support promotion by Local Authorities	£70,000	NHS Cheshire & Merseyside provided £10,000 to each of its Local Authorities to support promotion of influenza vaccination.	Provided by communication between NICE and NHS England, Neil Gaye
Pilot of drug and alcohol services	£10,000	NHS Cheshire & Merseyside asked all providers of drug and alcohol services to vaccine people who they provided support to. Those receiving support would often have an underlying condition that made them eligible for vaccination. Felt that a better channel than using GP invitation or signposting.	Provided by communication between NICE and NHS England, Neil Gaye
Support for maternity providers	£12,290	Five year plan by NHSE Cheshire and Merseyside aimed to improve the quality of local service delivery/methods, to reduce unwarranted variation in the local maternal immunisation offer, to shape local services in line with the national maternity review, to achieve high coverage rates and to achieve best value for money and sustainable service delivery models.	Provided by communication between NICE and NHS England, Neil Gaye
Support for GPs to deliver to housebound	£15,000	NHS Cheshire and Merseyside funded GPs buying portable vaccine storage and pump primed Sefton being able to vaccinate the housebound.	Provided by communication between NICE and NHS England, Neil Gaye
Sending letters to patients	42p (+ VAT) per one-side A4 letter. Includes printing and posting	Information about the study into strategies to increase influenza vaccination in GP practices but only one cost provided. Report highlights that a service is available (and used by an increasing number of GP practices) which prints and posts letters on the practice's behalf.	Work conducted in collaboration with Warwickshire County Council and Coventry City Council. Provided by communication between NICE and Katie Newby
Contacting low performing GP practices offering support and advice to improve vaccination uptake	Approximately £12,000 (30% of 1.4wte Band 7 for 3 months)	Nurses contacted the GP practices with the highest rates of uptake in 2-3 year old children. Ideas that were collected were sent to all GP practices in the region. Practices with low uptake rates were contacted by telephone and received support and advice.	Oxford AHSN Children's Network. Provided by communication between NICE and Tim Gustafson

Intervention	Total cost	Notes	Source
		Resources used staff time, telephone calls, email, production of the best practice tips and website design.	
Focussed work on one CCG with low vaccine uptake	Approximately £2,400. £300 per visit to each centre (10% of 1.4wte Band 7 for 2 months)	Nurses undertook promotional work in Children's centres. Parents were offered educational materials in a variety of languages. Vaccine demonstrators were displayed and a promotional film shown.	Oxford AHSN Children's Network. Provided by communication between NICE and Tim Gustafson
Improving awareness of effects of flu and the flu vaccine amongst children	Approximately £2,000 (20% of 0.6 wte Band 7 for 5 months)	Primary school children in years 1 and 2 were invited to enter a poster competition. 800+ schools were contacted by email and competition posted on the AHSN website. 12 top entries made in to a calendar and distributed to local and national flu stakeholders. Resources used staff time, travel costs, telephone calls, email, promotional materials, and website design.	Oxford AHSN Children's Network. Provided by communication between NICE and Tim Gustafson
Development of flu information webpages	£1,500 for set up and further £800 for redevelopment	Oxford AHSN Children's Network flu webpages were developed as a 'one-stop shop' of key information and resources needed by different groups with an interest in children's flu. Resources used staffing time and web design.	Oxford AHSN Children's Network. Provided by communication between NICE and Tim Gustafson

* *Cost updated based on reference provided in NG34*

2.4 COST-EFFECTIVENESS ANALYSIS

2.4.1 Modelling Outputs

The model was designed to report the following types of outcomes:

- Total costs for the population and cost per patient, for each scenario;
- Total QALYs for the population and per patient, for each scenario;
- Total number of events (cases, ILI, ARI, deaths, GP consultations, hospitalisations and secondary cases of ILI) for the cohort;
- Disaggregated results for costs and QALYs by type;
- Scenario analysis, sensitivity analysis and threshold analysis;
- Cost per averted case of influenza;

- Cost per uptake of an influenza vaccination;
- Net monetary benefit.

The net monetary benefit (NMB) was calculated using a threshold of £20,000 per QALY. A negative net monetary benefit indicates that the intervention that changes vaccination uptake by the level for the specified scenario (i.e. increase by 10% from baseline for scenario 3 for carers) is not cost-effective. The net monetary benefit of a scenario represents the maximum willingness to pay for the intervention per targeted person.

The cost per averted case of influenza was calculated using the total incremental cost for the whole population and the total incremental cases of influenza.

The cost per uptake of vaccine was calculated using the total incremental cost for the whole population and the number of the targeted population vaccinated.

2.4.2 Scenarios

2.4.2.1 Children and clinical risk groups

The cost-effectiveness analysis of interventions targeting children and patients clinical risk groups took a threshold analysis approach. This involved running a range of scenarios based around different potential vaccine uptake rates rather than incorporating evidence on how specific interventions improve uptake.

Table 2.18 presents the scenarios that were undertaken:

- Scenario 1 represented the baseline scenario, defined by current coverage levels described in Section 2.3.3;
- Scenarios 2 to 6 explored the impact of interventions to increase vaccination uptake in adults in clinical risk groups;
- Scenarios 7 to 11 focused on pregnant women (increasing uptake in both low risk and high risk women simultaneously, since these groups aren't targeted separately);
- Scenarios 12 to 15 focused on all children (increasing uptake in both low risk and high risk children simultaneously);
- Scenarios 16 to 19 focused on children in clinical risk groups;
- Scenario 20 focused on children not in a clinical risk group.

Table 2.18: Scenarios for threshold analysis in children and clinical risk groups

Scenario	Adults clinical risk	Pregnant women		Children	
		Low risk	High risk	Low risk	High risk
1 (baseline)	47.7%	40.6%	56.0%	See Table 2.6	See Table 2.6
2	Baseline -5% (40.7%)	Baseline	Baseline	Baseline	Baseline
3	Baseline +5% (50.7%)	Baseline	Baseline	Baseline	Baseline
4	Baseline +15% (60.7%)	Baseline	Baseline	Baseline	Baseline
5	Baseline +30% (75.7%)	Baseline	Baseline	Baseline	Baseline
6	Baseline +40% (85.7)	Baseline	Baseline	Baseline	Baseline
7	Baseline	-5% (35.6%)	-5% (51.0%)	Baseline	Baseline
8	Baseline	+5% (45.6%)	+5% (61.0%)	Baseline	Baseline
9	Baseline	+15% (55.6)	+15% (71.0%)	Baseline	Baseline
10	Baseline	+25% (65.6%)	+25% (81.0%)	Baseline	Baseline
11	Baseline	+35% (75.6%)	+35% (91.0%)	Baseline	Baseline
12	Baseline	Baseline	Baseline	Baseline -5%	Baseline -5%
13	Baseline	Baseline	Baseline	Baseline +10%	Baseline +10%
14	Baseline	Baseline	Baseline	Baseline +25%	Baseline +25%
15	Baseline	Baseline	Baseline	Baseline +35%	Baseline +35%
16	Baseline	Baseline	Baseline	Baseline	Baseline -5%
17	Baseline	Baseline	Baseline	Baseline	Baseline +10%
18	Baseline	Baseline	Baseline	Baseline	Baseline +25%
19	Baseline	Baseline	Baseline	Baseline	Baseline +35%
20	Baseline	Baseline	Baseline	Baseline +10%	Baseline

The coverage levels in each of the scenarios were determined by adding (or subtracting) a set number of percentage points to the baseline coverage rate in the targeted population. The meaningful measureable difference was noted as being 5% at an early PHAC meeting, however, given that there was a limit to the number of scenarios able to be run in the PHE dynamic model, wider intervals between uptake levels were modelled. Where there is evidence for a specific intervention that falls within a modelled interval, the total costs and QALYs for that intervention were interpolated via a range of techniques (linear and non-linear interpolation) so that a more precise estimate could be calculated. The most appropriate means of interpolation was explored (results presented in Section 3).

The uptake level upper limit for each patient group was determined by the national targets for vaccine coverage, to allow the PHAC to determine whether an intervention that has the evidence to support whether these levels can be achieved is cost-effective. The aspirational target for vaccine coverage in 2015 to 2016 is to reach or exceed 75% uptake for people aged 65 years and over as recommended by the World Health Organization (WHO). For children, an approximate 30% coverage is said to reduce transmission significantly. Some scenarios modelled coverage slightly under the current levels in order to assess relative impact of interventions in areas with below-average coverage.

2.4.2.2 Carers and health and social care workers

The cost-effectiveness analysis of interventions targeting carers and health and social care workers also took a scenario analysis approach for the preliminary analysis.

Table 2.19 outlines the scenarios run for the carer and health and social care worker populations.

Table 2.19: Scenarios for threshold analysis carers and health and social care workers

Scenario	Carers	Health and social care workers
1 (baseline)	37.4%	50.6%
2	Baseline -5%	Baseline -5%
3	Baseline +10%	Baseline +10%
4	Baseline +25%	Baseline +25%
5	Baseline +35%	Baseline +35%
6	Uptake is 100%	Uptake is 100%

2.4.3 Sensitivity Analysis

Deterministic sensitivity analysis

Univariate sensitivity analyses were performed to examine the effect of changes in key model parameters. Deterministic sensitivity analysis (DSA) was performed where each parameter was varied according to the measure of dispersion (95% confidence intervals and standard deviations where applicable). All parameters considered to have sufficient uncertainty in their expected value were varied in order to identify the greatest causes of uncertainty in the model. Where confidence intervals were unavailable, the standard deviation was assumed to be 20% of the mean.

The sensitivity analyses that will be undertaken in the cost-effectiveness models are described in Appendix C. Certain parameters, such as those used to model disease transmission were varied explicitly in the carer and health and social worker models by varying the relevant parameters directly. In the children and clinical risk group models, these parameters were varied implicitly, where the intermediate outcome (the output of the PHE models, for example, the number of cases of ILI, GP consultations) was varied.

Probabilistic sensitivity analysis

Probabilistic sensitivity analysis (PSA) was included in the cost-effectiveness models to take account of the simultaneous effect of uncertainty relating to model parameter values. This allowed the uncertainty in the results to be quantified and the likely range of values that the results of the models may take to be estimated. Appendix C reports the parameters included in the PSA, and the assumptions around variation.

Parameters in the PHE model, such as whether or not the vaccine was well-matched to the circulating strain of the influenza virus, were varied stochastically due to the dynamic nature of the model. The model for children and clinical risk groups incorporated the output of the PHE model, which included 1,000 iterations for each specific outcome (cases, ILI, ARI, *etc*). This allowed for the parameter uncertainty to be represented for each outcome, as estimated by the sample standard error, which implicitly captured the variation in the PHE model inputs. Appendix C provides information on which parameters were explicitly varied in each population model.

The model was run for 1,000 simulations to generate total costs and QALYs for each scenario by varying event rates, costs, risks and utilities and population characteristics simultaneously. Parameters were all varied independently. The PSA was run for a large number of iterations to estimate when the results converged and to determine an appropriate number of iterations to use for the analysis. A chart plotting the cumulative was visually inspected to determine at which point the results converged. This was after approximately 1,000 iterations. Figures 2.5 and 2.6 show the variance over a number of iterations to determine where the mean outcome stabilised.

Figure 2.5: PSA stabilisation graph for incremental costs per targeted population member

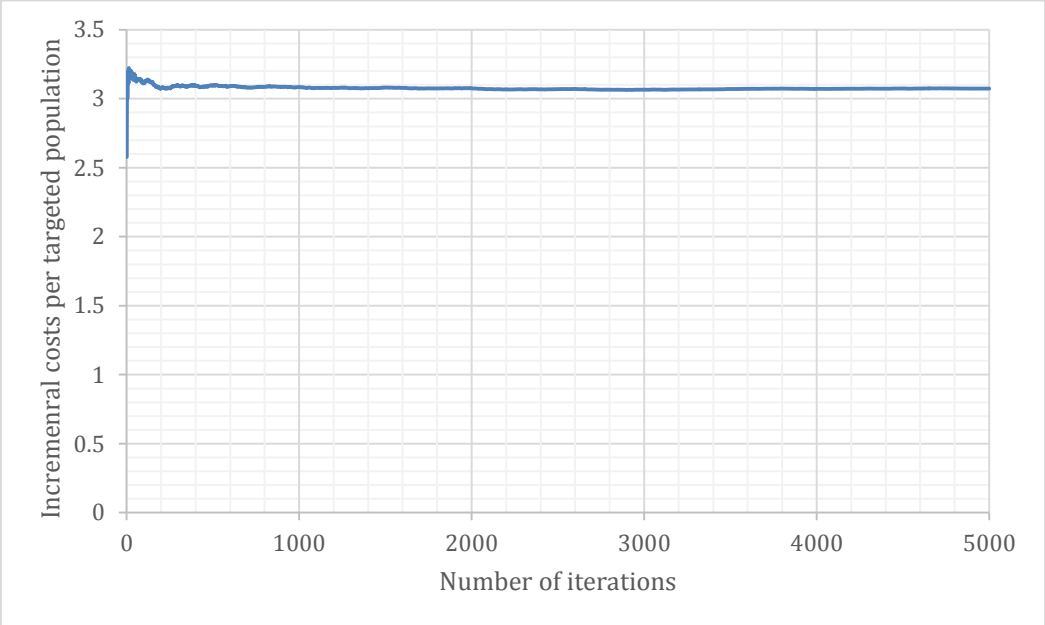
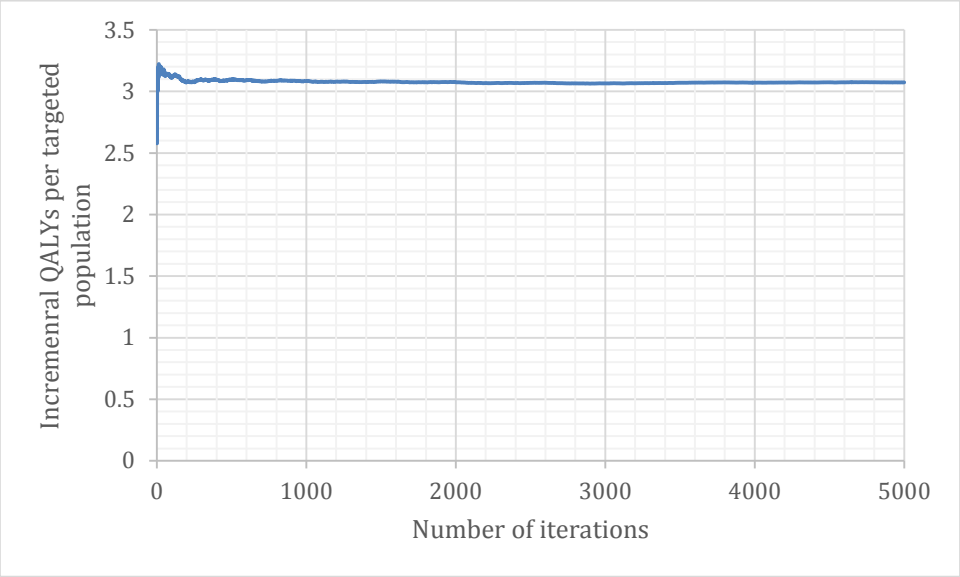


Figure 2.6: PSA stabilisation graph for incremental QALYs per targeted population member



A number of probability distributions were employed including the beta, Dirichlet, lognormal and gamma distributions.

Probabilities, such as event probabilities of dichotomous outcomes, were sampled from a beta distribution. This distribution is bounded by 0 and 1. The parameterisation consists of denoting the shape parameter (i.e. alpha) as the number of events and the scale parameter (i.e. beta) as the number of non-events. Patient numbers obtained from the trials or from published estimates were used to represent this source of variation. Where possible, alpha and beta was estimated by calculating the mean alpha (number of events), and the mean beta (number of non-events) over the season or trial period. Standard errors around the point estimate were taken from the published literature or assumed to be 20% of the point estimate. The values of alpha (α) and beta (β) used to parameterize the distribution were calculated from the mean (μ) and standard error of the utility value, using the following equations:

$$\alpha = \frac{1-\mu}{\left(\frac{s}{\mu}\right)2} - \mu \qquad \beta = \frac{\alpha}{\mu} - \alpha$$

The Dirichlet distribution was used to sample inputs pertaining to the distribution of patients amongst a number of different occurrences, such as employment status. The Dirichlet distribution is a multivariate generalization of the beta distribution, and a series of conditional beta distributions was utilised [79] which involves the decomposition of a multi-branch node into a series of conditional dichotomous nodes.

Number of days ill and QALY losses were assumed to be distributed according to a lognormal distribution. Confidence intervals around these parameters were estimated on the log-scale, and the logarithm of the risk was assumed to be normally distributed. The standard error around the RRs was estimated from the reported 95% confidence intervals, by taking the natural logarithms of the upper and lower limit, and dividing the width of the adjusted interval by 1.96*2 [79].

Costs were sampled from a gamma distribution, since this distribution has a lower bound of 0 and therefore avoids the generation of any negative costs. The distribution can be highly skewed to reflect the natural skew in costs. Standard deviations were used along with the mean to obtain the shape and scale parameters of the gamma distribution. Standard errors around the point estimate were taken from the published literature, and where data wasn't reported, a 20% standard error around the mean value was assumed. The values of alpha (α) and beta (β) used to parameterize the distribution were calculated from the mean (μ) and standard error (s) of the value, using the following equations:

$$\alpha = \mu^2 - s^2 \qquad \beta = \frac{s^2}{\mu}$$

Section 3: Results

3.1 CHILDREN

Table 3.1 presents a summary of the different scenarios evaluated in the children subanalysis. Table 3.2 gives the baseline coverage for low and high risk children.

Table 3.1: Summary of scenarios

Scenario	Impact on uptake
Scenario 1	Baseline (no impact on uptake)
Scenario 12	Uptake by all children is 5% lower than the baseline rate
Scenario 13	Uptake by all children is 10% higher than the baseline rate
Scenario 14	Uptake by all children is 25% higher than the baseline rate
Scenario 15	Uptake by all children is 35% higher than the baseline rate
Scenario 20	Uptake by low-risk children is 10% higher than the baseline rate

Please note that interventions increasing the uptake of vaccination on high-risk children only are discussed in Section 3.2.

Table 3.2 Baseline coverage for low and high risk children

Age	<2	2	3	4	5	6	7	8	9	10	11-15
Low risk	0.0%	35.0%	37.0%	21.1%	54.4%	52.9%	57.2%	56.2%	56.0%	54.7%	0.0%
High risk	18.6%	48.3%	52.3%	47.3%	39.2%	39.2%	39.2%	39.2%	39.2%	39.2%	39.2%

3.1.1 Base case analysis

Scenario 15 was associated with the highest increase in vaccination uptake and, therefore, the lowest number of cases of influenza and related events in the population. As expected, targeting low-risk children had a similar effect to targeting all children (given the low rate of complications in this age group, the size of the low risk population is similar to that of all children).

Results are based on the whole of England population of 54,786,327 individuals (for population breakdown by age, see Appendix B). Note that the whole population was assessed (rather than just children) as the impact on vaccinating children was expected to impact on the transmission of influenza in other age groups as well as other children who were not vaccinated. A breakdown of the total number of events, costs and QALYs for each scenario are given in Appendix D1 to D3 respectively.

Table 3.3 presents the cost-effectiveness results for each scenario compared with the baseline scenario. These costs do not include the cost of an intervention, and so the true cost-effectiveness result for a given intervention will be higher than that reported in the table. The net benefit of a scenario represents the maximum willingness to pay for the intervention per targeted child. Net benefit was calculated using a threshold of £20,000 per QALY.

Higher levels of vaccination uptake are associated with higher estimates of net benefit, and higher cost per averted case of influenza and cost per uptake of vaccine.

Table 3.3: Cost-effectiveness results for each scenario

Scenario	ICER	Net benefit*	Cost per averted case of influenza	Cost per uptake of vaccine
Scenario 1	-	-	-	-
Scenario 12	Intervention less effective	-£2.12	Intervention does not avert cases of flu	Intervention does not increase uptake of vaccination
Scenario 13	£2,645.41	£5.50	£9.94	£9.57
Scenario 14	£3,226.10	£11.48	£12.13	£10.09
Scenario 15	£3,654.57	£14.25	£13.75	£10.40
Scenario 20	£2,327.28	£4.96	£8.73	£8.46

* Net monetary benefit (NMB) was calculated using a threshold of £20,000 per QALY.

** Note that these results do not include intervention costs. Results are from NHS and PSS perspective.

The link between model outcomes (total costs, total QALYs and net benefit) and uptake rate in scenarios 12 to 15 was assessed by interpolating between values. This may allow the costs at uptake rates to be predicted between these thresholds.

It appears from a visual inspection of the charts that the relationship between uptake rate and total population costs and QALYs is relatively linear. However, this assessment is based on a limited number of data points. It might be possible that the relationship is non-linear at higher uptakes, but it is not possible to say without undertaking these additional analyses. While the linear interpolation could be considered a justifiable fit for the net benefit, the second order polynomial curve appeared to fit better (with a higher R squared value). Figure 3.1 presents the interpolation of each outcome with uptake rate.

Figure 3.1: Interpolation of results for children

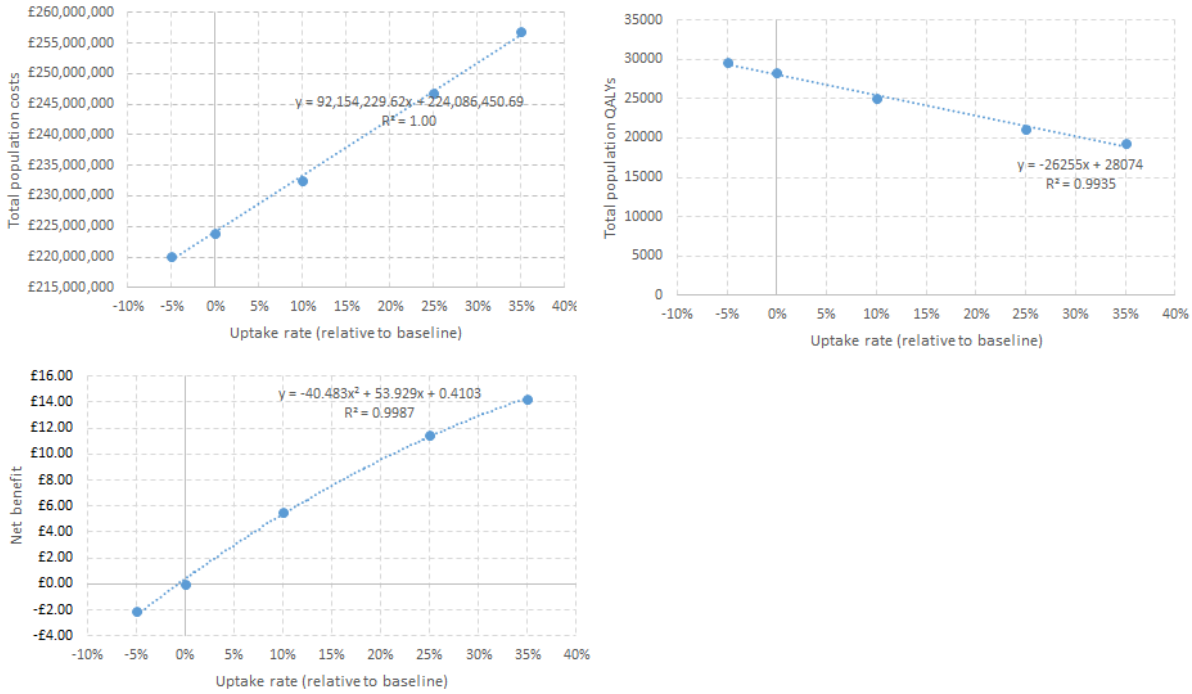


Table 3.4 presents the interpolated outcomes for uptake rates between those which have been modelled. Net benefit was calculated using a threshold of £20,000 per QALY. Extrapolated values for uptake rates beyond the range of those that have been modelled should be interpreted with caution, since it is not possible to determine the nature of the relationship between uptake rate and outcome beyond that which has been modelled.

Table 3.4: Interpolated values for different uptake rates

Uptake rate	Total population cost	Total population QALYs	Net benefit**
-10%	£214,871,028	30,700	-£5.39
-5%*	£219,478,739	29,387	-£2.39
0%*	£224,086,451	28,074	£0.41
5%	£228,694,162	26,761	£3.01
10%*	£233,301,874	25,449	£5.40
15%	£237,909,585	24,136	£7.59
20%	£242,517,297	22,823	£9.58
25%*	£247,125,008	21,510	£11.36
30%	£251,732,720	20,198	£12.95
35%*	£256,340,431	18,885	£14.33
40%	£260,948,143	17,572	£15.50
45%	£265,555,854	16,259	£16.48
50%	£270,163,566	14,947	£17.25

* Table gives values according to the line of best fit (i.e. interpolated values)

** Compared to baseline and based on a cost-effectiveness threshold of £20,000 per QALY gained

Table 3.5 presents the maximum willingness to pay for the intervention at which an intervention is cost-effective at a threshold of £20,000 per QALY, as coverage changes from one level to another. Coverage level is presented as relative to baseline coverage from the NHS and PSS perspective.

Table 3.5: Maximum willingness to pay for the intervention: Children

		Coverage level with intervention				
		-5%	**Baseline**	**10%**	**25%**	**35%**
Coverage level without intervention	-5%	No change	£2.12	£7.61	£13.60	£16.37
	Baseline	No benefit	No change	£5.50	£11.48	£14.25
	10%	No benefit	No benefit	No change	£5.98	£8.76
	25%	No benefit	No benefit	No benefit	No change	£2.77
	35%	No benefit	No benefit	No benefit	No benefit	No change

Interventions are associated with a higher maximum willingness to pay for the intervention if the intervention is associated with a greater increase in uptake. For example, moving from -5% below baseline coverage to 35% above baseline coverage (an absolute change of 40% percentage points) is associated with the highest maximum willingness to pay per child, of £16.37. The maximum willingness to pay is not linear, that is, the maximum willingness to pay is dependent on the uptake before the intervention is introduced. The results shown in Table 3.5 imply that increasing uptake at lower coverage rates is more cost-effective than increasing uptake at higher coverage rates, where the group approaches herd immunity.

3.1.2 Sensitivity Analysis

3.1.2.1 Deterministic sensitivity analysis

A range of parameters were evaluated and their impact on the results assessed (for a full list, see Section 2.4.3). The tornado diagram for each scenario compared with the baseline scenario is provided in Appendix G. Each tornado diagram presents the impact on the maximum intervention cost per targeted population member. In the analysis where vaccine uptake is increased by 5%, varying the parameters does not result in the net benefit to be below £0, indicating that the results are robust to the parameter inputs and their associated range of values.

The parameters that had the biggest impact on the results of the analysis were as follows:

- The number of ILI cases;
- The number of influenza-related deaths;
- QALY loss for ILI;
- Cost of vaccine.

Two of the parameters with a large impact on the results were the number of ILI cases and the number of deaths. It should be noted that these were outputs of the dynamic model and that the true drivers in this instance are likely to be those related to disease transmission, i.e. the vaccine efficacy, probability of a matched year. However, it was not possible to vary these parameters in the sensitivity analysis for the children and clinical risk group populations.

Following the comments from the public consultation, one-way sensitivity analysis has been conducted around the cost of hospitalisation. Varying the cost of hospitalisation from the base case value (£1,209) between £1,000 and £11,000 has a small impact on the maximum willingness to pay for the intervention from the NHS and PSS perspective. The results for scenarios 12 to 15 and scenario 20 are given in Appendix O.

3.1.2.2 Probabilistic sensitivity analysis

The distribution of incremental cost and QALY estimates for each scenario compared with the baseline scenario is presented in a range of PSA scatterplots, which are provided in Appendix K.

Table 3.6 presents the results of the probabilistic sensitivity analysis in this analysis. In all scenarios that increased uptake of vaccination, none of the estimates were cost saving and all scenarios were associated with increased QALYs. Cost-effectiveness results were calculated using a threshold of £20,000 per QALY. Probabilistic results were similar to the deterministic results, although the interventions were estimated as being less likely to be cost-effective in the probabilistic analysis. The probabilistic ICERs tending to be lower than the corresponding deterministic ICERs, and the probabilistic net benefits higher than the corresponding deterministic net benefit. From re-analysis of the PSA (removing select parameters from being varied), it appears that this is largely due to the number of ILIs occurring in the population. This parameter was varied according to a normal distribution based on a visual inspection of the spread of data, and while it appeared to be the best fit it may be that this distribution provides more pessimistic estimates of the number of ILIs to the mean value.

Table 3.6: Results of PSA in children

	Mean incremental cost per targeted population member (SE)	Mean incremental QALYs per targeted population member (SE)	Probabilistic ICER	Probabilistic net benefit*	Probability of cost-effectiveness	Proportion of estimates that save costs	Proportion of estimates that increase QALYs
Scenario 1	-	-	-	-	-	-	-
Scenario 12	-£0.36 (£0.001)	-0.00014 (0.000002)	Intervention less effective	-£2.45	0%	100%	0%
Scenario 13	£0.83 (£0.001)	0.00035, (0.000005)	£2,391.15	£6.13	100%	0%	100%
Scenario 14	£2.20 (£0.004)	0.00077 (0.000011)	£2,838.68	£13.27	100%	0%	100%
Scenario 15	£3.17 (£0.005)	0.001 (0.000016)	£3,162.76	£16.88	100%	0%	100%
Scenario 20	£0.65 (£0.001)	0.00031 (0.000005)	£2,069.37	£5.61	100%	0%	100%

* Based on a cost-effectiveness threshold of £20,000 per QALY gained.

3.2 CLINICAL RISK GROUPS

Table 3.7 presents a summary of the different scenarios evaluated in the clinical risk groups subanalysis. Table 3.8 gives the baseline coverage for those in clinical risk groups.

Table 3.7: Summary of scenarios

Scenario	Impact on uptake
Scenario 1	Baseline (no impact on uptake)
Scenario 2	Uptake by adults in a clinical risk group is 5% lower than the baseline rate
Scenario 3	Uptake by adults in a clinical risk group is 5% higher than the baseline rate
Scenario 4	Uptake by adults in a clinical risk group is 15% higher than the baseline rate
Scenario 5	Uptake by adults in a clinical risk group is 30% higher than the baseline rate
Scenario 6	Uptake by adults in a clinical risk group is 40% higher than the baseline rate
Scenario 7	Uptake by pregnant women is 5% lower than the baseline rate
Scenario 8	Uptake by pregnant women is 5% higher than the baseline rate
Scenario 9	Uptake by pregnant women is 15% higher than the baseline rate
Scenario 10	Uptake by pregnant women is 25% higher than the baseline rate
Scenario 11	Uptake by pregnant women is 35% higher than the baseline rate
Scenario 16	Uptake by high risk children is 5% lower than the baseline rate
Scenario 17	Uptake by high risk children is 10% higher than the baseline rate
Scenario 18	Uptake by high risk children is 25% higher than the baseline rate
Scenario 19	Uptake by high risk children is 35% higher than the baseline rate

Table 3.8: Baseline coverage for clinical risk groups

Clinical risk group	Baseline coverage (%)
<2	18.6
2	48.3
3	52.3
4	47.3
5	39.2
6	39.2
7	39.2
8	39.2
9	39.2
10	39.2
11 to 15	39.2
16 to 65	45.7
>65	71.0
Pregnant	55.9

3.2.1 Base Case Analysis

Results are based on the whole of England population of 54,786,327 individuals (for population breakdown by age, see Appendix B). Note that the whole population was assessed (rather than just those in clinical risk groups) as the impact on vaccinating these patients was expected to impact on the transmission of influenza in the rest of the population.

A breakdown of the total number of events, costs and QALYs for each scenario are given in Appendix E1 to E3 respectively.

Table 3.9 presents the cost-effectiveness results for each scenario compared with the baseline scenario. These costs do not include the cost of an intervention, and so the true cost-effectiveness result for a given intervention will be higher than that reported in the table. The net benefit of a scenario represents the maximum willingness to pay per targeted child for the intervention to be cost-effective. Children in clinical risk groups were associated with the highest ICER of the three clinical risk subgroups. This is due to a number of factors, including population size and the relative impact of increased levels of vaccination costs compared with the reduction in hospitalisation and GP costs.

Higher levels of vaccination uptake is associated with higher estimates of net benefit, and higher cost per averted case of influenza and cost per uptake of vaccine.

Table 3.9: Cost-effectiveness results for each scenario

Scenario	ICER	Net benefit*	Cost per averted case of influenza	Cost per uptake of vaccine
Scenario 1	-	-	-	-
Scenario 2	Intervention less effective	-£3.96	Intervention does not avert cases of flu	Intervention does not increase uptake of vaccination
Scenario 3	£3,039.77	£3.96	£11.65	£13.69
Scenario 4	£3,044.82	£11.87	£11.66	£13.69
Scenario 5	£3,087.05	£23.25	£11.80	£13.72
Scenario 6	£3,203.97	£30.01	£12.23	£13.79
Scenario 7	Intervention less effective	-£4.47	Intervention does not avert cases of flu	Intervention does not increase uptake of vaccination
Scenario 8	£2,535.34	£4.47	£9.58	£12.99
Scenario 9	£2,537.85	£13.41	£9.59	£12.99
Scenario 10	£2,536.62	£22.37	£9.58	£13.00
Scenario 11	£2,536.92	£31.32	£9.58	£13.00
Scenario 16	Intervention less effective	-£2.43	Intervention does not avert cases of flu	Intervention does not increase uptake of vaccination
Scenario 17	£4,735.34	£4.84	£17.96	£17.35
Scenario 18	£4,780.06	£11.96	£18.12	£17.37
Scenario 19	£4,819.47	£16.58	£18.27	£17.40

* Net monetary benefit (NMB) was calculated using a threshold of £20,000 per QALY.

** Note that these results do not include intervention costs. Results are from NHS and PSS perspective.

The link between model outcomes (total costs, total QALYs and net benefit) and uptake rate in scenarios 2 to 6 (adults), scenarios 7 to 11 (pregnant women) and scenarios 16 to 19 (children) was assessed by interpolating between values. This may allow the costs at uptake rates to be predicted between these thresholds.

It appears from a visual inspection of the charts that the relationship between uptake rate and total population costs and QALYs is relatively linear. A similar points holds as with the interpolation of outcomes in children - this assessment is based on a limited number of data points, and it is not possible to say how the trend may continue beyond those that have been modelled. Figures 3.2 to 3.4 present the interpolation of each outcome with uptake rate.

Figure 3.2: Interpolation of results for adults in clinical risk groups

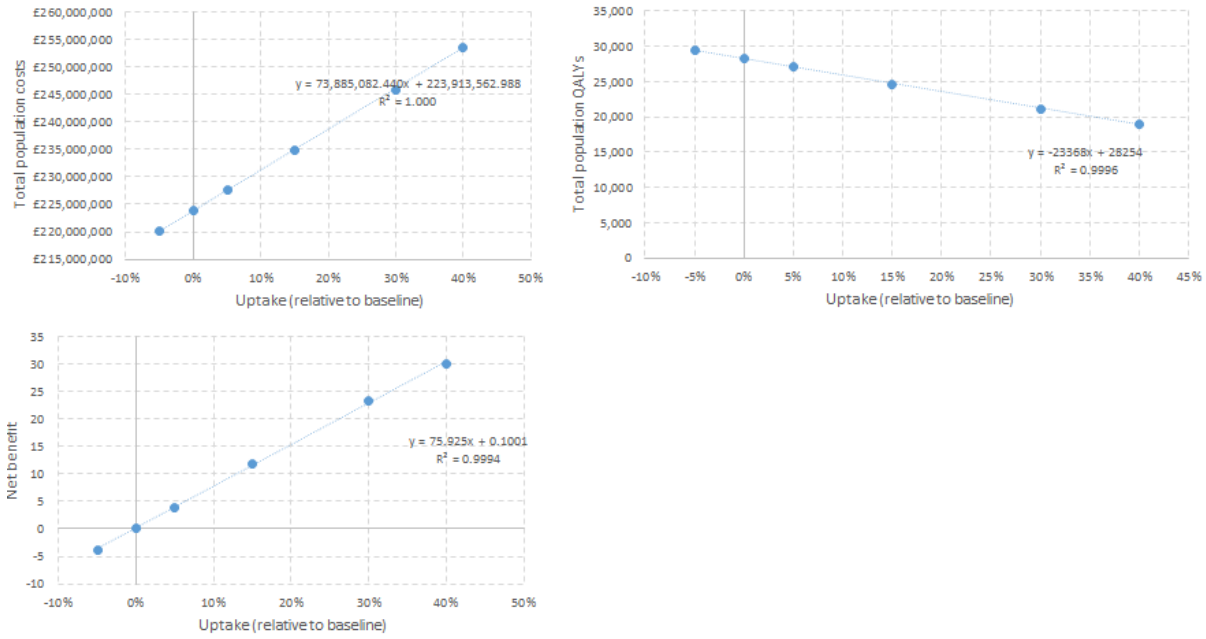


Figure 3.3: Interpolation of results for pregnant women

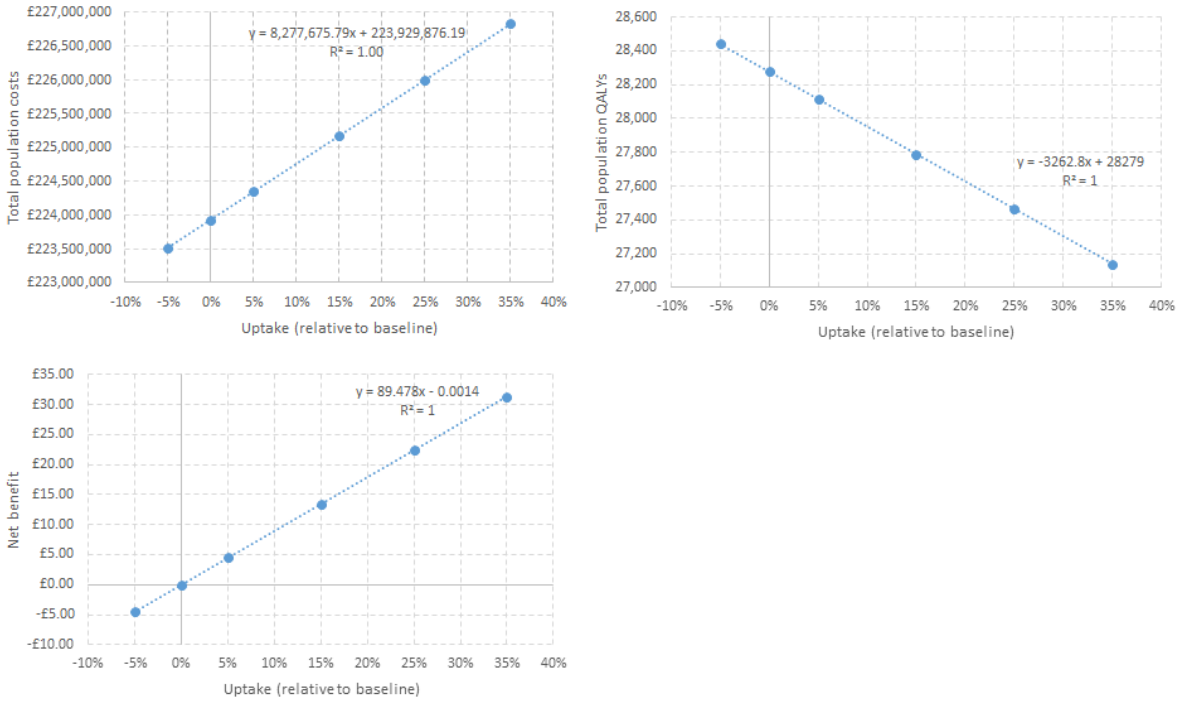


Figure 3.4: Interpolation of results for children in clinical risk groups

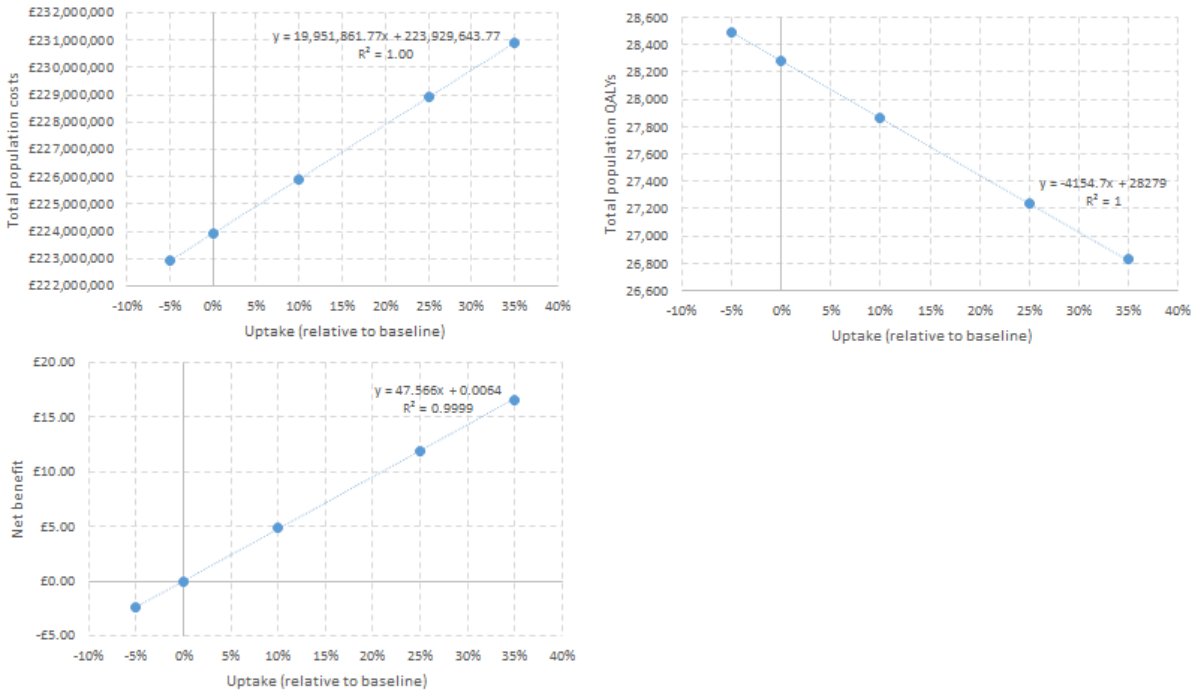


Table 3.10 to Table 3.12 present the interpolated outcomes for uptake rates between those which have been modelled for the adult, pregnant women and child high risk populations respectively. Net benefit was calculated using a threshold of £20,000 per QALY. Extrapolated values for uptake rates beyond the range of those that have been modelled should be interpreted with caution, since it is not possible to determine the nature of the relationship between uptake rate and outcome beyond that which has been modelled.

Table 3.10: Interpolated values for different uptake rates – adults in clinical risk groups

Uptake rate	Total population cost	Total population QALY loss	Net benefit**
-10%	£216,525,055	30,591	-£7.49
-5%*	£220,219,309	29,422	-£3.70
0%*	£223,913,563	28,254	£0.10
5%	£227,607,817	27,086	£3.90
10%	£231,302,071	25,917	£7.69
15%*	£234,996,325	24,749	£11.49
20%	£238,690,579	23,580	£15.29
25%	£242,384,834	22,412	£19.08
30%*	£246,079,088	21,244	£22.88
35%	£249,773,342	20,075	£26.67
40%*	£253,467,596	18,907	£30.47
45%	£257,161,850	17,738	£34.27
50%	£260,856,104	16,570	£38.06

* Table gives values according to the line of best fit (i.e. interpolated values).

** Compared to baseline and based on a cost-effectiveness threshold of £20,000 per QALY gained.

Table 3.11: Interpolated values for different uptake rates – pregnant women

Uptake rate	Total population cost	Total population QALY loss	Net benefit**
-10%	£223,102,109	28,605	-£8.95
-5%*	£223,515,992	28,442	-£4.47
0%*	£223,929,876	28,279	£0.00
5%	£224,343,760	28,116	£4.48
10%	£224,757,644	27,953	£8.95
15%*	£225,171,528	27,790	£13.42
20%	£225,585,411	27,626	£17.90
25%*	£225,999,295	27,463	£22.37
30%	£226,413,179	27,300	£26.84
35%*	£226,827,063	27,137	£31.32
40%	£227,240,947	26,974	£35.79
45%	£227,654,830	26,811	£40.27
50%	£228,068,714	26,648	£44.74

* Table gives values according to the line of best fit (i.e. interpolated values).

** Compared to baseline and based on a cost-effectiveness threshold of £20,000 per QALY gained.

Table 3.12: Interpolated values for different uptake rates – children in clinical risk groups

Uptake rate	Total population cost	Total population QALY loss	Net benefit**
-10%	£221,934,458	28,694	-£4.76
-5%*	£222,932,051	28,487	-£2.38
0%*	£223,929,644	28,279	-£0.01
5%	£224,927,237	28,071	£2.37
10%	£225,924,830	27,864	£4.75
15%*	£226,922,423	27,656	£7.13
20%	£227,920,016	27,448	£9.51
25%*	£228,917,609	27,240	£11.89
30%	£229,915,202	27,033	£14.26
35%*	£230,912,795	26,825	£16.64
40%	£231,910,388	26,617	£19.02
45%	£232,907,982	26,409	£21.40
50%	£233,905,575	26,202	£23.78

* Table gives values according to the line of best fit (i.e. interpolated values).

** Compared to baseline and based on a cost-effectiveness threshold of £20,000 per QALY gained.

Tables 3.13 to 3.15 present the maximum willingness to pay for the intervention per targeted person at which an intervention is cost-effective at a threshold of £20,000 per QALY, as coverage changes from one level to another. Coverage level is presented as relative to baseline coverage in pregnant women and children.

Table 3.13: Maximum willingness to pay for the intervention: Adults in clinical risk groups

	Coverage level with intervention						
		40.7%	**45.7%**	**50.7%**	**60.7%**	**75.7%**	**85.7%**
Coverage level without intervention	40.7%	No change	£3.96	£7.92	£15.83	£27.20	£33.96
	45.7%	No benefit	No change	£3.96	£11.87	£23.25	£30.01
	50.7%	No benefit	No benefit	No change	£7.91	£19.28	£26.05
	60.7%	No benefit	No benefit	No benefit	No change	£11.37	£18.14
	75.7%	No benefit	No benefit	No benefit	No benefit	No change	£6.76
	85.7%	No benefit	No benefit	No benefit	No benefit	No benefit	No change

In adults, the maximum willingness to pay follows a more linear trend, that is, the maximum willingness to pay is similar for a given increase in percentage points, regardless of the uptake before the intervention is introduced, although there is a small association with higher uptake rates being associated with lower maximum willingness to pay. This is likely due to the fact that while there is some onwards transmission in these groups, it is not as great as in the children group. Increasing uptake by 5% percentage points from -5% to baseline is similar (£3.96) to moving from baseline to 5% (£3.96), while increasing uptake from -5% to 5% (£7.92) is greater than increasing uptake from 30% to 40% (£6.76). Increasing uptake by 15% percentage points from baseline to 15% (£11.87) is similar to increasing uptake from 15% to 30% (£11.37).

Table 3.14: Maximum willingness to pay for the intervention: Pregnant women

		Coverage level with intervention					
		-5%	**Baseline**	**5%**	**15%**	**25%**	**35%**
Coverage level without intervention	-5%	No change	£4.47	£8.94	£17.88	£26.84	£35.78
	Baseline	No benefit	No change	£4.47	£13.41	£22.37	£31.32
	5%	No benefit	No benefit	No change	£8.94	£17.89	£26.84
	15%	No benefit	No benefit	No benefit	No change	£8.96	£17.91
	25%	No benefit	No benefit	No benefit	No benefit	No change	£8.95
	35%	No benefit	No benefit	No benefit	No benefit	No benefit	No change

A similar trend was observed in the pregnant women analysis to the adult in clinical risk group analysis, whereby the maximum willingness to pay is similar for a given increase in percentage points, regardless of the uptake before the intervention is introduced.

Table 3.15: Maximum willingness to pay for the intervention: Children in clinical risk groups

		Coverage level with intervention				
		-5%	**Baseline**	**10%**	**25%**	**35%**
Coverage level without intervention	-5%	No change	£2.43	£7.27	£14.39	£19.02
	Baseline	No benefit	No change	£4.84	£11.96	£16.58
	10%	No benefit	No benefit	No change	£7.12	£11.75
	25%	No benefit	No benefit	No benefit	No change	£4.63
	35%	No benefit	No benefit	No benefit	No benefit	No change

The trend in maximum willingness to pay in children in clinical risk groups is similar to that observed in the children group in Table 3.5. Children in clinical risk groups, however, are associated with lower maximum willingness to pay per person for the intervention compared with the whole children group when uptake is increased by 10%, and associated with a higher maximum willingness to pay per person for the intervention when uptake is increased by 25% and 35%. There is a greater number of children at low risk, leading to a larger increase in the absolute number of children in the population being vaccinated with increased uptake compared with the clinical risk group scenario. These additional children being vaccinated results in lower hospitalisations, GP visits and deaths, but also increased vaccine and vaccine-related side-effect costs. The additional cost of vaccination appears to be more of a contributing factor to cost-effectiveness when uptake is increased by a smaller amount in the clinical risk group analysis. This implies that the concept of herd immunity, disease transmission and the higher risk of complications in this group are likely to result in higher increases in uptake in the clinical risk groups being more cost-effective; factors which cannot be disentangled as easily within the economic model as these were parameters in the dynamic model.

3.2.2 Sensitivity Analysis

3.2.2.1 Deterministic sensitivity analysis

A range of parameters were evaluated and their impact on the results assessed (for a full list, see Section 2.4.3). The tornado diagram for each scenario compared with the baseline scenario is provided in Appendix H. Each tornado diagram presents the impact on the maximum intervention cost per targeted population member. In the analysis where vaccine uptake is increased by 5%, varying the parameters does not result in the net benefit to be below £0, indicating that the results are robust to the parameter inputs and their associated range of values.

Similarly to the analyses in children in Section 3.1.2, the parameters that had the biggest impact on the results of the analysis were as follows:

- The number of ILI;
- The number of deaths;
- QALY loss for ILI;
- Average (weighted) cost of an adult vaccine;
- The number of ARI cases.

Following the comments from the public consultation, one-way sensitivity analysis has been conducted around the cost of hospitalisation. Varying the cost of hospitalisation from the base case value (£1,209) between £1,000 and £11,000 has a small impact on the maximum willingness to pay for the intervention from the NHS and PSS perspective. The results for scenarios 12 to 15 and scenario 20 are given in Appendix O.

3.2.2.2 Probabilistic sensitivity analysis

The distribution of incremental cost and QALY estimates for each scenario compared with the baseline scenario is presented in a range of PSA scatterplots, which are provided in Appendix L.

Table 3.16 presents the results of the probabilistic sensitivity analysis in this analysis. In all scenarios that increased uptake of vaccination, none of the estimates were cost saving and all were associated with a higher number of QALYs compared to baseline. Cost-effectiveness results were calculated using a threshold of £20,000 per QALY. Table 3.7 summarises each scenario.

Table 3.16: Results of PSA in clinical risk groups

	Mean incremental cost per targeted population member (SE)	Mean incremental QALY loss per targeted population member (SE)	Probabilistic ICER	Probabilistic net benefit*	Probability of cost-effectiveness*	Proportion of estimates that save costs	Proportion of estimates that increase QALYs
Scenario 1	-	-	-	-	-	-	-
Scenario 2	-£0.71 (£0.001)	-0.00026 (0.000004)	Intervention less effective	-£4.46	0%	100%	0%
Scenario 3	£0.71 (£0.001)	0.00027 (0.000004)	£2,609.81	£4.70	100%	0%	100%
Scenario 4	£2.12 (£0.004)	0.00079 (0.000011)	£2,673.36	£13.76	100%	0%	100%
Scenario 5	£4.22 (£0.007)	0.00154 (0.000022)	£2,747.69	£26.52	100%	0%	100%
Scenario 6	£5.71 (£0.01)	0.00199 (0.000028)	£2,867.10	£34.12	100%	0%	100%
Scenario 7	-£0.65 (£0.001)	-0.00029 (0.000004)	Intervention less effective	-£5.09	0%	100%	0%
Scenario 8	£0.65 (£0.001)	0.00029 (0.000004)	£2,201.30	£5.23	100%	0%	100%
Scenario 9	£1.94 (£0.004)	0.00088 (0.000013)	£2,196.86	£15.73	100%	0%	100%
Scenario 10	£3.24 (£0.006)	0.00147 (0.000022)	£2,203.41	£26.17	100%	0%	100%
Scenario 11	£4.53 (£0.008)	0.00208 (0.000032)	£2,173.59	£37.16	100%	0%	100%
Scenario 16	-£0.75 (£0.001)	-0.00018 (0.000003)	Intervention less effective	-£2.76	0%	100%	0%
Scenario 17	£1.49 (£0.002)	0.00036 (0.000005)	£4,174.97	£5.67	100%	0%	100%
Scenario 18	£3.74 (£0.004)	0.00088 (0.000013)	£4,243.11	£13.89	100%	0%	100%
Scenario 19	£5.25 (£0.006)	0.00122 (0.000018)	£4,322.25	£19.05	100%	0%	100%

* Based on a cost-effectiveness threshold of £20,000 per QALY gained.

3.3 CARERS

Table 3.17 presents a summary of the different scenarios evaluated in the carers analysis.

Table 3.17: Summary of scenarios

Scenario	Impact on uptake
Scenario 1	Baseline (37.4%) (no impact on uptake)
Scenario 2	Uptake by carers is 5% lower than the baseline rate (32.4%)
Scenario 3	Uptake by carers is 10% higher than the baseline rate (47.4%)
Scenario 4	Uptake by carers is 25% higher than the baseline rate (62.4%)
Scenario 5	Uptake by carers is 35% higher than the baseline rate (72.4%)
Scenario 6	Uptake by carers is 100% (62.6% higher than in the basecase)

3.3.1 Base Case Analysis

A breakdown of the total number of events, costs and QALYs for each scenario are given in Tables 3.18 to 3.20 below. Costs and QALY loss due to influenza and related illness in the carer and secondary cases are reported for the whole targeted population (all carers), individual-level targeted population (per carer) and individual-level vaccinated person (vaccinated carer) in the targeted population.

Table 3.18: Results of carers analyses – events

	Vaccinated (difference from baseline)	Cases of influenza*(difference from baseline)	ILI (difference from baseline)	Non-ILI respiratory illness (difference from baseline)	Deaths (difference from baseline)	GP consultations (difference from baseline)	Hospitalisations (difference from baseline)	Secondary cases of ILI (difference from baseline)
Targeted population-level results – total number of events								
Baseline	219,295	80,280	14,450	4,014	4	3,486	654	2,464
Baseline - 5%	189,978 (-29,318)	83,658 (3,377)	15,058 (608)	4,183 (169)	4 (0)	3,633 (147)	682 (28)	2,568 (104)
Baseline +10%	277,930 (58,635)	73,526 (-6,755)	13,235 (-1216)	3,676 (-338)	4 (0)	3,193 (-293)	599 (-55)	2,257 (-207)
Baseline +25%	365,883 (146,588)	63,393 (-16,887)	11,411 (-3040)	3,170 (-844)	3 (-1)	2,753 (-733)	517 (-138)	1,946 (-518)
Baseline +35%	424,518 (205,223)	56,639 (-23,642)	10,195 (-4256)	2,832 (-1182)	3 (-1)	2,460 (-1027)	462 (-193)	1,739 (-726)
Uptake is 100%	586,351 (367,056)	37,996 (-42,285)	6,839 (-7611)	1,900 (-2114)	2 (-2)	1,650 (-1836)	310 (-345)	1,166 (-1298)
Individual-level results – number of events per targeted person								
Baseline	0.374	0.137	0.025	0.007	0.000	0.006	0.001	0.004
Baseline - 5%	0.324 (-0.676)	0.143 (0.00576)	0.0257 (0.001)	0.007 (0.0003)	0.000 (0.0000003)	0.006 (0.000250)	0.001 (0.000047)	0.004 (0.000177)
Baseline +10%	0.474 (-0.526)	0.125 (-0.01152)	0.0226 (-0.0021)	0.006 (-0.0006)	0.000 (-0.0000006)	0.005 (-0.000500)	0.001 (-0.000094)	0.004 (-0.000354)
Baseline +25%	0.624 (-0.376)	0.108 (-0.0288)	0.0195 (-0.0052)	0.005 (-0.0014)	0.000 (-0.0000014)	0.005 (-0.001251)	0.001 (-0.000235)	0.003 (-0.000884)
Baseline +35%	0.724 (-0.276)	0.097 (-0.04032)	0.0174 (-0.0073)	0.005 (-0.0020)	0.000 (-0.0000020)	0.004 (-0.001751)	0.001 (-0.000329)	0.003 (-0.001238)
Uptake is 100%	1 (0)	0.065 (-0.072115)	0.0117 (-0.013)	0.003 (-0.0036)	0.000 (-0.0000036)	0.003 (-0.003132)	0.001 (-0.000588)	0.002 (-0.002214)
Individual-level results – number of events per vaccinated person								
Baseline	1	0.366	0.066	0.018	0.000	0.016	0.003	0.011
Baseline - 5%	1 (0)	0.44 (0.074272)	0.0793 (0.0134)	0.022 (0.0037)	0.00002 (0.000004)	0.019 (0.003226)	0.004 (0.000605)	0.014 (0.002280)
Baseline +10%	1 (0)	0.265 (-0.101537)	0.0476 (-0.0183)	0.0132 (-0.0051)	0.00001 (-0.000005)	0.011 (-0.004410)	0.002 (-0.000828)	0.008 (-0.003117)
Baseline +25%	1 (0)	0.173 (-0.192822)	0.0312 (-0.0347)	0.0087 (-0.0096)	0.00001 (-0.000010)	0.008 (-0.008374)	0.001 (-0.001571)	0.005 (-0.005919)
Baseline +35%	1 (0)	0.133 (-0.232665)	0.024 (-0.0419)	0.0067 (-0.0116)	0.00001 (-0.000012)	0.006 (-0.010104)	0.001 (-0.001896)	0.004 (-0.007142)

	Vaccinated (difference from baseline)	Cases of influenza*(difference from baseline)	ILI (difference from baseline)	Non-ILI respiratory illness (difference from baseline)	Deaths (difference from baseline)	GP consultations (difference from baseline)	Hospitalisations (difference from baseline)	Secondary cases of ILI (difference from baseline)
Uptake is 100%	1 (0)	0.065 (-0.301283)	0.0117 (-0.0542)	0.0032 (-0.0151)	0.000003 (-0.000015)	0.003 (-0.013084)	0.001 (-0.002455)	0.002 (-0.009248)

Table 3.19: Results of carers analyses – costs

	Vaccine	Vaccine side-effects	GP consultations	Hospitalisations	Replacement care	Secondary cases	Total (NHS and PSS perspective)	Replacement care (local authority)
Targeted population-level results – total cost (difference from baseline)								
Baseline	£3,456,899	£135,963	£124,431	£673,436	£922,301	£845,404	**£6,158,434**	£642,934
Baseline -5%	£2,994,747 (-£462,152)	£117,786 (-£18,177)	£129,666 (£5,235)	£701,767 (£28,331)	£961,102 (£38,801)	£880,970 (£35,566)	**£5,786,038** **(-£372,396)**	£669,982 (£27,048)
Baseline +10%	£4,381,204 (£924,305)	£172,317 (£36,354)	£113,961 (-£10,470)	£616,773 (-£56,663)	£844,699 (-£77,602)	£774,272 (-£71,132)	**£6,903,226** **(£744,792**	£588,838 (-£54,096)
Baseline +25%	£5,767,660 (£2,310,761)	£226,847 (£90,884)	£98,257 (-£26,174)	£531,779 (-£141,657)	£728,296 (-£194,005)	£667,574 (-£177,830)	**£8,020,414** **(£1,861,980)**	£507,693 (-£135,241)
Baseline +35%	£6,691,965 (£3,235,066)	£263,201 (£127,238)	£87,787 (-£36,644)	£475,117 (-£198,319)	£650,694 (-£271,607)	£596,442 (-£248,962)	**£8,765,206** **(£2,606,772)**	£453,597 (-£189,337)
Uptake is 100%	£9,243,046 (£5,786,147)	£363,538 (£227,575)	£58,891 (-£65,540)	£318,728 (-£354,708)	£436,512 (-£485,789)	£400,118 (-£445,287)	**£10,820,832** **(4,662,397)**	£304,291 (-£338,643)
Individual-level results – total cost per targeted person (difference from baseline)								
Baseline	£5.90	£0.23	£0.21	£1.15	£1.57	£1.44	**£11**	£1.10
Baseline -5%	£5.107 (-£0.788)	£0.201 (-£0.031)	£0.221 (£0.009)	£1.197 (£0.048)	£1.639 (0.066)	£1.50 (£0.06)	**£9.87** **(-£0.64)**	£1.14 (£0.05)
Baseline +10%	£7.472 (£1.576)	£0.294 (£0.062)	£0.194 (-£0.018)	£1.052 (-£0.097)	£1.441 (-£0.132)	£1.32 (-£0.12)	**£11.77** **(£1.27)**	£1.00 (-£0.09)
Baseline +25%	£9.837 (£3.941)	£0.387 (£0.155)	£0.168 (-£0.045)	£0.907 (-£0.242)	£1.242 (-£0.331)	£1.14 (-£0.30)	**£13.68** **(£3.18)**	£0.87 (-£0.23)
Baseline +35%	£11.413 (£5.517)	£0.449 (£0.217)	£0.150 (-£0.062)	£0.810 (-£0.338)	£1.110 (-£0.463)	£1.02 (-£0.43)	**£14.95** **(£4.45)**	£0.77 (-£0.32)
Uptake is 100%	£15.764 (£9.868)	£0.620 (£0.388)	£0.100 (-£0.112)	£0.544 (-£0.605)	£0.744 (-£0.828)	£0.68 (-£0.76)	**£18.45** **(£7.95)**	£0.52 (-£0.58)
Individual-level results – total cost per vaccinated person (difference from baseline)								
Baseline	£15.76	£0.62	£0.57	£3.07	£4.21	£3.86	**£28**	£2.93

	Vaccine	Vaccine side-effects	GP consultations	Hospitalisations	Replacement care	Secondary cases	Total (NHS and PSS perspective)	Replacement care (local authority)
Baseline -5%	£15.76 (£0.00)	£0.62 (£0.00)	£0.68 (£0.12)	£3.694 (£0.623)	£5.059 (£0.853)	£4.64 (£0.78)	**£30.46** **(£2.37)**	£3.53 (£0.59)
Baseline +10%	£15.76 (£0.00)	£0.62 (£0.00)	£0.41 (-£0.16)	£2.219 (-£0.852)	£3.039 (-£1.167)	£2.79 (-£1.07)	**£24.84** **(-£3.24)**	£2.12 (-£0.81)
Baseline +25%	15.764 (0.00000)	0.620 (0,000)	£0.27 (-£0.30)	£1.45 (-£1.62)	£1.99 (-£2.22)	£1.83 (-£2.03)	**£21.92** **(-£6.16)**	£1.39 (-£1.54)
Baseline +35%	£15.76 (£0.00)	£0.62 (£0.00)	£0.21 (-£0.36)	£1.12 (-£1.95)	£1.53 (-£2.67)	£1.41 (-£2.45)	**£20.65** **(-£7.44)**	£1.07 (£1.86)
Uptake is 100%	15.76 (£0.00)	£0.62 (£0.00)	£0.27 (-£0.36)	£1.119 (-£1.952)	£1.533 (-£2.673)	£0.68 (-£3.17)	**£18.45** **(-£9.63)**	£0.52 (-£2.41)

Table 3.20: Results of carers analyses – QALY loss

	Vaccine side-effects	ILI	Non-ILI respiratory illness	Hospitalisations	Death	Cared for losing carer	Cared for losing carer – temporary	Secondary cases	Total
Targeted population-level results – total QALY loss (difference from baseline)									
Baseline	7	116	4	12	24	0	0	20	**181**
Baseline - 5%	6 (-1)	120 (5)	4 (0)	12 (0)	25 (1)	0 (0)	0 (0)	21 (1)	**188** **(6)**
Baseline +10%	8 (2)	106 (-10)	4 (0)	11 (-1)	22 (-2)	0 (0)	0 (0)	18 (-2)	**168** **(-13)**
Baseline +25%	11 (4)	91 (-24)	3 (-1)	9 (-2)	19 (-5)	0 (0)	0 (0)	16 (-4)	**149** **(-32)**
Baseline +35%	13 (6)	82 (-34)	3 (-1)	8 (-3)	17 (-7)	0 (0)	0 (0)	14 (-6)	**136** **(-45)**
Uptake is 100%	18 (11)	55 (-61)	2 (-2)	6 (-6)	11 (-12)	0 (0)	0 (0)	9 (-10)	**100** **(-81)**
Individual-level results – QALY loss per targeted person (difference from baseline)									
Baseline	0.00001	0.000197	0.000007	0.000020	0.000040	0	0	0.000034	**0.0003**
Baseline - 5%	0.00001 (-0.000002)	0.00021 (0.000008)	0.000007 (0.0000003)	0.0000209 (0.00000084)	0.0000419 (0.000002)	0.0 (0.0)	0.0 (0.0)	0.000035 (0.000001)	**0.0003** **(0.00001)**
Baseline +10%	0.00001 (0.000003)	0.00018 (-0.000017)	0.000006 (-0.0000006)	0.0000184 (-0.00000169)	0.0000368 (-0.000003)	0.0 (0.0)	0.0 (0.0)	0.000031 **(**-0.000003**)**	**0.0003** **(-0.00002)**
Baseline +25%	0.00002 (0.000008)	0.00016 (-0.000041)	0.000005 (-0.0000015)	0.0000159 (-0.00000422)	0.0000318 (-0.000008)	0.0 (0.0)	0.0 (0.0)	0.000027 **(**-0.000007**)**	**0.0003** **(-0.00006)**

	Vaccine side-effects	ILI	Non-ILI respiratory illness	Hospitalisations	Death	Cared for losing carer	Cared for losing carer – temporary	Secondary cases	Total
Baseline +35%	0.00002 (0.000011)	0.00014 (-0.000058)	0.000005 (-0.0000020)	0.0000142 (-0.00000591)	0.0000284 (-0.000012)	0.0 (0.0)	0.0 (0.0)	0.000024 (-0.000010)	**0.0002 (-0.00008)**
Scenario 6	0.00003 (0.000019)	0.00009 (-0.000104)	0.000003 (-0.0000036)	0.0000095 (-0.00001058)	0.0000190 (-0.000021)	0.0 (0.0)	0.0 (0.0)	0.000016 (-0.000018)	**0.0002 (-0.00014)**
Individual-level results – QALY loss per vaccinated person (difference from baseline)									
Baseline	0.000030	0.000527	0.000018	0.000054	0.000108	0	0	0.000090	**0.0008**
Baseline - 5%	0.00003 (0.0)	0.000634 (0.0001070)	0.000022 (0.0000038)	0.000065 (0.00001)	0.000129 (0.00002)	0.0 (0.0)	0 (0.0)	0.000108 (0.000018)	**0.0010 (0.0002)**
Baseline +10%	0.00003 (0.0)	0.000381 (-0.0001462)	0.000013 (-0.0000051)	0.000039 (-0.00001)	0.000078 (-0.00003)	0.0 (0.0)	0 (0.0)	0.000065 (-0.000025)	**0.0006 (-0.0002)**
Baseline +25%	0.00003 (0.0)	0.000249 (-0.0002777)	0.000009 (-0.0000097)	0.000025 (-0.00003)	0.000051 (-0.00006)	0.0 (0.0)	0 (0.0)	0.000043 (-0.000047)	**0.0004 (-0.0004)**
Baseline +35%	0.00003 (0.0)	0.000192 (-0.0003350)	0.000007 (-0.0000117)	0.000020 (-0.00003)	0.000039 (-0.00007)	0.0 (0.0)	0 (0.0)	0.000033 (-0.000057)	**0.0003 (-0.0005)**
Uptake is 100%	0.00003 (0.0)	0.000093 (-0.0004338)	0.000003 (-0.0000152)	0.000010 (-0.00004)	0.000019 (-0.00009)	0.0 (0.0)	0 (0.0)	0.000016 (-0.000074)	**0.0002 (-0.0007)**

The results for scenarios 3 to 6 show that, when vaccine uptake is increased from the base line uptake rate, there are fewer cases of influenza, ILI, non-ILI respiratory illness, deaths, influenza-related resource use, secondary cases of ILI and fewer replacement workers required. This is reflected in the reported incremental costs and QALY loss. Due to fewer people being vaccinated in scenario 2 than in the base case, there are higher numbers of the outcomes listed above.

The greatest contributor to cost to the NHS included in the analysis was the cost of vaccination. For scenarios 3 to 6 the greatest total cost difference between baseline and the comparator scenario was for the cost of providing replacement care if a carer is not able to carry out their caring duties because of influenza related illness. This was followed by the cost of secondary cases of ILI and hospitalisation costs for the carer.

The greatest QALY loss was associated with ILI, followed by death for the carer and the QALY loss from the secondary cases of ILI.

The cost-effectiveness results are presented Table 3.21 for each scenario compared with the baseline levels of uptake. These results do not include the cost of the intervention, and so the true cost-effectiveness result for a given intervention will be higher than that reported in the table.

Compared with baseline levels of uptake, none of the scenarios for the carer population that increased vaccination uptake resulted in a positive net monetary benefit in the base case analysis, as shown in Table 3.21. The base case ICER was £57,547

From a local authority perspective, increasing uptake from baseline to 100% results in cost savings of £338,643 as fewer individuals require provision of a replacement carer or the permanent replacement carer if the carer dies.

Table 3.21: Cost-effectiveness results for each scenario from the NHS and PSS perspective

Scenario	ICER	Net monetary benefit*	Cost per averted case of influenza**	Cost per uptake of vaccine**
Baseline - 5%	Intervention less effective	£0.41	Intervention does not avert cases of flu	Intervention does not increase uptake of vaccination
Baseline +10%	£57,547	-£0.83	£110.26	£12.70
Baseline +25%	£57,547	-£2.07	£110.26	£12.70
Baseline +35%	£57,547	-£2.90	£110.26	£12.70
Uptake is 100%	£57,547	-£5.19	£110.26	£12.70

* Net monetary benefit (NMB) was calculated using a threshold of £20,000 per QALY.

** The ICER, cost per averted case of influenza and the cost per uptake of the vaccine did not vary by scenario. This is due to the proportional effect.

In this analysis, given that intervention costs were not included in the calculations, the net benefit of a scenario represents the maximum willingness to pay for the intervention per targeted carer for the intervention to be cost-neutral. Table 3.22 presents the maximum willingness to pay for the intervention per targeted carer at a threshold of £20,000 per QALY, as coverage changes from one level to another from the NHS and PSS perspective. Coverage level is presented as relative to baseline coverage.

Table 3.22: Maximum willingness to pay for the intervention per targeted carer

Coverage level (37.4% at baseline)	Maximum willingness to pay for the intervention per targeted person
32.4% (-5% from baseline)	Intervention less effective
47.4% (+10% from baseline)	-£0.83
62.4% (+25% from baseline)	-£2.07
72.4% (+35% from baseline)	-£2.90
100% (+ 62.6% from baseline)	-£5.19

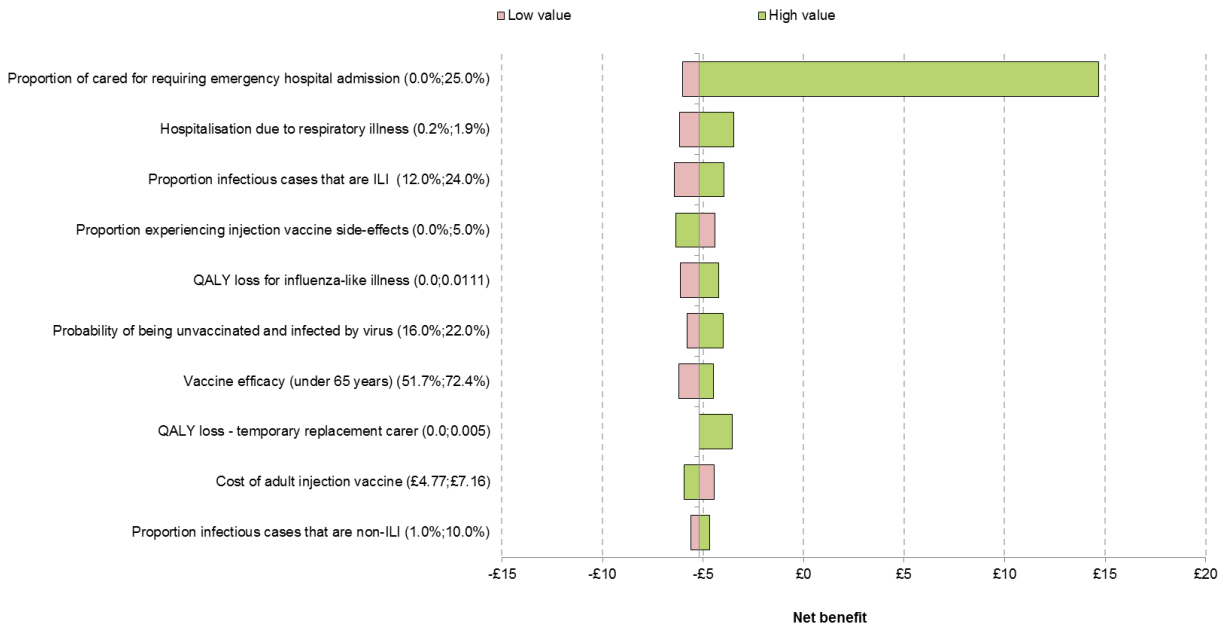
For carers, the maximum willingness to pay for the intervention per targeted person was never positive when uptake was increased from baseline levels in the model base case. The Committee were interested in conducting scenario analysis around some of the assumptions around the consequences of cases for carers. This is presented in Section 3.3.2.

3.3.2 Sensitivity Analysis

3.3.2.1 Deterministic sensitivity analysis

Extensive univariate sensitivity analyses have been carried out, whereby one parameter within the model (for a full list, see Section 2.4.3) is varied in isolation to assess its impact on the model's results. These sensitivity analyses have been presented in a tornado diagram. Tornado diagrams allow many univariate sensitivity analyses to be reported in one diagram. Presenting the univariate sensitivity analyses in a tornado diagram allows the key drivers of the model to be identified as many univariate sensitivity analyses are viewed alongside each other. Each tornado diagram presents the impact on the net benefit for the NHS and PSS perspective. Given that the vaccination of carers is not cost-effective in the base case of the model an example tornado diagram for this population is presented below, Figure 3.5. The tornado diagram shows the impact on the maximum willingness to pay for the intervention when uptake increases from baseline to 100%. The tornado diagrams for each scenario compared with the baseline scenario are shown in Appendix I.

Figure 3.5: Example tornado diagram for carers – Scenario 6 (post-intervention uptake is 100% compared to baseline uptake rate), NHS and PSS perspective



* The diagram does not show a bar for the low value for QALY loss for a temporary replacement carer because the value in the base case is zero and the lower limit is zero.

Figure 3.5 shows that the key drivers of the models results from the NHS and PSS perspective are (listed in descending order of greatest impact):

- Proportion of cared for requiring emergency hospital admission;
- Hospitalisation due to respiratory illness;
- Proportion of infectious cases that are ILI;
- Proportion experiencing injection vaccine side-effects;
- QALY loss for ILI.

It is clear from Figure 3.5 that the only parameter in the model that would change the direction of the results when varied within the limits shown in the diagram is the proportion of cared for individuals who require emergency care provided by the NHS. When the proportion of cared for individuals who require emergency care provided by the NHS was 7.3% the direction of the results change (i.e. the value where the green bar in Figure 3.5 crosses zero net benefit).

Following the comments from the public consultation, one-way sensitivity analysis has been conducted around the cost of hospitalisation for the average episode. The cost of hospitalisation was varied between £1,000 and £11,000 (the base case value is £1,209) and the results are presented in Appendix O. In all scenarios where uptake is increased from the base line level, the maximum willingness to pay for the intervention is positive when the cost of hospitalisation is greater than £6,000. Therefore, depending on the cost of the intervention

itself, if the cost of hospitalisation for the average patient is greater than £6,000 then an intervention to increase the uptake of the influenza vaccination in carers may be cost effective.

Two-way sensitivity analysis was conducted whereby the QALY loss to the cared for if a temporary replacement carer was required and the average cost of emergency care per episode was varied simultaneously. The average cost of emergency care per episode was generated based on the proportion of cared for individuals who required emergency care and the cost of the emergency care (i.e. the value of the average cost of emergency care is dependent on the proportion of those requiring the care. It could be 100% of people requiring care that costs £500, or 10% of people requiring care that costs £5,000). All other inputs in the model base case remained unchanged. The impact on the maximum willingness to pay for the intervention per targeted person was analysed and is presented in Table 3.23. This analysis was conducted with the vaccine coverage level changing from baseline (37.4%) to 100% from the NHS and PSS perspective.

Table 3.23: Maximum willingness to pay for the intervention per targeted carer when the QALY loss to the cared for requiring a replacement carer and the average cost of emergency care is varied from the base case simultaneously

		Average cost of emergency care per episode				
QALY loss to the cared for if a temporary replacement carer is required		£0	£250	£500	£750	£1,000
	0	-£6.02	-£1.87	£2.28	£6.42	£10.57
	0.001	-£5.68	-£1.54	£2.61	£6.76	£10.90
	0.002	-£5.35	-£1.21	£2.94	£7.09	£11.23
	0.003	-£5.02	-£0.87	£3.27	£7.42	£11.57
	0.004	-£4.69	-£0.54	£3.60	£7.75	£11.90
	0.005	-£4.36	-£0.21	£3.94	£8.08	£12.23

Table 3.23 shows that when the average cost of emergency care per episode was £500 or higher, the maximum willingness to pay for the intervention was positive (i.e. there was a positive net benefit) irrespective of the value for the QALY loss to the cared for individual.

Sensitivity analysis was conducted around the QALY loss to the care recipient if they lose their carer temporarily. When the baseline level of uptake was compared against 100% uptake of the vaccination and the QALY loss to the care recipient was varied whilst all other model parameters remained as in the base case, the QALY loss would need to be 0.016 for the intervention to increase uptake to be cost-effective, willingness to pay per targeted carer was £0.12. This QALY loss is very high, equivalent to just under 6 days of being dead compared to in full health.

Further sensitivity analysis was conducted around the rate of onward transmission in the carers model. The rate of onward transmission was 19% in the base case. For the sensitivity analysis this value was varied from 0% to 100% using increments of 10% and all other parameters were kept constant. The results of this sensitivity analysis are given in Table 3.24.

Table 3.24: Maximum willingness to pay for the intervention per targeted carer when onward transmission is varied

Onward transmission	Maximum willingness to pay for the intervention per targeted person*
0%	-£6.30
10%	-£5.72
20%	-£5.13
30%	-£4.54
40%	-£3.96
50%	-£3.37
60%	-£2.78
70%	-£2.20
80%	-£1.61
90%	-£1.03
100%	-£0.44

* Calculated using a cost-effectiveness threshold of £20,000 per QALY.

The results in Table 3.24 show that when uptake was increased to 100% from baseline, irrespective of the value for onward transmission, an intervention to increase uptake would not be cost-effective. When onward transmission was 100% (i.e. every susceptible individual who has contact with a carer who has ILI or non-ILI respiratory illness becomes a secondary case of ILI), the net benefit (or maximum wiliness to pay for the intervention) was -£0.44 and the ICER was £22,062.

Three-way sensitivity analysis was conducted to investigate the impact of varying the average cost of emergency care, onward transmission and vaccine efficacy for those aged under 65 years simultaneously. In the base case of the model the average cost of emergency care was approximately £50, 19% of carers gave one additional case of ILI and vaccine efficacy was 64% for those under 65 years of age. Tables 3.25, 3.26 and 3.27 show the maximum willingness to pay for an intervention that increases uptake by 10% from baseline from the NHS and PSS perspective. Tables 3.25, 3.26 and 3.27 give the results when vaccine efficacy is 64%, 74% and 84%, respectively.

Table 3.25: Maximum willingness to pay for the intervention per targeted carer when the onward transmission and the average cost of emergency care is varied from the base case simultaneously. Vaccine efficacy for carers is 64%

		Average cost of emergency care per episode			
		£0	£50	£250	£500
Onward transmission	0%	-£1.14	-£1.01	-£0.48	£0.19
	20%	-£0.95	-£0.82	-£0.29	£0.37
	40%	-£0.76	-£0.63	-£0.10	£0.56
	60%	-£0.58	-£0.44	£0.09	£0.75
	80%	-£0.39	-£0.26	£0.27	£0.93
	100%	-£0.20	-£0.07	£0.46	£1.12

Table 3.26: Maximum willingness to pay for the intervention per targeted carer when the onward transmission and the average cost of emergency care is varied from the base case simultaneously. Vaccine efficacy for carers is 74%

		Average cost of emergency care per episode			
		£0	£50	£250	£500
Onward transmission	0%	-£1.05	-£0.90	-£0.29	£0.48
	20%	-£0.84	-£0.69	-£0.07	£0.69
	40%	-£0.63	-£0.47	£0.14	£0.90
	60%	-£0.41	-£0.26	£0.35	£1.12
	80%	-£0.20	-£0.05	£0.56	£1.33
	100%	£0.01	£0.16	£0.78	£1.54

Table 3.27: Maximum willingness to pay for the intervention per targeted carer when the onward transmission and the average cost of emergency care is varied from the base case simultaneously. Vaccine efficacy for carers is 84%

		Average cost of emergency care per episode			
		£0	£50	£250	£500
Onward transmission	0%	-£0.96	-£0.79	-£0.09	£0.77
	20%	-£0.73	-£0.55	£0.14	£1.01
	40%	-£0.49	-£0.32	£0.38	£1.25
	60%	-£0.26	-£0.08	£0.61	£1.48
	80%	-£0.02	£0.15	£0.85	£1.72
	100%	£0.22	£0.39	£1.09	£1.96

3.3.2.2 Probabilistic sensitivity analysis

The distribution of incremental cost and QALY estimates for each scenario compared with the baseline scenario is presented in a range of PSA scatterplots, which are provided in the Appendix M.

Table 3.28 presents the results of the probabilistic sensitivity analysis in the base case analysis from the NHS and PSS perspective.

Table 3.28: Results of PSA for carers from a NHS and PSS perspective

	Mean incremental cost per targeted population member (SE)	Mean incremental QALYs per targeted population member (SE)	Probabilistic ICER	Probabilistic net benefit*	Proportion of estimates that save costs	Proportion of estimates that increase QALYs
Baseline	-	-	-	-	-	-
Baseline -5%	-£0.63 (£0.002)	-0.00001 (0.0000001)	Programme less effective	£0.85	100%	0%
Baseline +10%	£1.26 (£0.004)	0.00002 (0.0000002)	£56,689	-£1.70	0%	100%
Baseline +25%	£3.15 (£0.01)	0.00006 (0.0000004)	£56,623	-£4.26	0%	100%
Baseline +35%	£4.43 (£0.01)	0.00008 (0.0000006)	£57,044	-£5.98	0%	100%
Uptake is 100%	£7.89 (£0.02)	0.00014 (0.0000011	£56,809	-£10.67	0%	100%

* Based on a cost-effectiveness threshold of £20,000 per QALY gained.

3.3.3 Scenario Analysis

Whilst in the base case of the model the cost of emergency care is based on the average person being cared for, the Committee discussed that there may be situations where a carer is caring for someone with more complex needs. The person being cared for may require emergency care that is more expensive than the average cost of emergency care used in the base case if the carer is temporarily unable to care for them. In the base case of the model, the average cost of emergency care was £50, based on 1% of cared for individuals requiring emergency hospitalisation at a cost of £4,995 per episode. Sensitivity analysis was conducted around the cost of emergency care, specifically when the cost of emergency care was higher than the base case value. This analysis found that the net benefit (willingness to pay for the intervention) becomes £0 when the average cost of emergency care is £363 and uptake is increased from baseline to 100%. This indicates that in a situation where the cost of emergency care is greater than £363 (i.e. for a person being cared for who has more complex care needs) then vaccination is likely to be cost-effective from an NHS and PSS perspective. The willingness-to-pay for an intervention to promote uptake will depend on the average cost of emergency care and other factors (as shown in Tables 3.25 to 3.27). At different levels of uptake compared to baseline the average cost of emergency care that gives zero net benefit varies very little. When uptake increased by 5% from baseline the net benefit was zero when the average cost of emergency care was £360. When uptake was 35% higher than baseline, net benefit was zero when the average cost of emergency care was £363.

When the cost of emergency care is £500, and all other model parameters are the values used in case analysis, the maximum willingness to pay for an intervention that increases uptake from baseline by 5% is £0.18.

3.4 HEALTH AND SOCIAL CARE WORKERS

3.4.1 Base Case Analysis

Table 3.29 presents a summary of the different scenarios evaluated in the health and social care worker analysis.

Table 3.29: Summary of scenarios

Scenario	Impact on uptake
Scenario 1	Baseline (no impact on uptake)
Scenario 2	Uptake by health and social care worker is 5% lower than the baseline rate (45.6%)
Scenario 3	Uptake by health and social care worker is 10% higher than the baseline rate (60.6%)
Scenario 4	Uptake by health and social care worker is 25% higher than the baseline rate (75.6%)
Scenario 5	Uptake by health and social care worker is 35% higher than the baseline rate (85.6%)
Scenario 6	Uptake by health and social care workers is 100% (49.4% higher than in the basecase)

A breakdown of the total number of events, costs and QALYs for each scenario are given in Appendix F1 to F3 respectively. Costs and QALY loss are reported for the whole targeted population (all health and social care workers), individual-level targeted population (per health and social care worker) and individual-level vaccinated person (vaccinated health and social care worker) in the targeted population.

Similar to the results for the carer population, the results for scenarios 3 to 6 show that when vaccine uptake is increased from the base line uptake rate there are fewer cases of influenza, ILI, non-ILI respiratory illness, deaths and influenza-related resource use, Appendix F. This is reflected in the reported incremental costs and QALY loss. Due to fewer people being vaccinated in scenario 2 than in the base case, there are a higher number of the outcomes such as cases of influenza and ILI. Compared to baseline levels of uptake, the scenarios that increased uptake, scenarios 3 to 6, health and social care worker resulted in a net monetary benefit and dominant ICER as shown in Table 3.30. In this analysis, given that intervention costs were not included in the calculations, the net benefit of a scenario represents the maximum willingness to pay for the intervention per targeted for the intervention to be cost-neutral.

Table 3.30: Cost-effectiveness results for each scenario from the NHS and PSS perspective

Scenario	ICER	Net monetary benefit*	Cost per averted case of influenza**	Cost per uptake of vaccine**
Baseline -5%	Dominated	-£2.15	Intervention does not avert cases of flu	Intervention does not increase uptake of vaccination
Baseline +10%	Dominant	£4.30	Intervention averts cases of flu and is cost saving overall	Intervention increases vaccination and is cost saving overall
Baseline +25%	Dominant	£10.75	Intervention averts cases of flu and is cost saving overall	Intervention increases vaccination and is cost saving overall
Baseline +35%	Dominant	£15.05	Intervention averts cases of flu and is cost saving overall	Intervention increases vaccination and is cost saving overall
Uptake is 100%	Dominant	£21.25	Intervention averts cases of flu and is cost saving overall	Intervention increases vaccination and is cost saving overall

* Net monetary benefit (NMB) was calculated using a threshold of £20,000 per QALY.

** Note that these results do not include intervention costs.

From a Local Authority perspective, the model reports cost savings of £735,759. This cost saving is generated despite the vaccination costs incurred as large cost savings are generated through the requirement for fewer replacement workers when vaccine uptake is higher than the baseline level.

Given that the net benefit is linear to the level of uptake, to assist the Committee in their discussion around the recommendations, Table 3.31 gives the net monetary benefit (or maximum willingness to pay for the intervention per targeted person) when the cost-effectiveness threshold is £20,000 and the level of uptake increases in 5% increments from baseline and compared against the baseline level of uptake. Intervention costs are not included.

Table 3.31: Maximum willingness to pay for the intervention per targeted health and social care worker

Change in uptake from baseline (uptake)	Net monetary benefit*
Baseline -5%	-£2.15
Baseline +5% (55.6%)	£2.15
Baseline +10% (60.6%)	£4.30
Baseline +15% (65.6%)	£6.45
Baseline +20% (70.6%)	£8.60
Baseline +25% (75.6%)	£10.75
Baseline +30% (80.6%)	£12.90
Baseline +35% (85.6%)	£15.05
Baseline +40% (90.6%)	£17.20
Baseline +45% (95.6%)	£19.36
Uptake is 100%	£21.25

* Net monetary benefit (NMB) was calculated using a threshold of £20,000 per QALY.

3.4.2 Sensitivity Analysis

As with the carers model (details given in Section 3.3.2), the univariate sensitivity analyses have been presented in a tornado diagram. The tornado diagrams are given in Appendix J. Each tornado diagram presents the impact on the maximum intervention cost per targeted population member when the cost-effectiveness threshold is £20,000.

The tornado diagrams show that the key drivers of the models results from the NHS and PSS perspective are (listed in descending order of greatest impact):

- Average number of extra ILI cases per HSCW;
- Cost of secondary case of influenza;
- Adult days off work due to influenza;
- Probability of being unvaccinated and infected by a virus;
- Vaccine efficacy (under 65 years old);
- QALY loss for influenza-like illness.

As with the scenario for carers one-way sensitivity analysis has been conducted around the cost of hospitalisation for the average episode. In all scenarios where uptake is increased from the base line level, the maximum willingness to pay for the intervention is greater than the base case result when the cost of hospitalisation is higher than the base case value. For example when the cost of hospitalisation is £6,000 as opposed to £1,029 in the base case, the maximum willingness to pay for the intervention per targeted population member is £43.40

as opposed to £15.05 in the base case when vaccination levels increase by 35% from baseline.

3.4.2.1 Probabilistic sensitivity analysis

The distribution of incremental cost and QALY estimates for each scenario compared with the baseline scenario is presented in a range of PSA scatterplots, which are provided in Appendix N.

Table 3.32 presents the results of the probabilistic sensitivity analysis in this analysis from the NHS and PSS perspective.

Table 3.32: Results of PSA for health and social care workers from a NHS and PSS perspective

	Mean incremental cost per targeted population member (SE)	Mean incremental QALYs per targeted population member (SE)	Probabilistic ICER	Probabilistic net benefit*	Proportion of estimates that save costs	Proportion of estimates that increase QALYs
Baseline	-	-	-	-	-	-
Baseline -5%	£1.39 (£0.0014)	-0.00004 (0.0000003)	Dominated	-£0.56	0%	0%
Baseline +10%	-£2.73 (£0.03)	0.00008 (0.000005)	Dominant	£1.08	100%	100%
Baseline +25%	-£6.81 (£0.07)	0.00021 (0.0000014)	Dominant	£2.70	100%	100%
Baseline +35%	-£9.46 (£0.09)	0.00029 (0.0000019)	Dominant	£3.68	100%	100%
Uptake is 100%	-£13.55 (£0.14)	0.00041 (0.000003)	Dominant	£5.39	100%	100%

* Based on a cost-effectiveness threshold of £20,000 per QALY gained.

3.4.3 Scenario Analysis

3.4.3.1 Vaccine uptake rates

Whilst this project was ongoing preliminary uptake rates for health care workers were published by Public Health England. This was cumulative data from September to the end of December and the reported uptake was 61.8% [32]. Given that the outcomes of the health and social care workers model are proportional to the number of individuals vaccinated, a change in baseline uptake by the same number of percentage points used in the base case analysis does not change the maximum willingness to pay for an intervention for each scenario. That is, if baseline uptake is 50.6% in 2015/16 and in 2016/17 baseline uptake is 61.8%, increasing uptake by 10% for both levels of baseline uptake results in a maximum willingness to pay for the intervention per targeted person of £4.30 in both scenarios.

3.4.3.2 Average number extra of ILI cases per health and social care worker

Given that the average number of extra ILI cases per HSCW was a key parameter in the health and social care worker model, the impact of varying this input was explored. The average number of extra ILI cases was varied whilst the other model input parameters remained at the value used in the base case. Uptake was 100% compared against baseline. The impact on the results for each scenario are given in Table 3.33.

Table 3.33: Varying the average number of extra ILI cases per HSCW

Value for the average number of extra ILI cases per HSCW	ICER	Net benefit*
0.7 (base case)	Dominant	£21.25
0	Dominant	£3.68
0.2	Dominant	£8.79

* Calculated using a threshold of £20,000 per QALY.

3.4.3.3 Proportion of extra ILI cases who are under 65 years old and 65 years and over

It was assumed in the base case of the model that the half of the extra ILI cases were under 65 years old whilst the remaining half were 65 years or over. These proportions were used to calculate the average cost of a secondary case of ILI as the resource use was dependent on the age. In the base the average cost of a secondary case of ILI was £289. In scenario analysis, the assumption made around the proportion of cases who are under and 65 years and over was explored. Table 3.34 shows the impact on the results for a scenario where 100% of the secondary cases were under 65 years and 0% were 65 years and over. The results of a second scenario are also given when the opposite was true.

Table 3.34: Varying the proportion of secondary cases of ILI under the age of 65 years and 65 years and over

Scenario	Average cost of secondary case of ILI	ICER	Net benefit*
50% under 65 years of age and 50% 65 years and over (base case)	£289.34	Dominant	£21.25
100% under 65 years of age and 0% 65 years and over	£155.03	Dominant	£16.00
0% under 65 years of age and 100% 65 years and over	£423.65	Dominant	£26.50

* Calculated using a threshold of £20,000 per QALY.

Section 4: Discussion

The economic evaluation has demonstrated that for children, clinical risk groups, health and social care workers and a sub-group of carers it is likely that interventions that increase the uptake of the influenza vaccination are likely to be cost-effective. The results of the analysis can be used as guidance when the Committee are considering whether the maximum willingness to pay for the intervention for it to be considered cost-effective is reasonable and whether they are able to make a decision on whether it can be recommended.

The base case analysis for carers showed that the maximum willingness to pay for the intervention per targeted person was never positive when uptake was increased from baseline levels. This indicates that the results of the model suggest that vaccinating all carers is not cost-effective in the base case from the NHS and PSS perspective and, as such, interventions aimed at increasing vaccination rates are not cost-effective. However, sensitivity analysis, conducted based on recommendations from the Committee, showed that, when the average cost of emergency care per episode is £363 or higher, the maximum willingness to pay for the intervention was positive (i.e. there was a positive net benefit). The Committee discussed a situation where a carer is caring for someone with more complex needs. In this situation, if the carer is not able to carry out their caring duties a person being cared for who has more complex needs may require emergency care that is more expensive than the average cost of emergency care used in the base case. In this case, the cost of emergency care per episode may exceed £363 and, therefore, an intervention to increase the uptake of the influenza vaccination in this group of carers may be cost-effective from the NHS and PSS perspective, depending on the cost of the intervention itself.

It is important to be mindful of the perspective that was used for the analysis. If the analysis was taken from a local authority perspective, the majority of cost-savings would not accrue to the local authority given that the costs saved are mostly NHS costs and costs saved from reduced productivity loss. For health and social care workers, given that Local Authorities employ approximately 10% of the workforce in the model, cost savings are generated for the local authorities when the vaccine uptake increases as fewer replacement workers are required. As the Local Authorities provide HomeCare services, again savings are generated for Local Authorities in the carers model when vaccination uptake increases as fewer carers require temporary replacement when they are unwell with flu. Other than for the carers model, cost savings are generated for the society when vaccine uptake is increased from baseline levels. This is generally through large savings from reduced productivity loss at higher levels of vaccine uptake.

Another point to note is that the influenza virus is constantly changing and so whilst effort is made every season to match the vaccine to the circulating strain, it may be that the strain used in the vaccine does not match the strain circulating during that flu season. In the model for children and clinical risk groups, the PHE model considers the benefits over each individual season and averages the benefits over a 14-year period. This method is used to generate produce results that are representative of an average year. In the static models used for carers and health and social care workers a more crude method was used to determine if the vaccination was matched to the circulating strain. Given the complexity of modelling vaccinations for an evolving virus, the methods used in the modelling recognised the challenges but by no means fully overcame them.

As with any economic evaluation, there are a number of limitations inherent within the model. The base case results of the analysis do not currently include any intervention costs. Data around intervention costs are scarce and the data that are available may not be applicable to other interventions of the same type. The maximum willingness to pay for the intervention would, therefore, be lower and the value of the "true" ICER would be higher in many cases. Furthermore, the Committee should consider not only the likely cost of an intervention, but the incremental cost over and above what is considered to be "current practice", since the NHS already has resources in place to promote and increase vaccination, such as posters in GP surgeries.

It is important to note that the results of these model results must be treated with some caution, given the uncertainties in the model, all of which reduce the reliability of any conclusions which may be drawn. As with any economic model, there is some uncertainty, which impacts upon the reliability of the conclusions. However, extensive sensitivity analysis (both deterministic and probabilistic) were undertaken in order to determine to the extent of the robustness of the conclusions.

Infectious disease modelling poses a number of challenges that could not fully be overcome within the remit of this project. This may mean that the impact of vaccination is underestimated in certain groups. In the carer and health and social group worker analysis a dynamic model was not used. Whilst onward transmission was included through calculating the number of secondary cases of ILI, this is a crude estimate and is a compromise given that a dynamic model was not available for these populations. Nonetheless, if the results of the model suggest that an intervention is cost-effective with the level of onward transmission included in the model, then incorporating the notion of herd protection may increase our level of confidence in this assessment. A further challenge of modelling influenza is that there is inter-seasonal variation in the circulating strain of the virus. The economic models attempted to address this issue through utilising data from the Health Protection Agency [11] to establish the match between the circulating and vaccine strains. This aimed to allow for predictions of the model to be applicable to an average season, rather than just a single, specific season. There remains the issue that in some seasons there may be a mismatch between the predicted circulating strain of the virus and the circulating strain and some types of vaccine may be more effective than others in these circumstances. Investigating the best type of vaccine to use in any given year was outside the scope of this project.

Lastly, there are likely to be some benefits of, and further issues related to, the vacation against influenza that have not been captured in this evaluation. For example, there may be a negative impact on an individual's quality of life (non-health-related) if their usual care provision is altered. There may also be some general economic gains from a reduced number of cases of influenza that are not captured by simple productivity gains. On balance, it is likely that the analyses presented here is cautious rather than optimistic.

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APPENDIX A

QALY Calculations

Table A.1: QALY loss calculations

Age	Probability of death	Proportion alive	Utility	Cumulative QALYs (discounted*)
0	0.003903	1.00	0.94	0.94
1	0.000297	1.00	0.94	1.85
2	0.000151	1.00	0.94	2.73
3	0.000121	1.00	0.94	3.57
4	0.000088	1.00	0.94	4.39
5	0.000081	1.00	0.94	5.18
6	0.000083	1.00	0.94	5.95
7	0.000089	1.00	0.94	6.68
8	0.000072	1.00	0.94	7.40
9	0.000079	1.00	0.94	8.09
10	0.000086	1.00	0.94	8.75
11	0.000073	1.00	0.94	9.39
12	0.000083	1.00	0.94	10.02
13	0.000106	1.00	0.94	10.62
14	0.000119	1.00	0.94	11.20
15	0.000147	1.00	0.94	11.76
16	0.000181	1.00	0.94	12.30
17	0.000213	1.00	0.94	12.82
18	0.000303	1.00	0.94	13.32
19	0.000333	1.00	0.94	13.81
20	0.000322	1.00	0.94	14.28
21	0.000334	1.00	0.94	14.74
22	0.000338	1.00	0.94	15.18
23	0.000381	1.00	0.94	15.60
24	0.000372	1.00	0.94	16.01
25	0.000401	1.00	0.94	16.41
26	0.000433	0.99	0.93	16.79
27	0.000432	0.99	0.93	17.15
28	0.000457	0.99	0.93	17.50
29	0.000492	0.99	0.93	17.84
30	0.000524	0.99	0.93	18.17
31	0.000555	0.99	0.93	18.49
32	0.000621	0.99	0.93	18.80
33	0.000637	0.99	0.93	19.09
34	0.000712	0.99	0.93	19.38
35	0.000761	0.99	0.91	19.65
36	0.000831	0.99	0.91	19.91
37	0.000880	0.99	0.91	20.16
38	0.001017	0.99	0.91	20.41
39	0.001078	0.99	0.91	20.64
40	0.001172	0.98	0.91	20.87
41	0.001273	0.98	0.91	21.09
42	0.001363	0.98	0.91	21.30
43	0.001447	0.98	0.91	21.50
44	0.001593	0.98	0.91	21.70
45	0.001768	0.98	0.85	21.87
46	0.001853	0.98	0.85	22.04
47	0.002020	0.97	0.85	22.21
48	0.002120	0.97	0.85	22.36
49	0.002369	0.97	0.85	22.52
50	0.002605	0.97	0.85	22.66
51	0.002789	0.96	0.85	22.81
52	0.003018	0.96	0.85	22.94
53	0.003334	0.96	0.85	23.07

Age	Probability of death	Proportion alive	Utility	Cumulative QALYs (discounted*)
54	0.003625	0.95	0.85	23.20
55	0.003997	0.95	0.80	23.32
56	0.004347	0.95	0.80	23.43
57	0.004846	0.94	0.80	23.53
58	0.005263	0.94	0.80	23.63
59	0.005827	0.93	0.80	23.73
60	0.006489	0.93	0.80	23.83
61	0.007032	0.92	0.80	23.92
62	0.007719	0.91	0.80	24.00
63	0.008430	0.90	0.80	24.09
64	0.009123	0.90	0.80	24.16
65	0.009835	0.89	0.78	24.24
66	0.010419	0.88	0.78	24.31
67	0.011567	0.87	0.78	24.38
68	0.012878	0.86	0.78	24.44
69	0.014210	0.84	0.78	24.50
70	0.015740	0.83	0.78	24.56
71	0.017358	0.82	0.78	24.62
72	0.019670	0.80	0.78	24.67
73	0.021843	0.78	0.78	24.72
74	0.024451	0.76	0.78	24.76
75	0.026802	0.74	0.73	24.81
76	0.029742	0.72	0.73	24.84
77	0.032670	0.70	0.73	24.88
78	0.036389	0.67	0.73	24.91
79	0.040895	0.64	0.73	24.95
80	0.046881	0.61	0.73	24.97
81	0.052327	0.58	0.73	25.00
82	0.059308	0.55	0.73	25.02
83	0.066575	0.51	0.73	25.05
84	0.075067	0.47	0.73	25.06
85	0.084614	0.43	0.73	25.08
86	0.094489	0.39	0.73	25.10
87	0.105970	0.35	0.73	25.11
88	0.118338	0.31	0.73	25.12
89	0.132488	0.27	0.73	25.13
90	0.146138	0.23	0.73	25.14
91	0.160464	0.19	0.73	25.14
92	0.179342	0.16	0.73	25.15
93	0.201530	0.13	0.73	25.15
94	0.218120	0.10	0.73	25.15
95	0.235742	0.08	0.73	25.16
96	0.253086	0.06	0.73	25.16
97	0.278607	0.04	0.73	25.16
98	0.304066	0.03	0.73	25.16
99	0.326562	0.02	0.73	25.16
100	0.346050	0.01	0.73	25.16

* In the model, these numbers are discounted from the age of loss (presently discounted from age 0 for illustrative purposes)

APPENDIX B

Population Numbers

Table B.1: Population estimates for 2016 (ONS 2016)

Age	England	England (female)	Pregnant	Not pregnant
0	662,977	322,748	0	662977
1	670,993	327,125	0	670993
2	688,932	335,543	0	688932
3	712,587	347,748	0	712587
4	699,191	341,128	0	699191
5	687,611	335,831	0	687,611
6	677,724	331,039	0	677724
7	683,397	333,321	0	683397
8	661,182	322,153	0	661182
9	647,549	316,214	0	647549
10	620,073	302,763	0	620073
11	609,790	297,780	0	609790
12	592,130	288,731	0	592130
13	581,609	283,828	0	581609
14	596,693	291,956	0	596693
15	612,676	298,386	13129	599547
16	631,635	307,539	13532	618103
17	641,107	312,086	13732	627375
18	661,031	321,759	14157	646874
19	666,840	323,005	14212	652628
20	673,761	328,147	14438	659323
21	701,685	341,451	15024	686661
22	712,095	348,590	15338	696757
23	740,862	366,730	16136	724726
24	763,854	374,871	16494	747360
25	754,595	369,929	25895	728700
26	749,216	371,857	26030	723186
27	759,356	379,320	26552	732804
28	742,544	374,487	26214	716330
29	752,257	374,995	26250	726007
30	754,383	376,358	26345	728038
31	737,768	369,406	25858	711910
32	744,176	373,691	26158	718018
33	742,944	374,267	26199	716745
34	748,757	376,423	26350	722407
35	749,992	376,740	26372	723620
36	719,287	360,640	25245	694042
37	670,798	335,705	23499	647299
38	660,061	330,155	23111	636950
39	670,780	337,036	23593	647187
40	683,903	343,758	24063	659840
41	694,559	349,909	24494	670065
42	724,677	364,274	25499	699178
43	754,561	379,488	26564	727997
44	778,754	393,885	0	778754
45	759,786	383,909	0	759786
46	777,437	393,603	0	777437
47	776,611	393,065	0	776611
48	787,611	397,316	0	787611
49	787,915	399,660	0	787915
50	791,066	401,127	0	791066
51	783,305	396,881	0	783305
52	765,857	387,546	0	765857
53	748,704	377,934	0	748704
54	722,068	364,134	0	722068

Age	England	England (female)	Pregnant	Not pregnant
55	692,374	349,338	0	692374
56	676,158	341,409	0	676158
57	661,089	333,803	0	661089
58	635,797	321,841	0	635797
59	612,904	310,270	0	612904
60	590,280	299,840	0	590280
61	591,581	301,716	0	591581
62	583,991	297,305	0	583991
63	567,596	290,531	0	567596
64	571,273	292,647	0	571273
65	582,595	299,998	0	582595
66	596,441	306,150	0	596441
67	629,564	323,972	0	629564
68	682,834	350,805	0	682834
69	525,701	271,426	0	525701
70	508,499	263,503	0	508499
71	504,922	262,068	0	504922
72	467,555	244,725	0	467555
73	415,572	219,236	0	415572
74	372,072	197,850	0	372072
75	385,501	205,465	0	385501
76	380,304	203,832	0	380304
77	367,100	197,446	0	367100
78	345,778	187,780	0	345778
79	325,545	178,815	0	325545
80	305,377	169,178	0	305377
81	278,932	156,542	0	278932
82	261,228	148,746	0	261228
83	249,194	143,927	0	249194
84	231,569	136,326	0	231569
85	210,446	126,611	0	210446
86	184,425	112,679	0	184425
87	160,779	100,078	0	160779
88	141,595	89,128	0	141595
89	123,076	79,462	0	123076
90	474,968	334,623	0	474968

APPENDIX C

Model Parameters

C.1: Parameters in the cost-effectiveness analysis

Parameter	Base case value	Values for DSA		Values for PSA		Source
		Lower limit	Upper limit	Distribution	Dispersion	
Population						
Number of children (2 to 17 years)	10,343,886	-	-	-	-	[22]
Number in a clinical risk group: adults	5,182,475	-	-	-	-	[11, 22] [25]
Number in a clinical risk group: pregnant women	636,892					[22] [24]
Number in a clinical risk group: children	1,327,057					[22]
Number of carers	586,351	-	-	-	-	[23, 25]
Number of health and social care workers	2,137,503	-	-	-	-	[29] [28]
Baseline coverage – carers	37.5%	-	-	-	-	[23]
Baseline coverage – HSCWs	50.6%	-	-	-	-	[29]
Proportion high risk, under 2 years of age	5.2%	-	-	-	-	[12]
Proportion high risk, 2 to 4 years of age	8.6%	-	-	-	-	
Proportion high risk, 5 to 16 years of age	12.9%	-	-	-	-	
Proportion high risk, 16 to 65 years of age	15.8%	-	-	-	-	
Proportion high risk, over 65 years of age	48.1%	-	-	-	-	
Proportion high risk, pregnant	11.0%	-	-	-	-	
Conception rate per 1,000 (15 to 24 years)	44.08	-	-	-	-	[24]
Conception rate per 1,000 (25 to 44 years)	69.51	-	-	-	-	
Quality of life						
QALY loss due to vaccine side effects	0.0015	0	0.003	Lognormal	95% CI -0.0005 to 0.0026	[43]
QALY loss due to ILI	0.008	0.005	0.011	Lognormal	NR in source, SE assumed 20% of mean value	[12]
QALY loss due to ARI	0.00101	0.001	0.001	Lognormal	SE 0.00008	
QALY loss due to hospitalisation	0.018	0.014	0.022	Lognormal	SE 0.0018	
Unit costs						
Vaccine injection cost per dose – adults	£5.96	£4.77	£7.16	Uniform	Varied by ± 20%	[53]
Vaccine injection cost per dose – children	£5.95	£4.76	£7.14	Uniform	Varied by ± 20%	[53]
Service payment	£9.80	-	-	-	-	[55, 57]
Cost of vaccine side effects	£31	-	-	-	-	[59]
Cost of hospitalisation	£1,029	-	-	-	-	[58]
Cost of GP appointment – in surgery	£31	-	-	-	-	[59]
Cost of GP appointment – out of surgery	£117	-	-	-	-	
Home care cost per hour (for permanent replacement carer)	£16.70	-	-	Gamma	NR in source, SE assumed 20% of mean value	[66]
Carers' allowance	£62.10	-	-	Gamma	NR in source, SE assumed 20% of mean value	[65]
Cost per hour of replacement HSCW	£26.27	-	-	Gamma	NR in source, SE assumed 20% of mean value	[59]
Average lifetime earnings	£660,927	£427,717	£944,070	Gamma	NR in source, SE assumed 20% of mean value	[69]

Parameter	Base case value	Values for DSA		Values for PSA		Source
		Lower limit	Upper limit	Distribution	Dispersion	
Travel cost to GP	£7.94	£2.16	£17.40	Gamma	NR in source, SE assumed 20% of mean value	[70]
Travel cost to hospital	£10.03	£2.73	£21.98	Gamma	NR in source, SE assumed 20% of mean value	
Over the counter medications	£5.09	£1.39	£11.16	Gamma	NR in source, SE assumed 20% of mean value	
Median gross weekly earnings – full-time employment	£539	-	-	Gamma	NR in source, SE assumed 20% of mean value	[80]
Median gross weekly earnings – part-time employment	£177	-	-	Gamma	NR in source, SE assumed 20% of mean value	[80]
Median gross weekly earnings – carer	£110	£0.00	£110	Gamma	NR in source, SE assumed 20% of mean value	Assumption
Resource use						
Proportion with vaccine side-effect incurring a treatment cost	100%	50%	100%	Beta	NR in source, estimated α and β assuming n=10	Assumption
Proportion of children aged 2 to 7 receiving nasal spray vaccine	90%	50%	100%	Beta	NR in source, estimated α and β assuming n=100	Assumption
Probability of GP consultation due to ILI	20.08%	15%	25%	Beta	α =48, β =239	[36]
Probability of GP consultation due to non-ILI respiratory illness	14.56%	12%	17%	Beta	α =108, β =742	
Probability of hospitalisation due to respiratory illness	0.82%	0.17%	1.94%	Beta	Estimated SE as 0.005	
Hours per week for permanent replacement carer	35	-	-	Gamma	NR in source, SE assumed 20% of mean value	Assumption
Proportion of ILI cases (in clinical risk group) visiting GP – carer & HSCW model	17%	10%	25%	Beta	α =17, β =83	[20]
Proportion of ILI cases (in clinical risk group) GP telephone consultation – carer & HSCW model	29%	21%	38%	Beta	α =29, β =71	
Proportion of ILI cases (in clinical risk group) requiring hospitalisation – carer & HSCW model	19%	12%	28%	Beta	α =19.4, β =81	
Proportion of ILI cases (in clinical risk group) requiring intensive care – carer & HSCW model	7%	3%	13%	Beta	α =7, β =93	
Proportion of cared for requiring provision of emergency residential care **–** carer & HSCW model	1%	0.03%	4%	Beta	α =1, β =99	
Proportion of cared for requiring emergency hospital admission **–** carer & HSCW model	1%	0.03%	4%	Beta	α =1, β =99	
Cost of secondary case of influenza (high risk group) – HSCW model	£289	-	-	Gamma	NR in source, SE assumed 20% of mean value	Calculated
Cost of secondary case of influenza (high risk group) – carer model	£343	-	-	Gamma	NR in source, SE assumed 20% of mean value	Calculated
Productivity						
Proportion of adults in full-time employment	70%	-	-	Dirichlet	α =23.2, β =33.38	[81]

Parameter	Base case value	Values for DSA		Values for PSA		Source
		Lower limit	Upper limit	Distribution	Dispersion	
Proportion of adults in part-time employment	26%	-	-	Dirichlet	α =8.56, β =33.38	
Proportion of adults unemployed	5%	-	-	Dirichlet	α = 1.62, β =33.38	
Proportion of HSCWs in full-time employment	81%	-	-	Beta	NR in source, estimated α and β assuming n=100	[28]
Proportion of carers in part-time employment	66%	57%	75%	Beta	NR in source, estimated α and β assuming n=100	[82]
Number of days absent from work – adult	2.5 days	1	10	Lognormal	NR in source, SE assumed 20% of mean value	[62]
Number of days absent from school – children	3.7 days			Lognormal	NR in source, SE assumed 20% of mean value	[68]
Remaining carer years (after carer death)	10	6.5	14.3	Gamma	NR in source, SE assumed 20% of mean value	Assumption
Disease transmission						
Vaccine efficacy, poorly-matched year (<65 years)	42%	32%	52%	Beta	Assumed SE of 0.05	[11]
Vaccine efficacy, well-matched year(<65 years)	70%	57%	78%	Beta	95% CI 57% to 78%	[11]
Probability of a well-matched year(<65 years)	79%	-	-	Beta	α =11, β =3	Calculated
Vaccine efficacy, poorly-matched year (>64 years)	28%	19%	38%	Beta	95% CI 19% to 38%	[11]
Vaccine efficacy, well-matched year(>64 years)	46%	36%	56%	Beta	95% CI 36% to 56%	[11]
Probability of a well-matched year(>64 years)	79%	-	-	Beta	α =11, β =3	Calculated
Rate of vaccine side effects (injection)	2%	0%	5%	Beta	NR in source, estimated α and β assuming n=100	[43]
Rate of vaccine side effects (nasal spray)	3.1%	0%	5%	Beta	NR in source, estimated α and β assuming n=100	[13, 38]
Probability of being unvaccinated and infected by virus	18.00%	16%	22%	Beta	95% CI 16% to 22%	[36]
Proportion infectious cases that are ILI	18.00%	12%	24%	Beta	95% CI 12% to 24%	
Proportion infectious cases that are non-ILI	5.00%	1%	10%	Beta	95% CI 1% to 10%	
Deaths per 1,000 hospitalisations - low risk	6.1	5.7	6.4	Beta	95% CI 5.7 to 6.4	[3]
Deaths per 1,000 hospitalisations - low risk – high risk	40.0	37	43	Beta	95% CI 37 to 43	[3]
Secondary attack rate - carers	19%	12%	28%	Beta		[34]
Average number of extra ILI cases per HSCW	0.69	0.14		Beta	α =25, β =0.03	Calculated

APPENDIX D

Breakdown of Events, Costs and QALYs
Children

Table D1: Results of children analyses - events

	Vaccinated (difference from baseline)	Cases of influenza* (difference from baseline)	ILI		ARI (difference from baseline)	Deaths		GP consultations (difference from baseline)	Hospitalisations (difference from baseline)
			Child (difference from baseline)	Adult (difference from baseline)		Child (difference from baseline)	Adult (difference from baseline)		
Population-level results – total number of events									
Scenario 1	13,067,472	7,290,821	726,578	2,227,666	1,754,155	3.78	1,145	327,162	7,028
Scenario 12	12,744,340 (-323,132)	7,632,118 (341,297)	780,433 (53,855)	2,312,144 (84,478)	1,836,109 (81,954)	4.14 (0.36)	1,193 (49)	348,776 (21,614)	7,426 (398)
Scenario 13	13,973,271 (905,799)	6,418,806 (-872,015)	589,894 (-136,684)	2,010,859 (-216,807)	1,544,819 (-209,336)	3.03 (-0.75)	1,024 (-121)	271,528 (-55,634)	6,072 (-956)
Scenario 14	15,331,970 (2,264,498)	5,407,572 (-1,883,249)	444,780 (-281,798)	1,746,191 (-481,475)	1,301,906 (-452,248)	2.18 (-1.59)	871 (-273)	212,329 (-114,833)	4,939 (-2,089)
Scenario 15	16,237,769 (3,170,297)	4,894,027 (-2,396,794)	384,912 (-341,666)	1,597,915 (-629,751)	1,178,410 (-575,744)	1.75 (-2.02)	785 (-359)	186,807 (-140,355)	4,356 (-2,671)
Scenario 20	13,865,456 (797,984)	6,517,939 (-772,882)	605,729 (-120,849)	2,035,203 (-192,463)	1,568,582 (-185,573)	3.29 (-0.49)	1,037 (-108)	278,107 (-49,056)	6,180 (-848)
Individual-level results – number of events per targeted child									
Scenario 1	1.263	0.705	0.070	0.215	0.170	0.0000004	0.0001	0.032	0.0007
Scenario 12	1.232 (-0.031)	0.738 (0.033)	0.075 (0.005)	0.224 (0.008)	0.178 (0.008)	0.00012 (0.000005)	0.034 (0.002)	0.001 (0.00004)	0.00012 (0.000005)
Scenario 13	1.351 (0.088)	0.621 (-0.084)	0.057 (-0.013)	0.194 (-0.021)	0.149 (-0.02)	0.0001 (-0.00001)	0.026 (-0.005)	0.001 (-0.00009)	0.0001 (-0.00001)
Scenario 14	1.482 (0.219)	0.523 (-0.182)	0.043 (-0.027)	0.169 (-0.047)	0.126 (-0.044)	0.00008 (-0.00003)	0.021 (-0.011)	0. (-0.0002)	0.00008 (-0.00003)
Scenario 15	1.57 (0.306)	0.473 (-0.232)	0.037 (-0.033)	0.154 (-0.061)	0.114 (-0.056)	0.00008 (-0.00003)	0.018 (-0.014)	0. (-0.00026)	0.00008 (-0.00003)
Scenario 20	1.34 (0.077)	0.63 (-0.075)	0.059 (-0.012)	0.197 (-0.019)	0.152 (-0.018)	0.0001 (-0.00001)	0.027 (-0.005)	0.001 (-0.00008)	0.0001 (-0.00001)
Individual-level results – number of events per vaccinated child									
Scenario 1	1.000	0.558	0.056	0.170	0.134	0.0000003	0.0001	0.025	0.0005
Scenario 12	1.000 (0.000)	0.599 (0.041)	0.061 (0.006)	0.181 (0.011)	0.144 (0.010)	0.0000003 (0.00000004)	0.0001 (0.00001)	0.027 (0.002)	0.001 (0.00004)
Scenario 13	1.000 (0.000)	0.459 (-0.099)	0.042 (-0.013)	0.144 (-0.027)	0.111 (-0.024)	0.0000002 (-0.00000007)	0.0001 (-0.00001)	0.019 (-0.006)	0.000 (-0.00010)
Scenario 14	1.000 (0.000)	0.353 (-0.205)	0.029 (-0.027)	0.114 (-0.057)	0.085 (-0.049)	0.0000001 (-0.00000015)	0.0001 (-0.00003)	0.014 (-0.011)	0.000 (-0.00022)
Scenario 15	1.000 (0.000)	0.301 (-0.257)	0.024 (-0.032)	0.098 (-0.072)	0.073 (-0.062)	0.0000001 (-0.00000018)	0.0000 (-0.00004)	0.012 (-0.014)	0.000 (-0.00027)
Scenario 20	1.000 (0.000)	0.470 (-0.088)	0.044 (-0.012)	0.147 (-0.024)	0.113 (-0.021)	0.0000002 (-0.00000005)	0.0001 (-0.00001)	0.020 (-0.005)	0.000 (-0.00009)

* Symptomatic and non-symptomatic cases, ILI: influenza-like illness. ARI: acute respiratory infection. GP: general practitioner

Table D2: Results of children analyses - costs

Scenario	Vaccine	Vaccine side-effects	GP consultations	Hospitalisation	Total (NHS and PSS perspective)	Productivity loss	OTC medication	Travel cost	Total (societal perspective)
Population-level results – total costs (difference from baseline)									
Scenario 1	£196,360,042	£8,659,961	£11,676,422	£7,233,504	£223,929,929	£695,442,163	£15,037,099	£2,486,321	£936,895,512
Scenario 12	£191,659,185 (-£4,700,857)	£8,395,946 (-£264,015)	£12,447,815 (£771,393)	£7,643,603 (£410,099)	£220,146,549 (-£3,783,380)	£730,094,090 (£34,651,927)	£15,741,215 (£704,115)	£2,649,917 (£163,596)	£968,631,772 (£31,736,259)
Scenario 13	£207,305,795 (£10,945,753)	£9,348,902 (£688,942)	£9,690,849 (-£1,985,574)	£6,249,625 (-£983,879)	£232,595,171 (£8,665,242)	£607,069,848 (-£88,372,315)	£13,237,831 (-£1,799,268)	£2,065,921 (-£420,400)	£854,968,771 (-£81,926,741)
Scenario 14	£223,724,425 (£27,364,382)	£10,382,315 (£1,722,355)	£7,578,022 (-£4,098,400)	£5,083,588 (-£2,149,916)	£246,768,350 (£22,838,421)	£505,979,434 (-£189,462,729)	£11,152,041 (-£3,885,059)	£1,617,418 (-£868,902)	£765,517,243 (-£171,378,269)
Scenario 15	£234,670,178 (£38,310,135)	£11,071,257 (£2,411,296)	£6,667,157 (-£5,009,266)	£4,483,912 (-£2,749,592)	£256,892,503 (£32,962,574)	£456,027,005 (-£239,415,158)	£10,092,587 (-£4,944,512)	£1,423,118 (-£1,063,203)	£724,435,214 (-£212,460,298)
Scenario 20	£205,125,215 (£8,765,173)	£9,268,402 (£608,441)	£9,925,621 (-£1,750,802)	£6,360,681 (-£872,823)	£230,679,918 (£6,749,989)	£617,229,913 (-£78,212,250)	£13,442,343 (-£1,594,756)	£2,115,577 (-£370,743)	£863,467,752 (-£73,427,760)
Individual-level results – cost per targeted child (difference from baseline)									
Scenario 1	£18.98	£0.84	£1.13	£0.70	£21.65	£67.23	£1.45	£0.24	£90.57
Scenario 12	£18.53 (-£0.45)	£0.81 (-£0.03)	£1.20 (£0.07)	£0.74 (£0.04)	£21.28 (-£0.37)	£70.58 (£3.35)	£1.52 (£0.07)	£0.26 (£0.02)	£93.64 (£3.07)
Scenario 13	£20.04 (£1.06)	£0.90 (£0.07)	£0.94 (-£0.19)	£0.60 (-£0.10)	£22.49 (£0.84)	£58.69 (-£8.54)	£1.28 (-£0.17)	£0.20 (-£0.04)	£82.65 (-£7.92)
Scenario 14	£21.63 (£2.65)	£1.00 (£0.17)	£0.73 (-£0.40)	£0.49 (-£0.21)	£23.86 (£2.21)	£48.92 (-£18.32)	£1.08 (-£0.38)	£0.16 (-£0.08)	£74.01 (-£16.57)
Scenario 15	£22.69 (£3.70)	£1.07 (£0.23)	£0.64 (-£0.48)	£0.43 (-£0.27)	£24.84 (£3.19)	£44.09 (-£23.15)	£0.98 (-£0.48)	£0.14 (-£0.10)	£70.04 (-£20.54)
Scenario 20	£19.83 (£0.85)	£0.90 (£0.06)	£0.96 (-£0.17)	£0.61 (-£0.08)	£22.30 (£0.65)	£59.67 (-£7.56)	£1.30 (-£0.15)	£0.20 (-£0.04)	£83.48 (-£7.10)
Individual-level results – cost per vaccinated child (difference from baseline)									
Scenario 1	£15.03	£0.66	£0.89	£0.55	£17.14	£53.22	£1.15	£0.19	£71.70
Scenario 12	£15.04 (£0.01)	£0.66 (£0.00)	£0.98 (£0.08)	£0.60 (£0.05)	£17.27 (£0.14)	£57.29 (£4.07)	£1.24 (£0.08)	£0.21 (£0.02)	£76.00 (£4.31)
Scenario 13	£14.84 (-£0.19)	£0.67 (£0.01)	£0.69 (-£0.20)	£0.45 (-£0.11)	£16.65 (-£0.49)	£43.45 (-£9.77)	£0.95 (-£0.20)	£0.15 (-£0.04)	£61.19 (-£10.51)
Scenario 14	£14.59 (-£0.43)	£0.68 (£0.01)	£0.49 (-£0.40)	£0.33 (-£0.22)	£16.10 (-£1.04)	£33.00 (-£20.22)	£0.73 (-£0.42)	£0.11 (-£0.08)	£49.93 (-£21.77)

Scenario	Vaccine	Vaccine side-effects	GP consultations	Hospitalisation	Total (NHS and PSS perspective)	Productivity loss	OTC medication	Travel cost	Total (societal perspective)
Scenario 15	£14.45 (-£0.57)	£0.68 (£0.02)	£0.41 (-£0.48)	£0.28 (-£0.28)	£15.82 (-£1.32)	£28.08 (-£25.13)	£0.62 (-£0.53)	£0.09 (-£0.10)	£44.61 (-£27.08)
Scenario 20	£14.79 (-£0.23)	£0.67 (£0.01)	£0.72 (-£0.18)	£0.46 (-£0.09)	£16.64 (-£0.50)	£44.52 (-£8.70)	£0.97 (-£0.18)	£0.15 (-£0.04)	£62.27 (-£9.42)

Table D3: Results of children analyses – QALYs

Scenario	Vaccine side-effects (difference from baseline)	ILI (difference from baseline)	ARI (difference from baseline)	Hospitalisation (difference from baseline)	Death (difference from baseline)	Total (difference from baseline)
Population-level results – total QALY loss						
Scenario 1	419	23,634	1,772	127	2,328	28,279
Scenario 12	406.26 (-12.77)	24,741 (1,107)	1,854 (83)	133.67 (7.17)	2,429 (101)	29,564 (1,285)
Scenario 13	452.37 (33.34)	20,806 (-2,828)	1,560 (-211)	109.29 (-17.21)	2,076 (-252)	25,004 (-3,276)
Scenario 14	502.37 (83.34)	17,528 (-6,106)	1,315 (-457)	88.90 (-37.60)	1,766 (-562)	21,200 (-7,079)
Scenario 15	535.71 (116.68)	15,863 (-7,771)	1,190 (-582)	78.42 (-48.09)	1,593 (-735)	19,260 (-9,020)
Scenario 20	448.47 (29.44)	21,127 (-2,506)	1,584 (-187)	111.24 (-15.26)	2,107 (-221)	25,379 (-2,900)
Individual-level results – QALY loss per targeted child						
Scenario 1	0.00004	0.00228	0.00017	0.00001	0.00023	0.00273
Scenario 12	0.0000 (-0.000001)	0.0024 (0.000107)	0.0002 (0.000008)	0.0000 (0.000001)	0.0002 (0.000010)	0.0029 (0.000124)
Scenario 13	0.0000 (0.000003)	0.0020 (-0.000273)	0.0002 (-0.000020)	0.0000 (-0.000002)	0.0002 (-0.000024)	0.0024 (-0.000317)
Scenario 14	0.0000 (0.000008)	0.0017 (-0.000590)	0.0001 (-0.000044)	0.0000 (-0.000004)	0.0002 (-0.000054)	0.0020 (-0.000684)
Scenario 15	0.0001 (0.000011)	0.0015 (-0.000751)	0.0001 (-0.000056)	0.0000 (-0.000005)	0.0002 (-0.000071)	0.0019 (-0.000872)
Scenario 20	0.0000 (0.000003)	0.0020 (-0.000242)	0.0002 (-0.000018)	0.0000 (-0.000001)	0.0002 (-0.000021)	0.0025 (-0.000280)
Individual-level results – QALY loss per vaccinated child						
Scenario 1	0.000032067	0.00181	0.00014	0.00001	0.00018	**0.002**
Scenario 12	0.00003 (0.00000)	0.0019 (0.0001)	0.0001 (0.00001)	0.00001 (0.000001)	0.0002 (0.00001)	0.0023 (0.0002)
Scenario 13	0.00003 (0.00000)	0.0015 (-0.0003)	0.0001 (-0.00002)	0.00001 (-0.000002)	0.0001 (-0.00003)	0.0018 (-0.0004)
Scenario 14	0.00003 (0.00000)	0.0011 (-0.0007)	0.0001 (-0.00005)	0.00001 (-0.000004)	0.0001 (-0.00006)	0.0014 (-0.0008)

Scenario	Vaccine side-effects (difference from baseline)	ILI (difference from baseline)	ARI (difference from baseline)	Hospitalisation (difference from baseline)	Death (difference from baseline)	Total (difference from baseline)
Scenario 15	0.00003 (0.00000)	0.0010 (-0.0008)	0.0001 (-0.00006)	0.00000 (-0.000005)	0.0001 (-0.00008)	0.0012 (-0.0010)
Scenario 20	0.00003 (0.00000)	0.0015 (-0.0003)	0.0001 (-0.00002)	0.00001 (-0.000002)	0.0002 (-0.00003)	0.0018 (-0.0003)

APPENDIX E

Breakdown of Events, Costs and QALYs
Clinical Risk Groups

Table E1: Results of clinical risk group analyses – events

	Vaccinated (difference from baseline)	Cases of influenza* (difference from baseline)	ILI (difference from baseline)		ARI (difference from baseline)	Deaths (difference from baseline)		GP consultations (difference from baseline)	Hospitalisations (difference from baseline)
			Child	Adult		Child	Adult		
Population-level results – total number of events (difference from baseline)									
Scenario 1	13,067,472	7,290,821	726,578	2,227,666	1,754,155	3.78	1,145	327,162	7,028
Scenario 2	12,798,509 (-268,963)	7,605,761 (314,940)	751,579 (25,002)	2,330,328 (102,662)	1,829,810 (75,655)	3.89 (0.11)	1,191 (46)	339,658 (12,496)	7,297 (269)
Scenario 3	13,336,435 (268,963)	6,974,784 (-316,037)	701,411 (-25,166)	2,124,746 (-102,920)	1,678,220 (-75,935)	3.66 (-0.11)	1,099 (-46)	314,624 (-12,538)	6,759 (-269)
Scenario 4	13,874,360 (806,888)	6,342,816 (-948,005)	650,826 (-75,751)	1,919,162 (-308,504)	1,526,361 (-227,794)	3.44 (-0.34)	1,007 (-138)	289,570 (-37,592)	6,223 (-805)
Scenario 5	14,670,489 (1,603,017)	5,426,952 (-1,863,869)	576,485 (-150,093)	1,622,354 (-605,312)	1,306,174 (-447,980)	3.09 (-0.68)	873 (-272)	253,102 (-74,060)	5,443 (-1,584)
Scenario 6	15,219,173 (2,151,701)	4,865,737 (-2,425,084)	529,867 (-196,711)	1,441,549 (-786,117)	1,171,209 (-582,946)	2.87 (-0.91)	790 (-355)	230,484 (-96,678)	4,955 (-2,073)
Scenario 7	13,035,627 (-31,845)	7,333,957 (43,136)	730,082 (3,504)	2,241,650 (13,984)	1,764,533 (10,378)	3.79 (0.02)	1,151 (6)	328,834 (1,672)	7,075 (47)
Scenario 8	13,099,317 (31,845)	7,247,653 (-43,168)	723,065 (-3,513)	2,213,668 (-13,998)	1,743,762 (-10,393)	3.76 (-0.02)	1,139 (-6)	325,488 (-1,674)	6,981 (-47)
Scenario 9	13,163,006 (95,534)	7,161,325 (-129,496)	716,043 (-10,534)	2,185,717 (-41,949)	1,722,992 (-31,163)	3.73 (-0.05)	1,127 (-17)	322,137 (-5,025)	6,887 (-140)
Scenario 10	13,226,695 (159,223)	7,074,846 (-215,975)	709,002 (-17,575)	2,157,702 (-69,964)	1,702,207 (-51,948)	3.70 (-0.08)	1,116 (-29)	318,783 (-8,379)	6,794 (-233)
Scenario 11	13,290,384 (222,912)	6,988,364 (-302,457)	701,962 (-24,616)	2,129,723 (-97,943)	1,681,397 (-72,758)	3.67 (-0.11)	1,104 (-41)	315,423 (-11,740)	6,702 (-326)
Scenario 16	13,010,096 (-57,376)	7,346,473 (55,652)	735,468 (8,891)	2,241,334 (13,668)	1,767,506 (13,351)	3.94 (0.16)	1,153 (8)	330,797 (3,635)	7,089 (61)
Scenario 17	13,182,224 (114,752)	7,180,008 (-110,813)	708,915 (-17,662)	2,200,397 (-27,269)	1,727,553 (-26,602)	3.47 (-0.31)	1,129 (-15)	319,900 (-7,262)	6,907 (-121)
Scenario 18	13,354,351 (286,879)	7,015,816 (-275,005)	682,880 (-43,698)	2,159,874 (-67,792)	1,688,144 (-66,011)	3.03 (-0.74)	1,107 (-38)	309,111 (-18,051)	6,728 (-300)
Scenario 19	13,469,103 (401,631)	6,908,416 (-382,405)	665,943 (-60,635)	2,133,232 (-94,434)	1,662,371 (-91,783)	2.76 (-1.02)	1,092 (-53)	302,061 (-25,101)	6,612 (-416)

	Vaccinated (difference from baseline)	Cases of influenza* (difference from baseline)	ILI (difference from baseline)		ARI (difference from baseline)	Deaths (difference from baseline)		GP consultations (difference from baseline)	Hospitalisations (difference from baseline)
			Child	Adult		Child	Adult		
Individual-level results – number of events per targeted person (difference from baseline)									
Scenario 1	2.521	1.407	0.140	0.430	0.338	0.0000007	0.0002	0.063	0.0014
Scenario 2	2.47 (-0.052)	1.468 (0.061)	0.145 (0.005)	0.45 (0.02)	0.353 (0.015)	0.000001 (0.00000002)	0.00023 (0.000009)	0.066 (0.002)	0.001 (0.00005)
Scenario 3	2.573 (0.052)	1.346 (-0.061)	0.135 (-0.005)	0.41 (-0.02)	0.324 (-0.015)	0.000001 (-0.00000002)	0.00021 (-0.00001)	0.061 (-0.002)	0.001 (-0.00005)
Scenario 4	2.677 (0.156)	1.224 (-0.183)	0.126 (-0.015)	0.37 (-0.06)	0.295 (-0.044)	0.000001 (-0.00000007)	0.00019 (-0.00003)	0.056 (-0.007)	0.001 (-0.00016)
Scenario 5	2.831 (0.309)	1.047 (-0.36)	0.111 (-0.029)	0.313 (-0.117)	0.252 (-0.086)	0.000001 (-0.00000013)	0.00017 (-0.00005)	0.049 (-0.014)	0.001 (-0.00031)
Scenario 6	2.937 (0.415)	0.939 (-0.468)	0.102 (-0.038)	0.278 (-0.152)	0.226 (-0.112)	0.000001 (-0.00000017)	0.00015 (-0.00007)	0.044 (-0.019)	0.001 (-0.0004)
Scenario 7	20.468 (-0.05)	11.515 (0.068)	1.146 (0.006)	3.52 (0.022)	2.771 (0.016)	0.000006 (0.00000003)	0.00181 (0.000009)	0.516 (0.003)	0.011 (0.00007)
Scenario 8	20.568 (0.05)	11.38 (-0.068)	1.135 (-0.006)	3.476 (-0.022)	2.738 (-0.016)	0.000006 (-0.00000002)	0.00179 (-0.00001)	0.511 (-0.003)	0.011 (-0.00007)
Scenario 9	20.668 (0.15)	11.244 (-0.203)	1.124 (-0.017)	3.432 (-0.066)	2.705 (-0.049)	0.000006 (-0.00000007)	0.00177 (-0.00003)	0.506 (-0.008)	0.011 (-0.00022)
Scenario 10	20.768 (0.25)	11.108 (-0.339)	1.113 (-0.028)	3.388 (-0.11)	2.673 (-0.082)	0.000006 (-0.00000012)	0.00175 (-0.00005)	0.501 (-0.013)	0.011 (-0.00037)
Scenario 11	20.868 (0.35)	10.973 (-0.475)	1.102 (-0.039)	3.344 (-0.154)	2.64 (-0.114)	0.000006 (-0.00000017)	0.00173 (-0.00006)	0.495 (-0.018)	0.011 (-0.00051)
Scenario 16	9.804 (-0.043)	5.536 (0.042)	0.554 (0.007)	1.689 (0.01)	1.332 (0.01)	0.000003 (0.00000012)	0.00087 (0.000006)	0.249 (0.003)	0.005 (0.00005)
Scenario 17	9.933 (0.086)	5.41 (-0.084)	0.534 (-0.013)	1.658 (-0.021)	1.302 (-0.02)	0.000003 (-0.00000023)	0.00085 (-0.00001)	0.241 (-0.005)	0.005 (-0.00009)
Scenario 18	10.063 (0.216)	5.287 (-0.207)	0.515 (-0.033)	1.628 (-0.051)	1.272 (-0.05)	0.000002 (-0.00000056)	0.00083 (-0.00003)	0.233 (-0.014)	0.005 (-0.00023)
Scenario 19	10.15 (0.303)	5.206 (-0.288)	0.502 (-0.046)	1.607 (-0.071)	1.253 (-0.069)	0.000002 (-0.00000077)	0.00082 (-0.00004)	0.228 (-0.019)	0.005 (-0.00031)
Individual-level results – number of events per vaccinated person (difference from baseline)									
Scenario 1	1.000	0.558	0.056	0.170	0.134	0.0000003	0.0001	0.025	0.0005
Scenario 2	1.000 (0.000)	0.594 (0.036)	0.059 (0.003)	0.182 (0.012)	0.143 (0.009)	0.0000003 (0.00000001)	0.0001 (0.00001)	0.027 (0.002)	0.001 (0.00003)

	Vaccinated (difference from baseline)	Cases of influenza* (difference from baseline)	ILI (difference from baseline)		ARI (difference from baseline)	Deaths (difference from baseline)		GP consultations (difference from baseline)	Hospitalisations (difference from baseline)
			Child	Adult		Child	Adult		
Scenario 3	1.000 (0.000)	0.523 (-0.035)	0.053 (-0.003)	0.159 (-0.011)	0.126 (-0.008)	0.0000003 (-0.00000001)	0.0001 (-0.00001)	0.024 (-0.001)	0.001 (-0.00003)
Scenario 4	1.000 (0.000)	0.457 (-0.101)	0.047 (-0.009)	0.138 (-0.032)	0.110 (-0.024)	0.0000002 (-0.00000004)	0.0001 (-0.00002)	0.021 (-0.004)	0.0004 (-0.00009)
Scenario 5	1.000 (0.000)	0.370 (-0.188)	0.039 (-0.016)	0.111 (-0.060)	0.089 (-0.045)	0.0000002 (-0.00000008)	0.0001 (-0.00003)	0.017 (-0.008)	0.0004 (-0.00017)
Scenario 6	1.000 (0.000)	0.320 (-0.238)	0.035 (-0.021)	0.095 (-0.076)	0.077 (-0.057)	0.0000002 (-0.00000010)	0.0001 (-0.00004)	0.015 (-0.010)	0.0003 (-0.00021)
Scenario 7	1.000 (0.000)	0.563 (0.005)	0.056 (0.000)	0.172 (0.001)	0.135 (0.001)	0.0000003 (0.00000000)	0.0001 (0.00000)	0.025 (0.000)	0.001 (0.00000)
Scenario 8	1.000 (0.000)	0.553 (-0.005)	0.055 (0.000)	0.169 (-0.001)	0.133 (-0.001)	0.0000003 (0.00000000)	0.0001 (0.00000)	0.025 (0.000)	0.001 (0.00000)
Scenario 9	1.000 (0.000)	0.544 (-0.014)	0.054 (-0.001)	0.166 (-0.004)	0.131 (-0.003)	0.0000003 (-0.00000001)	0.0001 (0.00000)	0.024 (-0.001)	0.0005 (-0.00001)
Scenario 10	1.000 (0.000)	0.535 (-0.023)	0.054 (-0.002)	0.163 (-0.007)	0.129 (-0.006)	0.0000003 (-0.00000001)	0.0001 (0.00000)	0.024 (-0.001)	0.0005 (-0.00002)
Scenario 11	1.000 (0.000)	0.526 (-0.032)	0.053 (-0.003)	0.160 (-0.010)	0.127 (-0.008)	0.0000003 (-0.00000001)	0.0001 (0.00000)	0.024 (-0.001)	0.0005 (-0.00003)
Scenario 16	1.000 (0.000)	0.565 (0.007)	0.057 (0.001)	0.172 (0.002)	0.136 (0.002)	0.0000003 (0.00000001)	0.0001 (0.00000)	0.025 (0.000)	0.001 (0.00001)
Scenario 17	1.000 (0.000)	0.545 (-0.013)	0.054 (-0.002)	0.167 (-0.004)	0.131 (-0.003)	0.0000003 (-0.00000003)	0.0001 (0.00000)	0.024 (-0.001)	0.001 (-0.00001)
Scenario 18	1.000 (0.000)	0.525 (-0.033)	0.051 (-0.004)	0.162 (-0.009)	0.126 (-0.008)	0.0000002 (-0.00000006)	0.0001 (0.00000)	0.023 (-0.002)	0.0005 (-0.00003)
Scenario 19	1.000 (0.000)	0.513 (-0.045)	0.049 (-0.006)	0.158 (-0.012)	0.123 (-0.011)	0.0000002 (-0.00000008)	0.0001 (-0.00001)	0.022 (-0.003)	0.0005 (-0.00005)

* Symptomatic and non-symptomatic cases

ILI: influenza-like illness. ARI: acute respiratory infection. GP: general practitioner

Table E2: Results of clinical risk group analyses – costs

Scenario	Vaccine	Vaccine side-effects	GP consultations	Hospitalisation	Total (NHS and PSS perspective)	Productivity loss	OTC medication	Travel cost	Total (societal perspective)
Population-level results – total costs (difference from baseline)									
Scenario 1	£196,360,042	£8,659,961	£11,676,422	£7,233,504	£223,929,929	£695,442,163	£15,037,099	£2,486,321	£936,895,512
Scenario 2	£192,120,346 (-£4,239,697)	£8,493,204 (-£166,757)	£12,122,394 (£445,972)	£7,510,473 (£276,969)	£220,246,416 (-£3,683,513)	£724,825,979 (£29,383,816)	£15,686,907 (£649,807)	£2,581,290 (£94,970)	£963,340,592 (£26,445,080)
Scenario 3	£200,599,739 (£4,239,697)	£8,826,717 (£166,757)	£11,228,927 (-£447,495)	£6,956,755 (-£276,749)	£227,612,138 (£3,682,209)	£665,952,642 (-£29,489,521)	£14,385,140 (-£651,960)	£2,391,038 (-£95,283)	£910,340,958 (-£26,554,554)
Scenario 4	£209,079,133 (£12,719,090)	£9,160,231 (£500,270)	£10,334,764 (-£1,341,658)	£6,405,456 (-£828,048)	£234,979,584 (£11,049,655)	£606,948,392 (-£88,493,771)	£13,081,240 (-£1,955,859)	£2,200,665 (-£285,656)	£857,209,881 (-£79,685,631)
Scenario 5	£221,628,635 (£25,268,593)	£9,653,831 (£993,871)	£9,033,221 (-£2,643,201)	£5,602,682 (-£1,630,822)	£245,918,370 (£21,988,441)	£521,349,238 (-£174,092,925)	£11,192,088 (-£3,845,011)	£1,923,555 (-£562,766)	£780,383,251 (-£156,512,261)
Scenario 6	£230,277,617 (£33,917,574)	£9,994,015 (£1,334,055)	£8,225,981 (-£3,450,441)	£5,099,648 (-£2,133,856)	£253,597,261 (£29,667,332)	£468,784,463 (-£226,657,700)	£10,034,506 (-£5,002,593)	£1,751,636 (-£734,684)	£734,167,867 (-£202,727,645)
Scenario 7	£195,858,083 (-£501,959)	£8,640,217 (-£19,744)	£11,736,096 (£59,674)	£7,281,877 (£48,374)	£223,516,274 (-£413,655)	£699,475,598 (£4,033,435)	£15,126,113 (£89,014)	£2,499,138 (£12,818)	£940,617,124 (£3,721,612)
Scenario 8	£196,862,001 (£501,959)	£8,679,704 (£19,744)	£11,616,670 (-£59,752)	£7,185,210 (-£48,293)	£224,343,586 (£413,657)	£691,403,469 (-£4,038,694)	£14,947,971 (-£89,128)	£2,473,487 (-£12,833)	£933,168,514 (-£3,726,999)
Scenario 9	£197,865,919 (£1,505,876)	£8,719,192 (£59,231)	£11,497,073 (-£179,349)	£7,089,019 (-£144,485)	£225,171,202 (£1,241,273)	£683,336,247 (-£12,105,916)	£14,769,960 (-£267,139)	£2,447,806 (-£38,515)	£925,725,216 (-£11,170,296)
Scenario 10	£198,869,836 (£2,509,794)	£8,758,679 (£98,718)	£11,377,376 (-£299,047)	£6,993,266 (-£240,238)	£225,999,157 (£2,069,228)	£675,249,525 (-£20,192,638)	£14,591,525 (-£445,574)	£2,422,107 (-£64,213)	£918,262,315 (-£18,633,197)
Scenario 11	£199,873,754 (£3,513,712)	£8,798,166 (£138,206)	£11,257,440 (-£418,983)	£6,898,006 (-£335,498)	£226,827,366 (£2,897,437)	£667,170,485 (-£28,271,678)	£14,413,276 (-£623,824)	£2,396,365 (-£89,956)	£910,807,491 (-£26,088,021)
Scenario 16	£195,215,129 (-£1,144,914)	£8,617,560 (-£42,401)	£11,806,156 (£129,733)	£7,296,526 (£63,022)	£222,935,370 (-£994,559)	£701,151,637 (£5,709,474)	£15,151,922 (£114,823)	£2,513,776 (£27,456)	£941,752,706 (£4,857,194)
Scenario 17	£198,649,869 (£2,289,827)	£8,744,762 (£84,801)	£11,417,231 (-£259,191)	£7,108,749 (-£124,755)	£225,920,611 (£1,990,682)	£684,078,943 (-£11,363,220)	£14,808,399 (-£228,701)	£2,431,479 (-£54,842)	£927,239,432 (-£9,656,081)
Scenario 18	£202,084,610 (£5,724,568)	£8,871,964 (£212,004)	£11,032,168 (-£644,254)	£6,925,139 (-£308,365)	£228,913,881 (£4,983,952)	£667,266,538 (-£28,175,625)	£14,469,617 (-£567,483)	£2,350,021 (-£136,300)	£913,000,057 (-£23,895,456)
Scenario 19	£204,374,437 (£8,014,395)	£8,956,766 (£296,805)	£10,780,564 (-£895,858)	£6,805,371 (-£428,133)	£230,917,138 (£6,987,209)	£656,273,737 (-£39,168,426)	£14,247,801 (-£789,299)	£2,296,797 (-£189,524)	£903,735,472 (-£33,160,040)
Individual-level results – cost per targeted person (difference from baseline)									
Scenario 1	£147.97	£6.53	£8.80	£5.45	£168.74	£524.05	£11.33	£1.87	£705.99

Scenario	Vaccine	Vaccine side-effects	GP consultations	Hospitalisation	Total (NHS and PSS perspective)	Productivity loss	OTC medication	Travel cost	Total (societal perspective)
Scenario 2	£37.07 (-£0.82)	£1.64 (-£0.03)	£2.34 (£0.09)	£1.45 (£0.05)	£42.50 (-£0.71)	£139.86 (£5.67)	£3.03 (£0.13)	£0.50 (£0.02)	£185.88 (£5.10)
Scenario 3	£38.71 (£0.82)	£1.70 (£0.03)	£2.17 (-£0.09)	£1.34 (-£0.05)	£43.92 (£0.71)	£128.50 (-£5.69)	£2.78 (-£0.13)	£0.46 (-£0.02)	£175.66 (-£5.12)
Scenario 4	£40.34 (£2.45)	£1.77 (£0.10)	£1.99 (-£0.26)	£1.24 (-£0.16)	£45.34 (£2.13)	£117.12 (-£17.08)	£2.52 (-£0.38)	£0.42 (-£0.06)	£165.41 (-£15.38)
Scenario 5	£42.77 (£4.88)	£1.86 (£0.19)	£1.74 (-£0.51)	£1.08 (-£0.31)	£47.45 (£4.24)	£100.60 (-£33.59)	£2.16 (-£0.74)	£0.37 (-£0.11)	£150.58 (-£30.20)
Scenario 6	£44.43 (£6.54)	£1.93 (£0.26)	£1.59 (-£0.67)	£0.98 (-£0.41)	£48.93 (£5.72)	£90.46 (-£43.74)	£1.94 (-£0.97)	£0.34 (-£0.14)	£141.66 (-£39.12)
Scenario 7	£307.52 (-£0.79)	£13.57 (-£0.03)	£18.43 (£0.09)	£11.43 (£0.08)	£350.95 (-£0.65)	£1098.26 (£6.33)	£23.75 (£0.14)	£3.92 (£0.02)	£1476.89 (£5.84)
Scenario 8	£309.10 (£0.79)	£13.63 (£0.03)	£18.24 (-£0.09)	£11.28 (-£0.08)	£352.25 (£0.65)	£1085.59 (-£6.34)	£23.47 (-£0.14)	£3.88 (-£0.02)	£1465.19 (-£5.85)
Scenario 9	£310.67 (£2.36)	£13.69 (£0.09)	£18.05 (-£0.28)	£11.13 (-£0.23)	£353.55 (£1.95)	£1072.92 (-£19.01)	£23.19 (-£0.42)	£3.84 (-£0.06)	£1453.50 (-£17.54)
Scenario 10	£312.25 (£3.94)	£13.75 (£0.16)	£17.86 (-£0.47)	£10.98 (-£0.38)	£354.85 (£3.25)	£1060.23 (-£31.70)	£22.91 (-£0.70)	£3.80 (-£0.10)	£1441.79 (-£29.26)
Scenario 11	£313.83 (£5.52)	£13.81 (£0.22)	£17.68 (-£0.66)	£10.83 (-£0.53)	£356.15 (£4.55)	£1047.54 (-£44.39)	£22.63 (-£0.98)	£3.76 (-£0.14)	£1430.08 (-£40.96)
Scenario 16	£147.10 (-£0.86)	£6.49 (-£0.03)	£8.90 (£0.10)	£5.50 (£0.05)	£167.99 (-£0.75)	£528.35 (£4.30)	£11.42 (£0.09)	£1.89 (£0.02)	£709.65 (£3.66)
Scenario 17	£149.69 (£1.73)	£6.59 (£0.06)	£8.60 (-£0.20)	£5.36 (-£0.09)	£170.24 (£1.50)	£515.49 (-£8.56)	£11.16 (-£0.17)	£1.83 (-£0.04)	£698.72 (-£7.28)
Scenario 18	£152.28 (£4.31)	£6.69 (£0.16)	£8.31 (-£0.49)	£5.22 (-£0.23)	£172.50 (£3.76)	£502.82 (-£21.23)	£10.90 (-£0.43)	£1.77 (-£0.10)	£687.99 (-£18.01)
Scenario 19	£154.01 (£6.04)	£6.75 (£0.22)	£8.12 (-£0.68)	£5.13 (-£0.32)	£174.01 (£5.27)	£494.53 (-£29.52)	£10.74 (-£0.59)	£1.73 (-£0.14)	£681.01 (-£24.99)
Individual-level results – cost per vaccinated person(difference from baseline)									
Scenario 1	£15.03	£0.66	£0.89	£0.55	£17.14	£53.22	£1.15	£0.19	£71.70
Scenario 2	£15.01 (-£0.02)	£0.66 (£0.00)	£0.95 (£0.05)	£0.59 (£0.03)	£17.21 (£0.07)	£56.63 (£3.41)	£1.23 (£0.07)	£0.20 (£0.01)	£75.27 (£3.57)
Scenario 3	£15.04 (£0.01)	£0.66 (£0.00)	£0.84 (-£0.05)	£0.52 (-£0.03)	£17.07 (-£0.07)	£49.93 (-£3.28)	£1.08 (-£0.07)	£0.18 (-£0.01)	£68.26 (-£3.44)

Scenario	Vaccine	Vaccine side-effects	GP consultations	Hospitalisation	Total (NHS and PSS perspective)	Productivity loss	OTC medication	Travel cost	Total (societal perspective)
Scenario 4	£15.07 (£0.04)	£0.66 (£0.00)	£0.74 (-£0.15)	£0.46 (-£0.09)	£16.94 (-£0.20)	£43.75 (-£9.47)	£0.94 (-£0.21)	£0.16 (-£0.03)	£61.78 (-£9.91)
Scenario 5	£15.11 (£0.08)	£0.66 (£0.00)	£0.62 (-£0.28)	£0.38 (-£0.17)	£16.76 (-£0.37)	£35.54 (-£17.68)	£0.76 (-£0.39)	£0.13 (-£0.06)	£53.19 (-£18.50)
Scenario 6	£15.13 (£0.10)	£0.66 (-£0.01)	£0.54 (-£0.35)	£0.34 (-£0.22)	£16.66 (-£0.47)	£30.80 (-£22.42)	£0.66 (-£0.49)	£0.12 (-£0.08)	£48.24 (-£23.46)
Scenario 7	£15.02 (£0.00)	£0.66 (£0.00)	£0.90 (£0.01)	£0.56 (£0.01)	£17.15 (£0.01)	£53.66 (£0.44)	£1.16 (£0.01)	£0.19 (£0.00)	£72.16 (£0.46)
Scenario 8	£15.03 (£0.00)	£0.66 (£0.00)	£0.89 (-£0.01)	£0.55 (-£0.01)	£17.13 (-£0.01)	£52.78 (-£0.44)	£1.14 (-£0.01)	£0.19 (£0.00)	£71.24 (-£0.46)
Scenario 9	£15.03 (£0.01)	£0.66 (£0.00)	£0.87 (-£0.02)	£0.54 (-£0.01)	£17.11 (-£0.03)	£51.91 (-£1.31)	£1.12 (-£0.03)	£0.19 (£0.00)	£70.33 (-£1.37)
Scenario 10	£15.04 (£0.01)	£0.66 (£0.00)	£0.86 (-£0.03)	£0.53 (-£0.02)	£17.09 (-£0.05)	£51.05 (-£2.17)	£1.10 (-£0.05)	£0.18 (-£0.01)	£69.42 (-£2.27)
Scenario 11	£15.04 (£0.01)	£0.66 (£0.00)	£0.85 (-£0.05)	£0.52 (-£0.03)	£17.07 (-£0.07)	£50.20 (-£3.02)	£1.08 (-£0.07)	£0.18 (-£0.01)	£68.53 (-£3.17)
Scenario 16	£15.00 (-£0.02)	£0.66 (£0.00)	£0.91 (£0.01)	£0.56 (£0.01)	£17.14 (£0.00)	£53.89 (£0.67)	£1.16 (£0.01)	£0.19 (£0.00)	£72.39 (£0.69)
Scenario 17	£15.07 (£0.04)	£0.66 (£0.00)	£0.87 (-£0.03)	£0.54 (-£0.01)	£17.14 (£0.00)	£51.89 (-£1.33)	£1.12 (-£0.03)	£0.18 (-£0.01)	£70.34 (-£1.36)
Scenario 18	£15.13 (£0.11)	£0.66 (£0.00)	£0.83 (-£0.07)	£0.52 (-£0.03)	£17.14 (£0.01)	£49.97 (-£3.25)	£1.08 (-£0.07)	£0.18 (-£0.01)	£68.37 (-£3.33)
Scenario 19	£15.17 (£0.15)	£0.66 (£0.00)	£0.80 (-£0.09)	£0.51 (-£0.05)	£17.14 (£0.01)	£48.72 (-£4.49)	£1.06 (-£0.09)	£0.17 (-£0.02)	£67.10 (-£4.60)

Table E3: Results of clinical risk group analyses – QALYs

Scenario	Vaccine side-effects (difference from baseline)	ILI (difference from baseline)	ARI (difference from baseline)	Hospitalisation (difference from baseline)	Death (difference from baseline)	Total (difference from baseline)
Population-level results – total QALY loss (difference from baseline)						
Scenario 1	392	23,634	1,772	127	2,328	**28,252**
Scenario 2	410.96 (-8.07)	24,655 (1,021)	1,848 (76)	131.34 (4.84)	2,443 (115)	29,488 (1,209)
Scenario 3	427.10 (8.07)	22,609 (-1,025)	1,695 (-77)	121.66 (-4.84)	2,215 (-113)	27,068 (-1,211)
Scenario 4	443.24 (24.21)	20,560 (-3,074)	1,542 (-230)	112.02 (-14.48)	1,993 (-335)	24,650 (-3,629)
Scenario 5	467.12 (48.09)	17,591 (-6,043)	1,319 (-452)	97.98 (-28.52)	1,681 (-647)	21,156 (-7,123)
Scenario 6	483.58 (64.55)	15,771 (-7,863)	1,183 (-589)	89.18 (-37.32)	1,493 (-835)	19,020 (-9,260)
Scenario 7	418.08 (-0.96)	23,774 (140)	1,782 (10)	127.35 (0.85)	2,341 (13)	28,442 (163)
Scenario 8	419.99 (0.96)	23,494 (-140)	1,761 (-10)	125.66 (-0.84)	2,315 (-13)	28,116 (-163)
Scenario 9	421.90 (2.87)	23,214 (-420)	1,740 (-31)	123.97 (-2.53)	2,290 (-38)	27,790 (-489)
Scenario 10	423.81 (4.78)	22,934 (-700)	1,719 (-52)	122.30 (-4.20)	2,264 (-64)	27,463 (-816)
Scenario 11	425.72 (6.69)	22,653 (-980)	1,698 (-73)	120.63 (-5.87)	2,239 (-89)	27,137 (-1,142)
Scenario 16	416.98 (-2.05)	23,814 (180)	1,785 (13)	127.60 (1.10)	2,346 (18)	28,490 (211)
Scenario 17	423.13 (4.10)	23,274 (-359)	1,745 (-27)	124.32 (-2.18)	2,292 (-36)	27,859 (-420)
Scenario 18	429.29 (10.26)	22,742 (-892)	1,705 (-67)	121.11 (-5.39)	2,239 (-89)	27,237 (-1,043)
Scenario 19	433.39 (14.36)	22,393 (-1,241)	1,679 (-93)	119.01 (-7.49)	2,205 (-123)	26,829 (-1,450)
Individual-level results – QALY loss per targeted person (difference from baseline)						
Scenario 1	0.00006	0.00334	0.00025	0.00002	0.00033	**0.00400**
Scenario 2	0.0001 (-0.000002)	0.0048 (0.000197)	0.0004 (0.000015)	0.0000 (0.000001)	0.0005 (0.000022)	0.0057 (0.000233)
Scenario 3	0.0001 (0.000002)	0.0044 (-0.000198)	0.0003 (-0.000015)	0.0000 (-0.000001)	0.0004 (-0.000022)	0.0052 (-0.000234)
Scenario 4	0.0001 (0.000005)	0.0040 (-0.000593)	0.0003 (-0.000044)	0.0000 (-0.000003)	0.0004 (-0.000065)	0.0048 (-0.000700)

Scenario	Vaccine side-effects (difference from baseline)	ILI (difference from baseline)	ARI (difference from baseline)	Hospitalisation (difference from baseline)	Death (difference from baseline)	Total (difference from baseline)
Scenario 5	0.0001 (0.000009)	0.0034 (-0.001166)	0.0003 (-0.000087)	0.0000 (-0.000006)	0.0003 (-0.000125)	0.0041 (-0.001374)
Scenario 6	0.0001 (0.000012)	0.0030 (-0.001517)	0.0002 (-0.000114)	0.0000 (-0.000007)	0.0003 (-0.000161)	0.0037 (-0.001787)
Scenario 7	0.0007 (-0.000001)	0.0373 (0.000220)	0.0028 (0.000016)	0.0002 (0.000001)	0.0037 (0.000020)	0.0447 (0.000256)
Scenario 8	0.0007 (0.000002)	0.0369 (-0.000220)	0.0028 (-0.000016)	0.0002 (-0.000001)	0.0036 (-0.000020)	0.0441 (-0.000256)
Scenario 9	0.0007 (0.000005)	0.0364 (-0.000659)	0.0027 (-0.000049)	0.0002 (-0.000004)	0.0036 (-0.000060)	0.0436 (-0.000768)
Scenario 10	0.0007 (0.000008)	0.0360 (-0.001100)	0.0027 (-0.000082)	0.0002 (-0.000007)	0.0036 (-0.000100)	0.0431 (-0.001281)
Scenario 11	0.0007 (0.000011)	0.0356 (-0.001539)	0.0027 (-0.000115)	0.0002 (-0.000009)	0.0035 (-0.000140)	0.0426 (-0.001793)
Scenario 16	0.0003 (-0.000002)	0.0179 (0.000136)	0.0013 (0.000010)	0.0001 (0.000001)	0.0018 (0.000014)	0.0215 (0.000159)
Scenario 17	0.0003 (0.000003)	0.0175 (-0.000271)	0.0013 (-0.000020)	0.0001 (-0.000002)	0.0017 (-0.000027)	0.0210 (-0.000317)
Scenario 18	0.0003 (0.000008)	0.0171 (-0.000672)	0.0013 (-0.000050)	0.0001 (-0.000004)	0.0017 (-0.000067)	0.0205 (-0.000786)
Scenario 19	0.0003 (0.000011)	0.0169 (-0.000935)	0.0013 (-0.000070)	0.0001 (-0.000006)	0.0017 (-0.000093)	0.0202 (-0.001092)
Individual-level results – QALY loss per vaccinated person (difference from baseline)						
Scenario 1	0.00003	0.00181	0.00014	0.00001 (-0.000008)	0.00019 (-0.000139)	**0.00230 (-0.001695)**
Scenario 2	0.00003 (0.00000)	0.0019 (0.0001)	0.0001 (0.00001)	0.00001 (0.000001)	0.0002 (0.00001)	0.0023 (0.0001)
Scenario 3	0.00003 (0.00000)	0.0017 (-0.0001)	0.0001 (-0.00001)	0.00001 (-0.000001)	0.0002 (-0.00001)	0.0020 (-0.0001)
Scenario 4	0.00003 (0.00000)	0.0015 (-0.0003)	0.0001 (-0.00002)	0.00001 (-0.000002)	0.0001 (-0.00003)	0.0018 (-0.0004)
Scenario 5	0.00003 (0.00000)	0.0012 (-0.0006)	0.0001 (-0.00005)	0.00001 (-0.000003)	0.0001 (-0.00006)	0.0014 (-0.0007)
Scenario 6	0.00003 (0.00000)	0.0010 (-0.0008)	0.0001 (-0.00006)	0.00001 (-0.000004)	0.0001 (-0.00008)	0.0012 (-0.0009)
Scenario 7	0.00003 (0.00000)	0.0018 (0.0000)	0.0001 (0.00000)	0.00001 (0.000000)	0.0002 (0.00000)	0.0022 (0.0000)
Scenario 8	0.00003 (0.00000)	0.0018 (0.0000)	0.0001 (0.00000)	0.00001 (0.000000)	0.0002 (0.00000)	0.0021 (0.0000)
Scenario 9	0.00003 (0.00000)	0.0018 (0.0000)	0.0001 (0.00000)	0.00001 (0.000000)	0.0002 (0.00000)	0.0021 (-0.0001)
Scenario 10	0.00003 (0.00000)	0.0017 (-0.0001)	0.0001 (-0.00001)	0.00001 (0.000000)	0.0002 (-0.00001)	0.0021 (-0.0001)

Scenario	Vaccine side-effects (difference from baseline)	ILI (difference from baseline)	ARI (difference from baseline)	Hospitalisation (difference from baseline)	Death (difference from baseline)	Total (difference from baseline)
Scenario 11	0.00003 (0.00000)	0.0017 (-0.0001)	0.0001 (-0.00001)	0.00001 (-0.000001)	0.0002 (-0.00001)	0.0020 (-0.0001)
Scenario 16	0.00003 (0.00000)	0.0018 (0.0000)	0.0001 (0.00000)	0.00001 (0.000000)	0.0002 (0.00000)	0.0022 (0.0000)
Scenario 17	0.00003 (0.00000)	0.0018 (0.0000)	0.0001 (0.00000)	0.00001 (0.000000)	0.0002 (0.00000)	0.0021 (-0.0001)
Scenario 18	0.00003 (0.00000)	0.0017 (-0.0001)	0.0001 (-0.00001)	0.00001 (-0.000001)	0.0002 (-0.00001)	0.0020 (-0.0001)
Scenario 19	0.00003 (0.00000)	0.0017 (-0.0001)	0.0001 (-0.00001)	0.00001 (-0.000001)	0.0002 (-0.00001)	0.0020 (-0.0002)

APPENDIX F

Breakdown of Events, Costs and QALYs
Health and Social Care Workers

Table F1: Results of health and social care workers analyses – events

	Vaccinated	Cases of influenza*	ILI	Non-ILI respiratory illness	Deaths	GP consultations	Hospitalisations	Secondary cases of ILI
Targeted population-level results – total number of events (difference from baseline)								
Baseline	1,081,577	260,153	46,828	13,008	13	11,298	2,120	178,757
Baseline -5%	974,701 (-106,875)	272,465 (12,312)	49,044 (2216)	13,623 (616)	14 (1)	11,833 (535)	2,221 (100)	187,216 (8460)
Baseline +10%	1,295,327 (213,750)	235,529 (-24,624)	42,395 (-4432)	11,776 (-1231)	12 (-1)	10,229 (-1069)	1,920 (-201)	161,837 (-16920)
Baseline +25%	1,615,952 (534,376)	198,593 (-61,560)	35,747 (-11081)	9,930 (-3078)	10 (-3)	8,625 (-2673)	1,619 (-502)	136,457 (-42299)
Baseline +35%	1,829,703 (748,126)	173,969 (-86,184)	31,314 (-15513)	8,698 (-4309)	9 (-4)	7,555 (-3743)	1,418 (-702)	119,538 (-59219)
Uptake is 100%	2,137,503 (1,055,926)	138,510 (-121,643)	24,932 (-21896)	6,926 (-6082)	7 (-6)	6,015 (-5283)	1,129 (-991)	95,173 (-83583)
Individual-level results – cost per targeted health and social care worker (difference from baseline)								
Baseline	0.506	0.122	0.022	0.006	0.000	0.005	0.001	0.084
Baseline -5%	0.456 (-0.544)	0.127 (0.00576)	0.0229 (0.001)	0.006 (0.0003)	0.000 (0.0000003)	0.006 (0.000250)	0.001 (0.000047)	0.088 (0.003958)
Baseline +10%	0.606 (-0.394)	0.11 (-0.01152)	0.0198 (-0.0021)	0.006 (-0.0006)	0.000 (-0.0000006)	0.005 (-0.000500)	0.001 (-0.000094)	0.076 (-0.007916)
Baseline +25%	0.756 (-0.244)	0.093 (-0.0288)	0.0167 (-0.0052)	0.005 (-0.0014)	0.000 (-0.0000014)	0.004 (-0.001251)	0.001 (-0.000235)	0.064 (-0.019789)
Baseline +35%	0.856 (-0.144)	0.081 (-0.04032)	0.0146 (-0.0073)	0.004 (-0.0020)	0.000 (-0.0000020)	0.004 (-0.001751)	0.001 (-0.000329)	0.056 (-0.027705)
Uptake is 100%	1. (0.)	0.065 (-0.056909)	0.0117 (-0.0102)	0.003 (-0.0028)	0.000 (-0.0000028)	0.003 (-0.002471)	0.001 (-0.000464)	0.045 (-0.039103)
Individual-level results – cost per vaccinated health and social care worker (difference from baseline)								
Baseline	1	0.241	0.043	0.012	0.000	0.010	0.002	0.165
Baseline -5%	1 (0)	0.28 (0.039006)	0.0503 (0.007)	0.014 (0.002)	0.0000139 (0.000002)	0.012 (0.001694)	0.002 (0.000318)	0.192 (0.026802)
Baseline +10%	1 (0)	0.182 (-0.058702)	0.0327 (-0.0106)	0.0091 (-0.0029)	0.0000090 (-0.000003)	0.008 (-0.002549)	0.001 (-0.000478)	0.125 (-0.040335)
Baseline +25%	1 (0)	0.123 (-0.117636)	0.0221 (-0.0212)	0.0061 (-0.0059)	0.0000061 (-0.000006)	0.005 (-0.005109)	0.001 (-0.000959)	0.084 (-0.080830)
Baseline +35%	1 (0)	0.095 (-0.145451)	0.0171 (-0.0262)	0.0048 (-0.0073)	0.0000047 (-0.000007)	0.004 (-0.006317)	0.001 (-0.001185)	0.065 (-0.099942)
Uptake is 100%	1 (0)	0.065 (-0.175731)	0.0117 (-0.0316)	0.0032 (-0.0088)	0.0000032 (-0.000009)	0.003 (-0.007632)	0.001 (-0.001432)	0.045 (-0.120749)

Table F2: Results of health and social care workers analyses – costs

	Vaccine	Vaccine side-effects	GP consultations	Hospitalisations	Replacement workers	Secondary cases of ILI	Total (NHS and PSS perspective)	Productivity loss	OTC medication	Travel cost	Total (societal perspective)
Population-level results – total costs (difference from baseline)											
Baseline	£2,794,282	£670,577	£403,225	£2,182,306	£12,767,488	£51,721,590	**£70,539,469**	£0	£238,352	£104,693	**£91,242,692**
Baseline -5%	£2,518,167 (-£276,115)	£604,315 (-£66,263)	£422,308 (£19,083)	£2,285,586 (£103,280)	£13,371,723 (£604,235)	£54,169,370 (£2,447,780)	**£73,371,469**	£0	£249,632 (£11,280)	£109,647 (£4,955)	**£94,520,223 (£3,277,531)**
Baseline +10%	£3,346,511 (£552,230)	£803,103 (£132,525)	£365,059 (-£38,166)	£1,975,746 (-£206,560)	£11,559,018 (-£1,208,470)	£46,826,030 (-£4,895,560)	**£64,875,467**	£0	£215,792 (-£22,561)	£94,783 (-£9,909)	**£84,687,631 (-£6,555,061)**
Baseline +25%	£4,174,856 (£1,380,574)	£1,001,890 (£331,313)	£307,810 (-£95,415)	£1,665,906 (-£516,400)	£9,746,313 (-£3,021,176)	£39,482,691 (-£12,238,900)	**£56,379,465**	£0	£181,951 (-£56,401)	£79,919 (-£24,773)	**£74,855,039 (-£16,387,653)**
Baseline +35%	£4,727,085 (£1,932,804)	£1,134,416 (£463,838)	£269,644 (-£133,581)	£1,459,346 (-£722,960)	£8,537,842 (-£4,229,646)	£34,587,131 (-£17,134,460)	**£50,715,464**	£0	£159,390 (-£78,962)	£70,010 (-£34,683)	**£68,299,978 (-£22,942,714)**
Uptake is 100%	£5,522,296 (£2,728,014)	£1,325,252 (£654,674)	£214,684 (-£188,541)	£1,161,900 (-£1,020,406)	£6,797,645 (-£5,969,843)	£27,537,524 (-£24,184,066)	**£42,559,301**	£0	£126,903 (-£111,449)	£55,740 (-£48,952)	**£58,860,690 (-£32,382,002)**
Population-level results – cost per targeted health and social care worker (difference from baseline)											
Baseline	£1.31	£0.31	£0.19	£1.02	£5.97	£24.20	**£33.00**	£0	£0.11	£0.05	**£42.69**
Baseline -5%	£1.18 (-£0.13)	£0.28 (-£0.03)	£0.20 (£0.01)	£1.07 (£0.05)	£6.26 (£0.28)	£25.34 (£1.15)	**£34.33**	£0	£0.12 (£0.01)	£0.05 (£0.00)	**£44.22 (£1.53)**
Baseline +10%	£1.57 (£0.26)	£0.38 (£0.06)	£0.17 (-£0.02)	£0.92 (-£0.10)	£5.41 (-£0.57)	£21.91 (-£2.29)	**£30.35**	£0	£0.10 (-£0.01)	£0.04 (-£0.01)	**£39.62 (-£3.07)**
Baseline +25%	£1.95 (£0.65)	£0.47 (£0.16)	£0.14 (-£0.05)	£0.78 (-£0.24)	£4.56 (-£1.41)	£18.47 (-£5.73)	**£26.38**	£0	£0.09 (-£0.03)	£0.04 (-£0.01)	**£35.02 (-£7.67)**
Baseline +35%	£2.21 (£0.91)	£0.53 (£0.22)	£0.13 (-£0.06)	£0.68 (-£0.34)	£3.99 (-£1.98)	£16.18 (-£8.02)	**£23.73**	£0	£0.08 (-£0.04)	£0.03 (-£0.02)	**£31.95 (-£10.73)**
Uptake is 100%	£2.58 (£1.28)	£0.62 (£0.31)	£0.10 (-£0.09)	£0.55 (-£0.48)	£3.18 (-£2.79)	£12.88 (-£11.31)	**£19.91**	£0	£0.06 (-£0.05)	£0.03 (-£0.02)	**£27.54 (-£15.15)**
Population-level results – cost per vaccinated health and social care worker (difference from baseline)											
Baseline	£2.58	£0.62	£0.37	£2.02	£11.80	£47.82	**£65.00**	£0	£0.22	£0.10	**£84.36**
Baseline -5%	£2.58 (£0.00)	£0.62 (£0.00)	£0.43 (£0.06)	£2.35 (£0.33)	£13.72 (£1.91)	£55.58 (£7.76)	**£75.28**	£0	£0.26 (£0.04)	£0.11 (£0.02)	**£96.97 (£12.61)**
Baseline +10%	£2.58 (£0.00)	£0.62 (£0.00)	£0.28 (-£0.09)	£1.53 (-£0.49)	£8.92 (-£2.88)	£36.15 (-£11.67)	**£50.08**	£0	£0.17 (-£0.05)	£0.07 (-£0.02)	**£65.38 (-£18.98)**
Baseline +25%	£2.58 (£0.00)	£0.62 (£0.00)	£0.19 (-£0.18)	£1.03 (-£0.99)	£6.03 (-£5.77)	£24.433 (-£23.39)	**£34.89**	£0	£0.11 (-£0.11)	£0.05 (-£0.05)	**£46.32 (-£38.04)**
Baseline +35%	£2.58 (£0.00)	£0.62 (£0.00)	£0.15 (-£0.23)	£0.80 (-£1.22)	£4.67 (-£7.14)	£18.90 (-£28.92)	**£27.72**	£0	£0.09 (-£0.13)	£0.04 (-£0.06)	**£37.33 (-£47.03)**
Uptake is 100%	£2.584 (£0.00)	£0.62 (£0.00)	£0.10 (-£0.27)	£0.54 (-£1.47)	£3.18 (-£8.62)	£12.88 (-£34.94)	**£19.91**	£0	£0.06 (-£0.16)	£0.03 (-£0.07)	**£27.54 (-£56.82)**

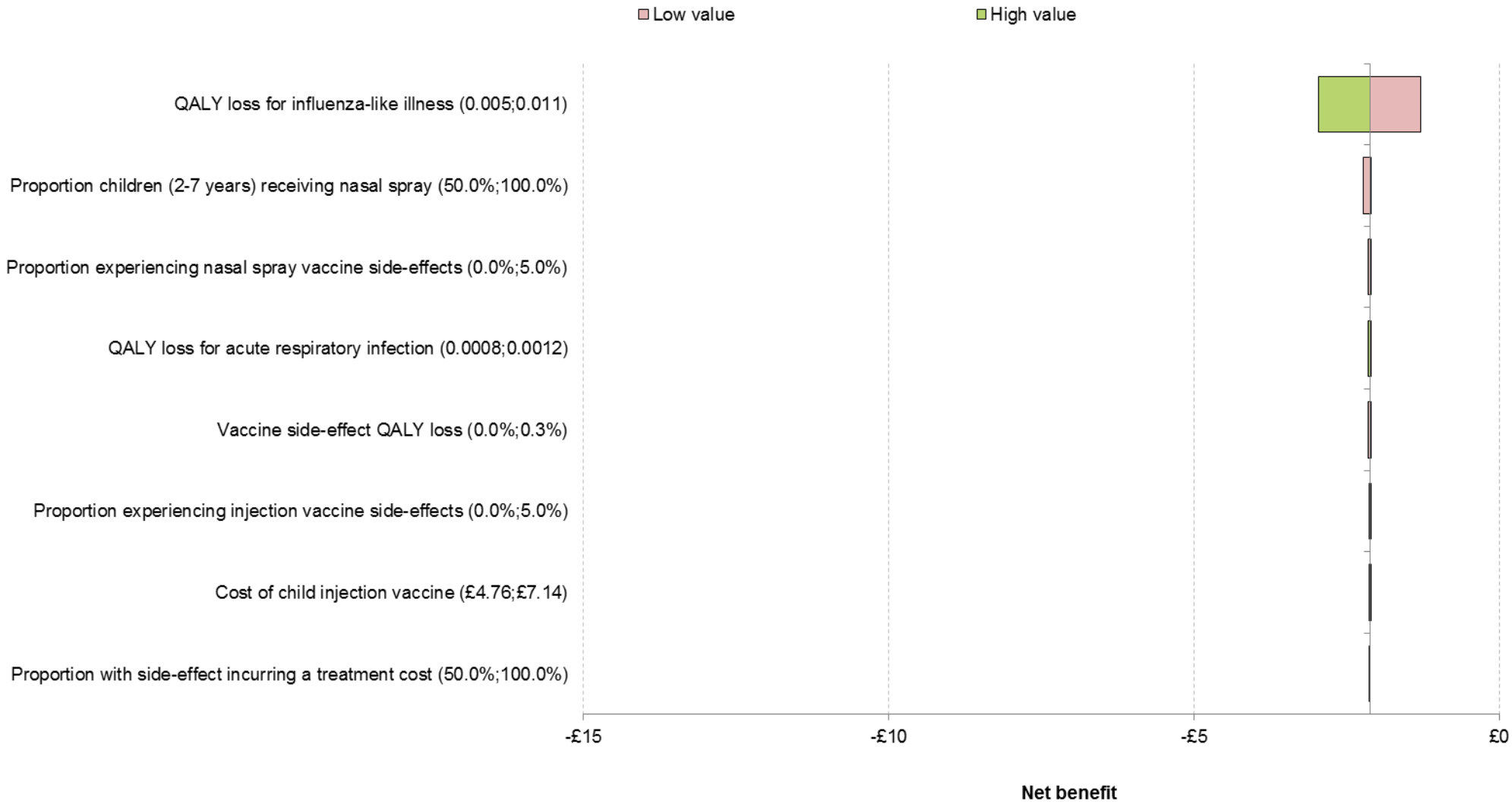
Table F3: Results of health and social care workers analyses – QALYs

	Vaccine side-effects (difference from baseline)	ILI (difference from baseline)	Non-ILI respiratory illness (difference from baseline)	Hospitalisations (difference from baseline)	Death (difference from baseline)	Secondary cases (difference from baseline)	Total (difference from baseline)
Targeted population-level results – total QALY loss							
Baseline	32	375	13	38	76	1,430.1	**1,965**
Baseline -5%	29 (-3)	392 (18)	14 (1)	40 (2)	80 (4)	1497.7 (67.7)	**2053.1** **(88.2)**
Baseline +10%	39 (6)	339 (-35)	12 (-1)	35 (-4)	69 (-7)	1294.7 (-135.4)	**1788.3** **(-176.5)**
Baseline +25%	48 (16)	286 (-89)	10 (-3)	29 (-9)	58 (-18)	1091.7 (-338.4)	**1523.6** **(-441.2)**
Baseline +35%	55 (22)	251 (-124)	9 (-4)	26 (-13)	51 (-25)	956.3 (-473.8)	**1347.1** **(-617.7)**
Uptake is 100%	64 (32)	199 (-175)	7 (-6)	20 (-18)	41 (-36)	761.4 (-668.7)	**1093.0** **(-871.9)**
Individual-level results – QALY loss per targeted health and social care worker							
Baseline	0.000015	0.000175	0.000006	0.000018	0.000036	0.000669	**0.0009**
Baseline -5%	0.00001 (-0.000002)	0.00018 (0.000008)	0.000006 (0.0000003)	0.0000187 (0.00000084)	0.0000374 (0.000002)	0.00070 (0.0000317)	**0.0010** **(0.0000)**
Baseline +10%	0.00002 (0.000003)	0.00016 (-0.000017)	0.000006 (-0.0000006)	0.0000162 (-0.00000169)	0.0000324 (-0.000003)	0.00061 (-0.0000633)	**0.0008** **(-0.0001)**
Baseline +25%	0.00002 (0.000008)	0.00013 (-0.000041)	0.000005 (-0.0000015)	0.0000136 (-0.00000422)	0.0000273 (-0.000008)	0.00051 (-0.0001583)	**0.0007** **(-0.0002)**
Baseline +35%	0.00003 (0.000011)	0.00012 (-0.000058)	0.000004 (-0.0000020)	0.0000119 (-0.00000591)	0.0000239 (-0.000012)	0.00045 (-0.0002216)	**0.0006** **(-0.0003)**
Uptake is 100%	0.00003 (0.000015)	0.00009 (-0.000082)	0.000003 (-0.0000029)	0.0000095 (-0.00000835)	0.0000190 (-0.000017)	0.00036 (-0.0003128)	**0.0005** **(-0.0004)**
Individual-level results – QALY loss per vaccinated health and social care worker							
Baseline	0.000030	0.000346	0.000012	0.000035	0.000071	0.001322	**0.0018**
Baseline -5%	0.00003 (0.0)	0.000403 (0.0000562)	0.000014 (0.0000020)	0.000041 (0.00001)	0.000082 (0.00001)	0.001537 (0.000214)	**0.0021** **(0.0003)**
Baseline +10%	0.00003 (0.0)	0.000262 (-0.0000845)	0.000009 (-0.0000030)	0.000027 (-0.00001)	0.000053 (-0.00002)	0.001000 (-0.000323)	**0.0014** **(-0.0004)**
Baseline +25%	0.00003 (0.0)	0.000177 (-0.0001694)	0.000006 (-0.0000059)	0.000018 (-0.00002)	0.000036 (-0.00003)	0.000676 (-0.000647)	**0.0009** **(-0.0009)**
Baseline +35%	0.00003 (0.0)	0.000137 (-0.0002094)	0.000005 (-0.0000073)	0.000014 (-0.00002)	0.000028 (-0.00004)	0.000523 (-0.000800)	**0.0007** **(-0.0011)**
Uptake is 100%	0.00003 (0.0)	0.000093 (-0.0002531)	0.000003 (-0.0000089)	0.000010 (-0.00003)	0.000019 (-0.00005)	0.000356 (-0.000966)	**0.0005** **(-0.0013)**

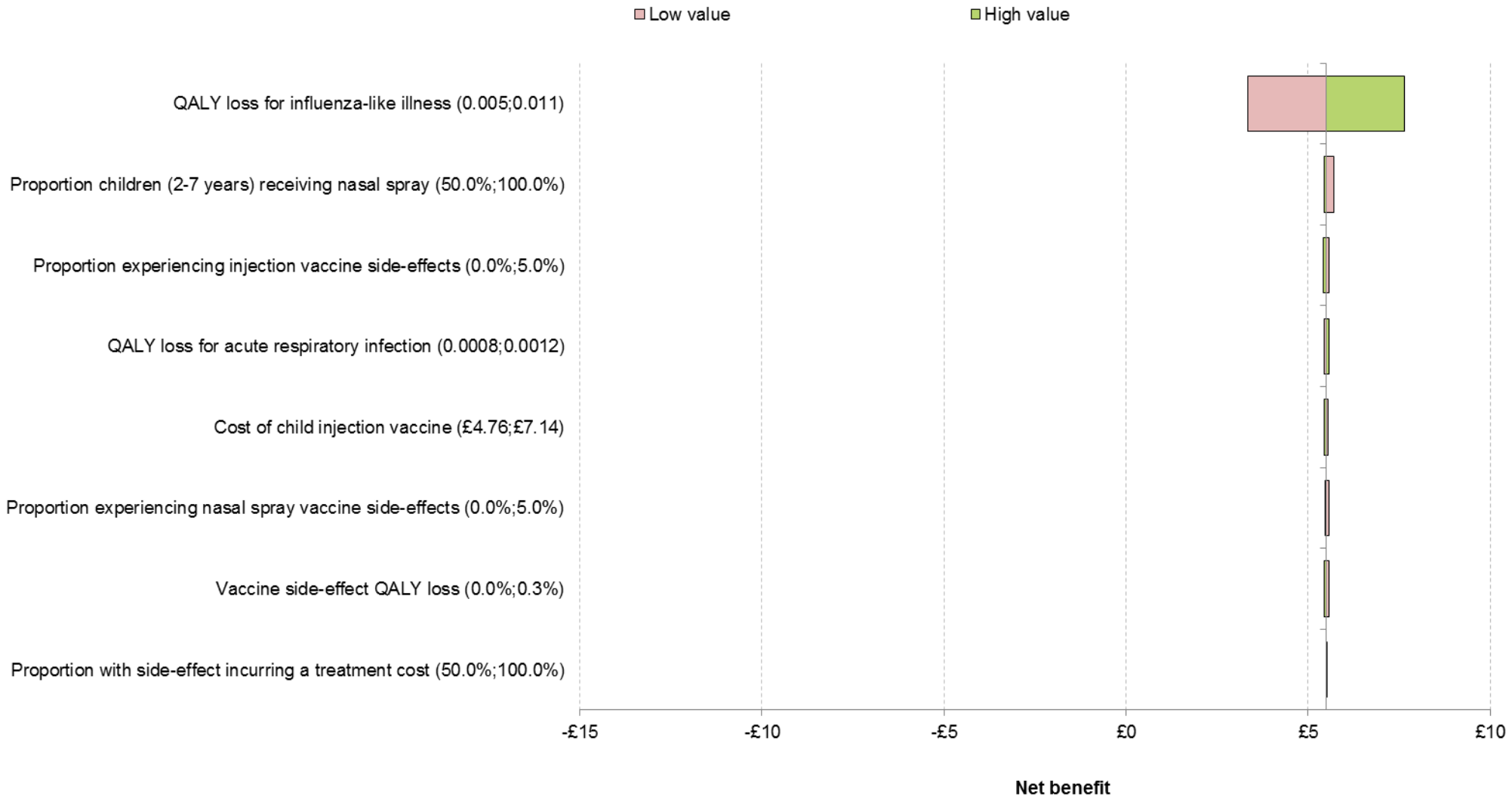
APPENDIX G

Tornado Diagrams
Children

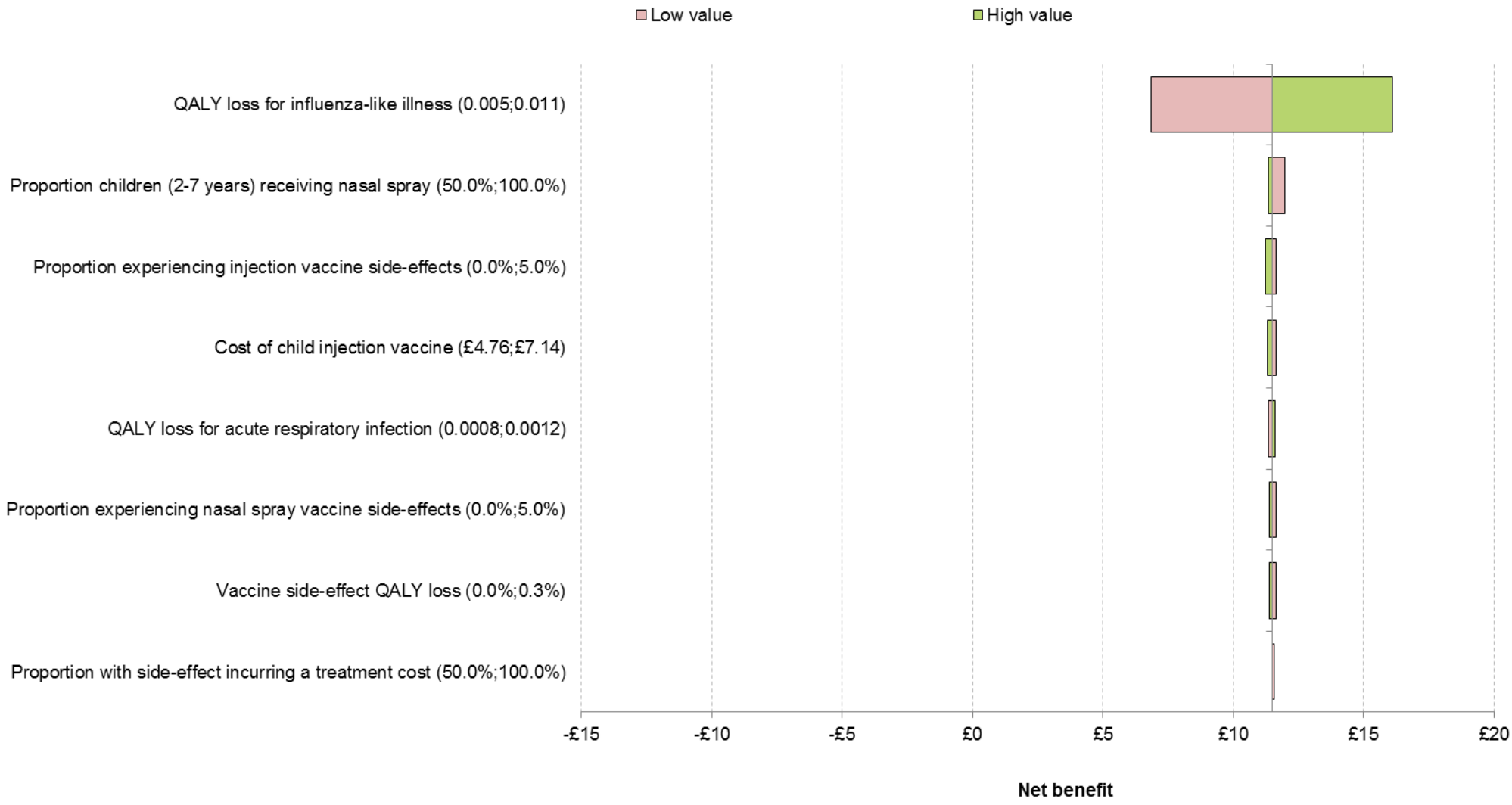
Scenario 12 (uptake in children between 2 and 17 years is 5% lower than the baseline rate)



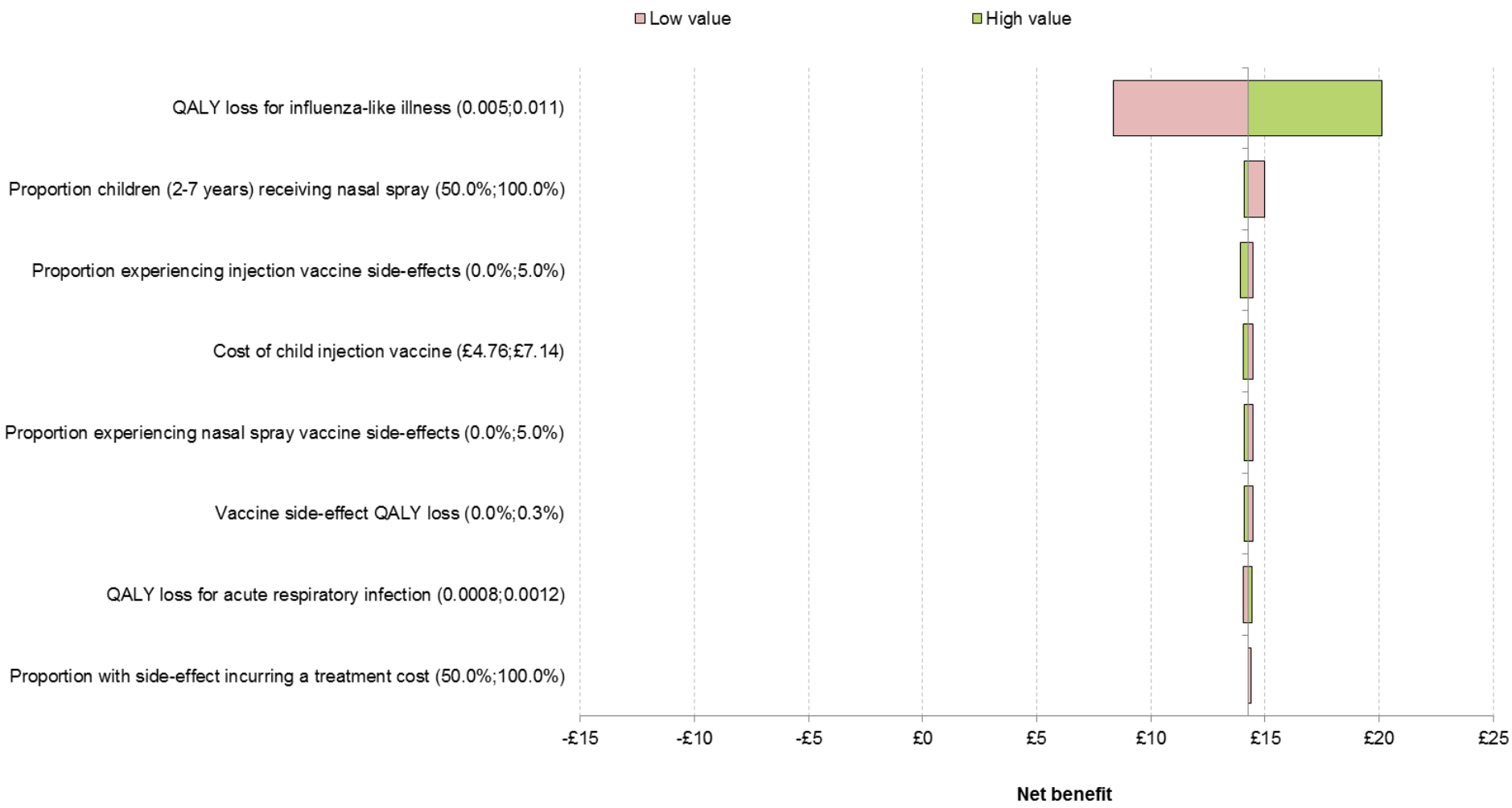
Scenario 13 (uptake in children between 2 and 17 years is 10% higher than the baseline rate)



Scenario 14 (uptake in children between 2 and 17 years is 25% higher than the baseline rate)



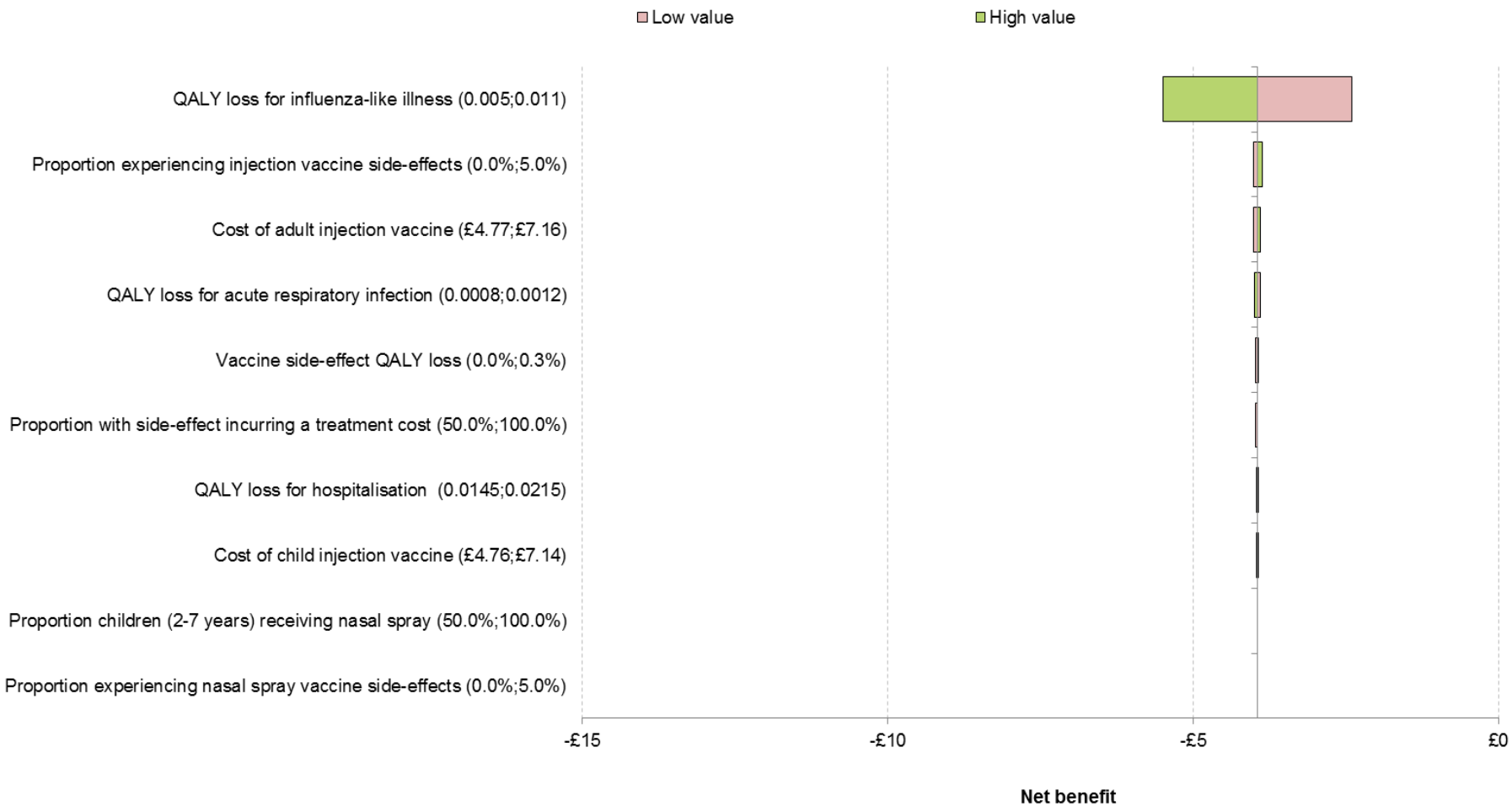
Scenario 15 (uptake in children between 2 and 17 years is 35% higher than the baseline rate)



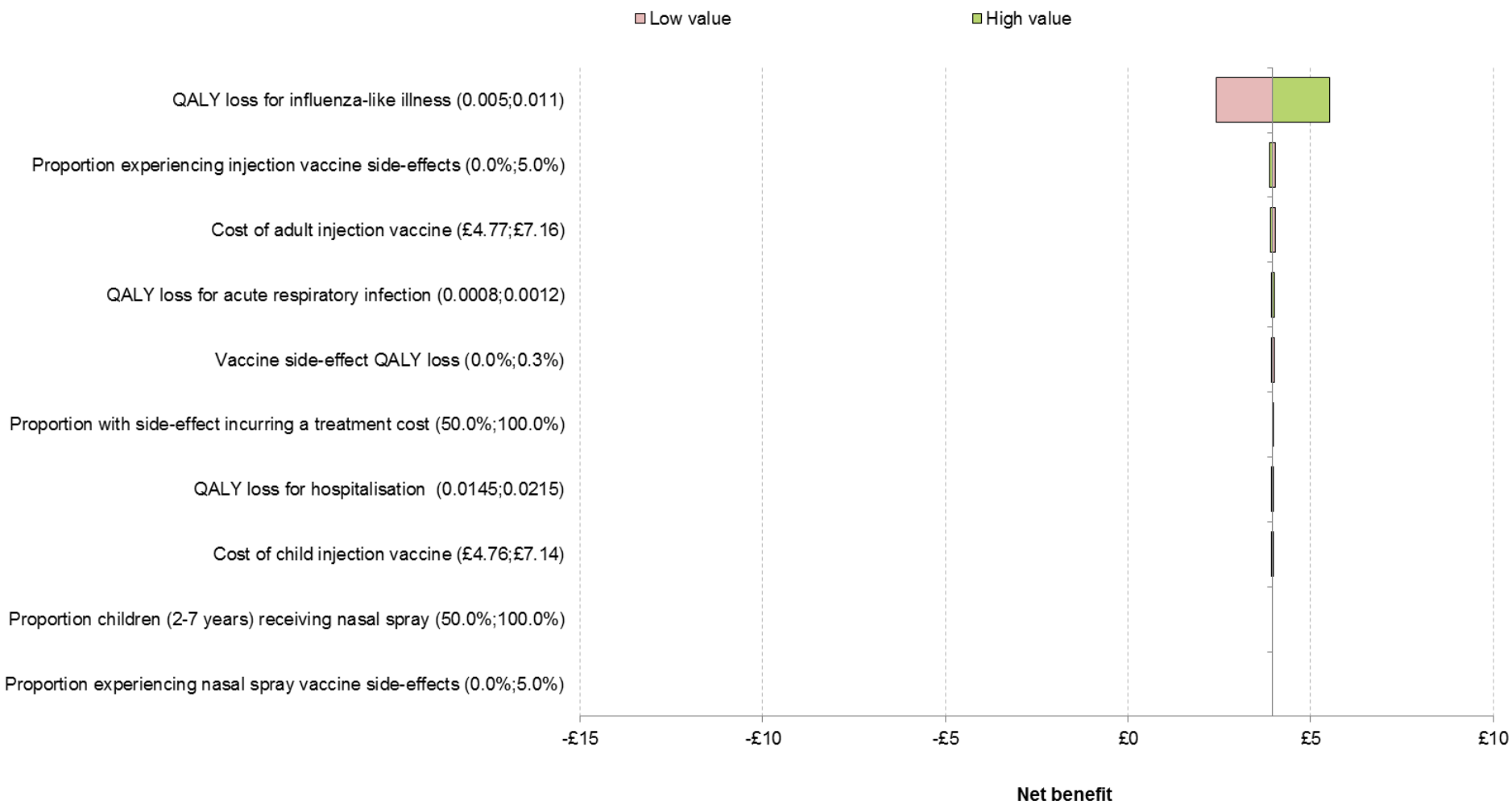
APPENDIX H

Tornado Diagrams
Clinical Risk Groups

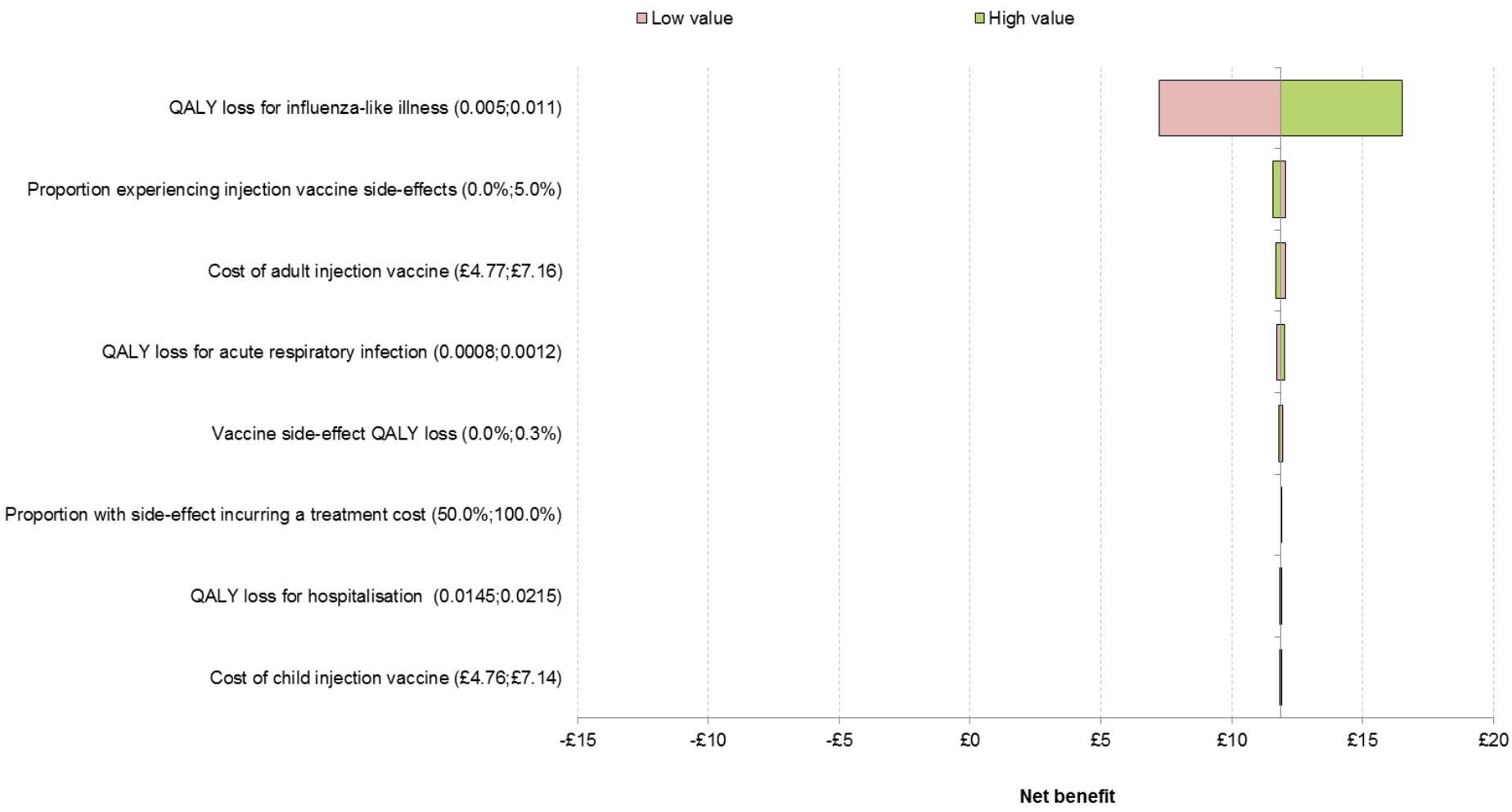
Scenario 2 (uptake by adults in a clinical risk group is 5% lower than the baseline rate)



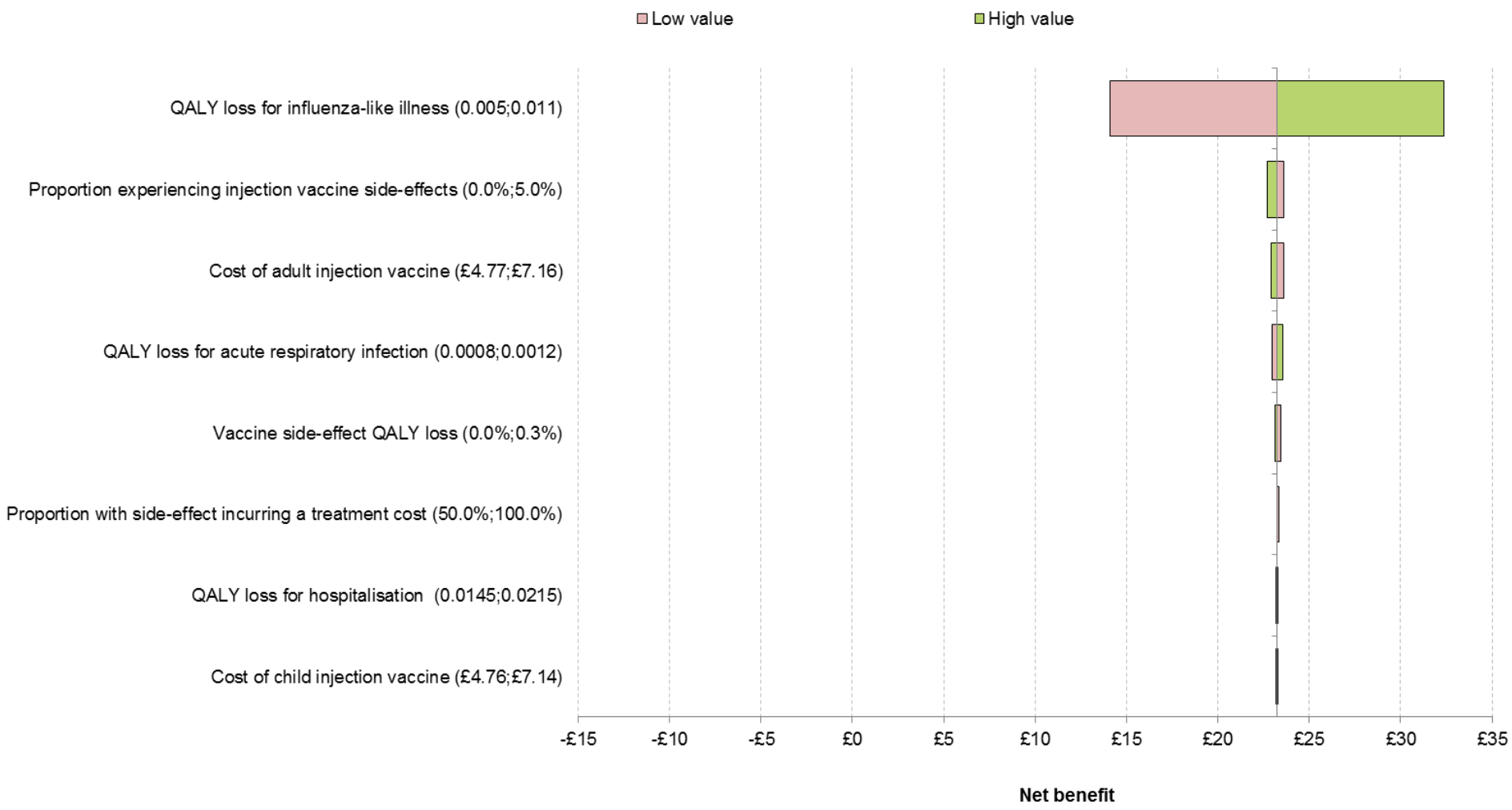
Scenario 3 (uptake by adults in a clinical risk group is 5% higher than the baseline rate)



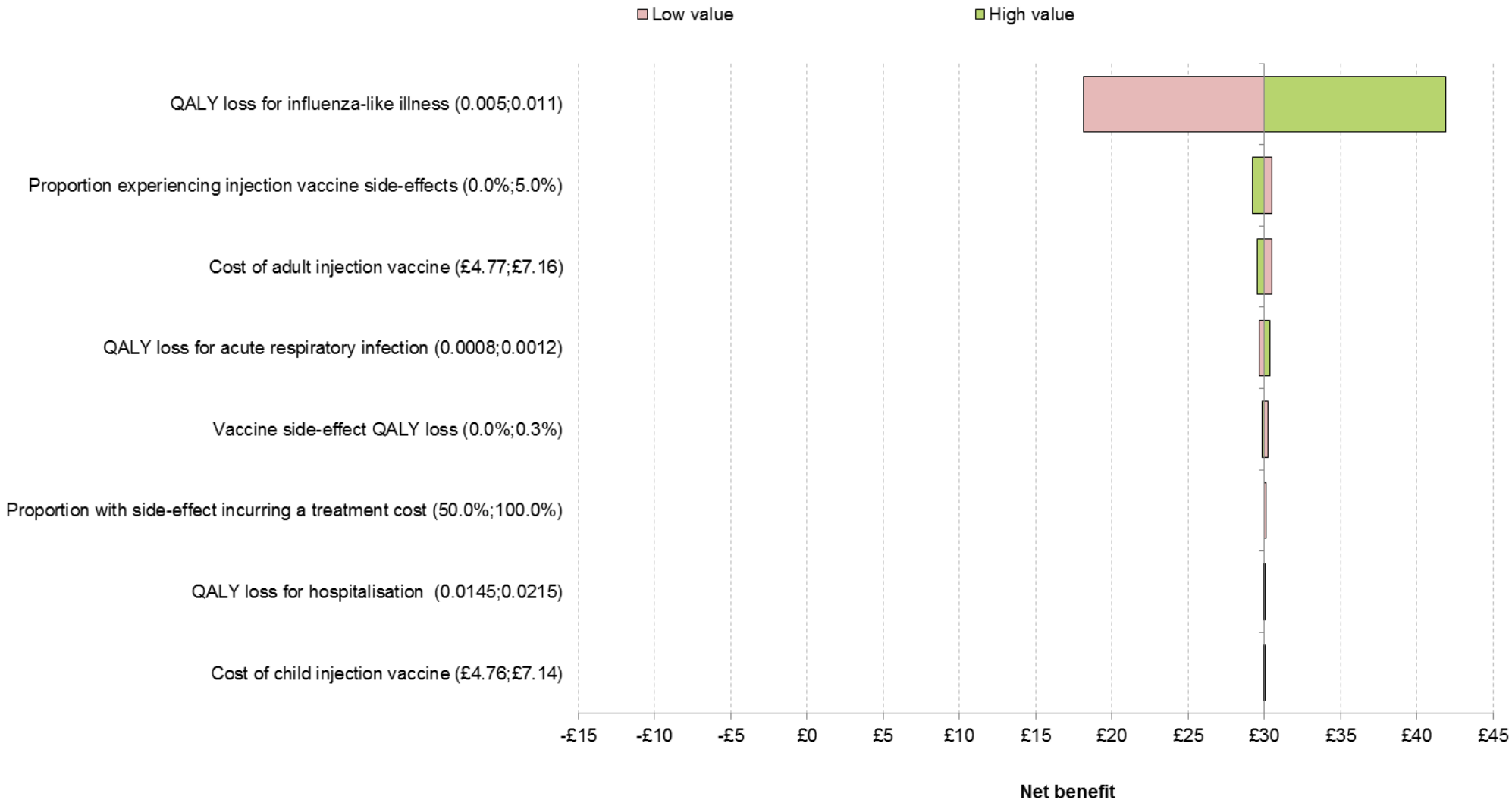
Scenario 4 (uptake by adults in a clinical risk group is 15% higher than the baseline rate)



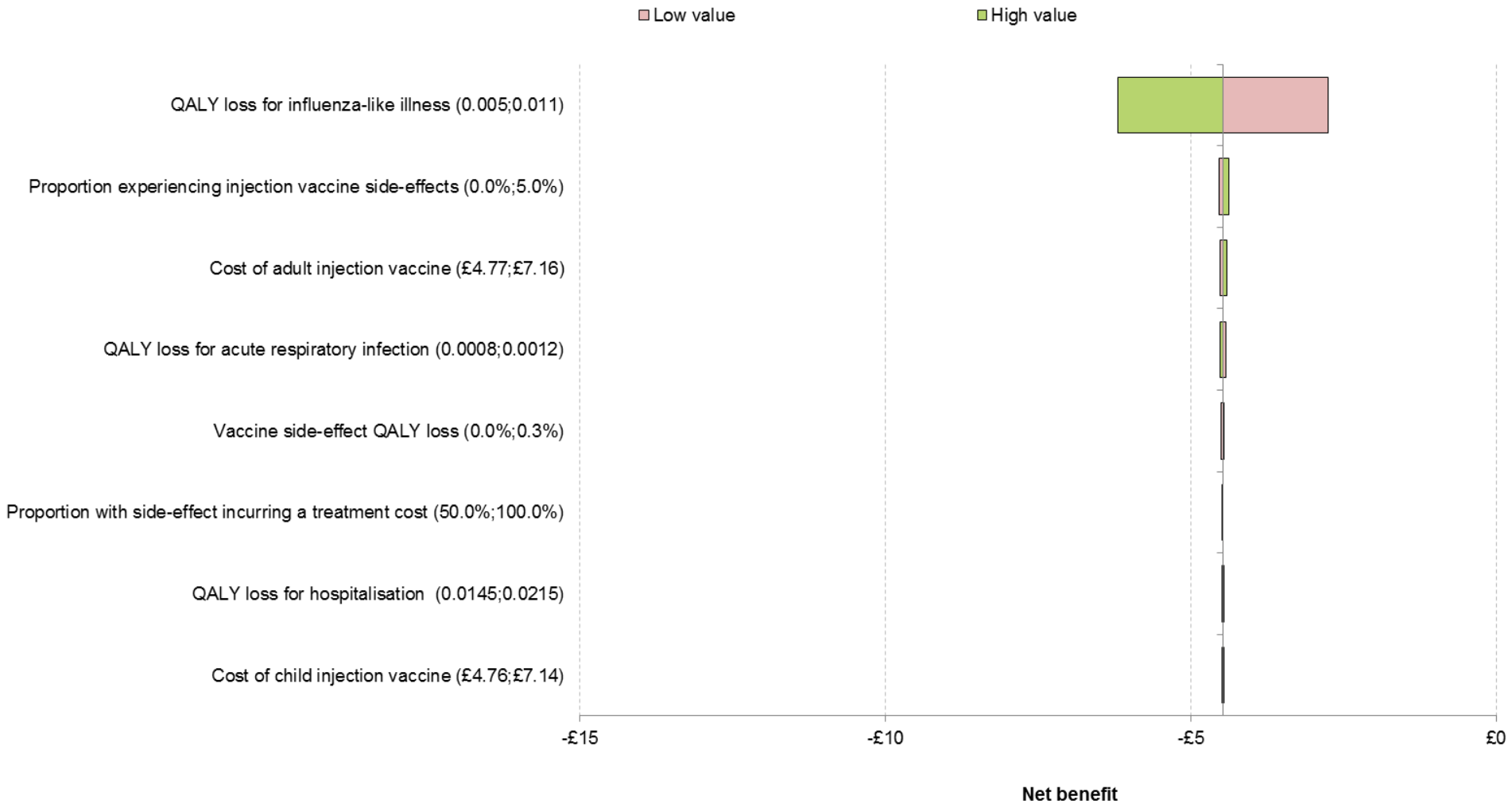
Scenario 5 (uptake by adults in a clinical risk group is 35% higher than the baseline rate)



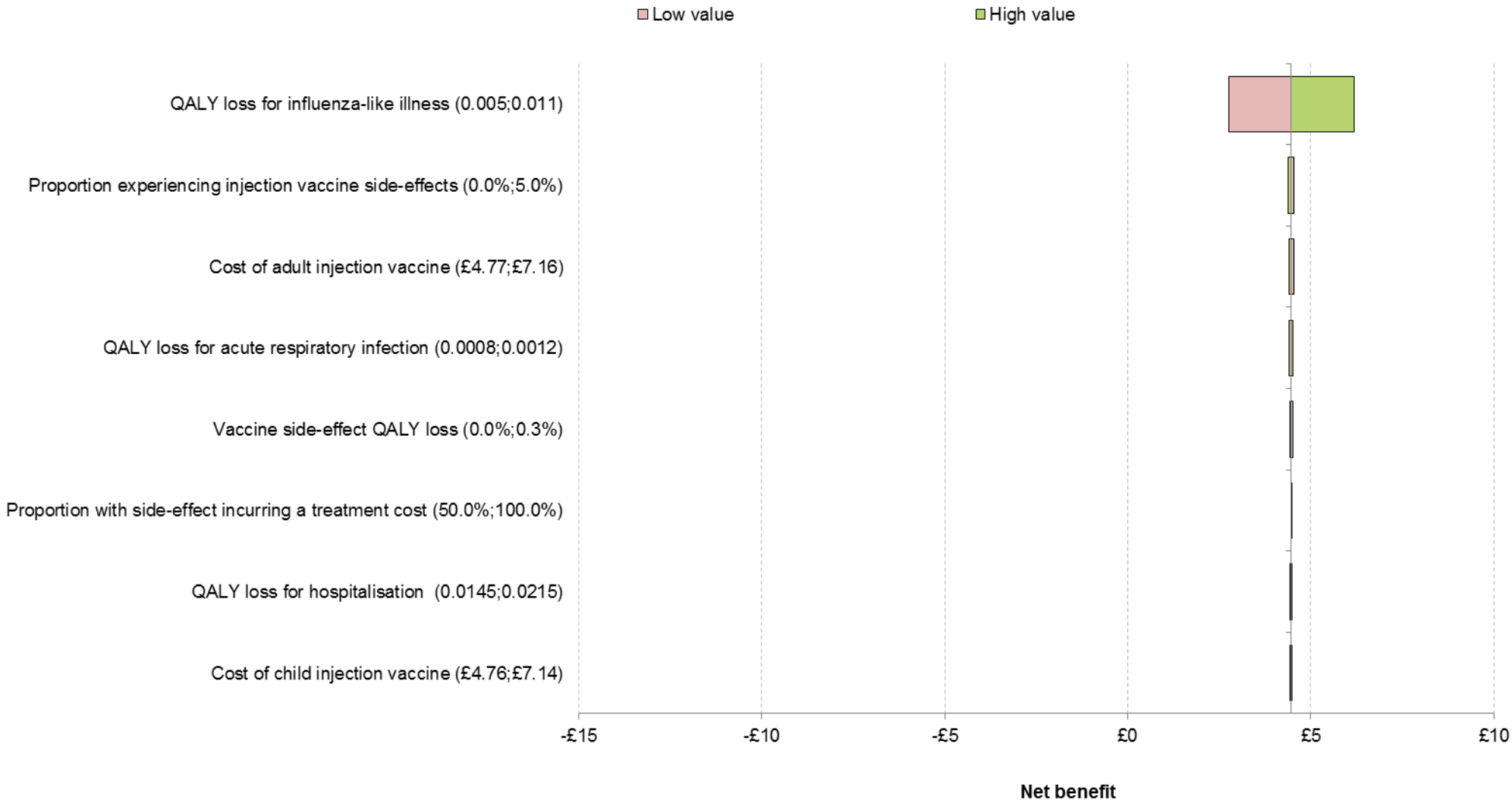
Scenario 6 (uptake by adults in a clinical risk group is 40% higher than the baseline rate)



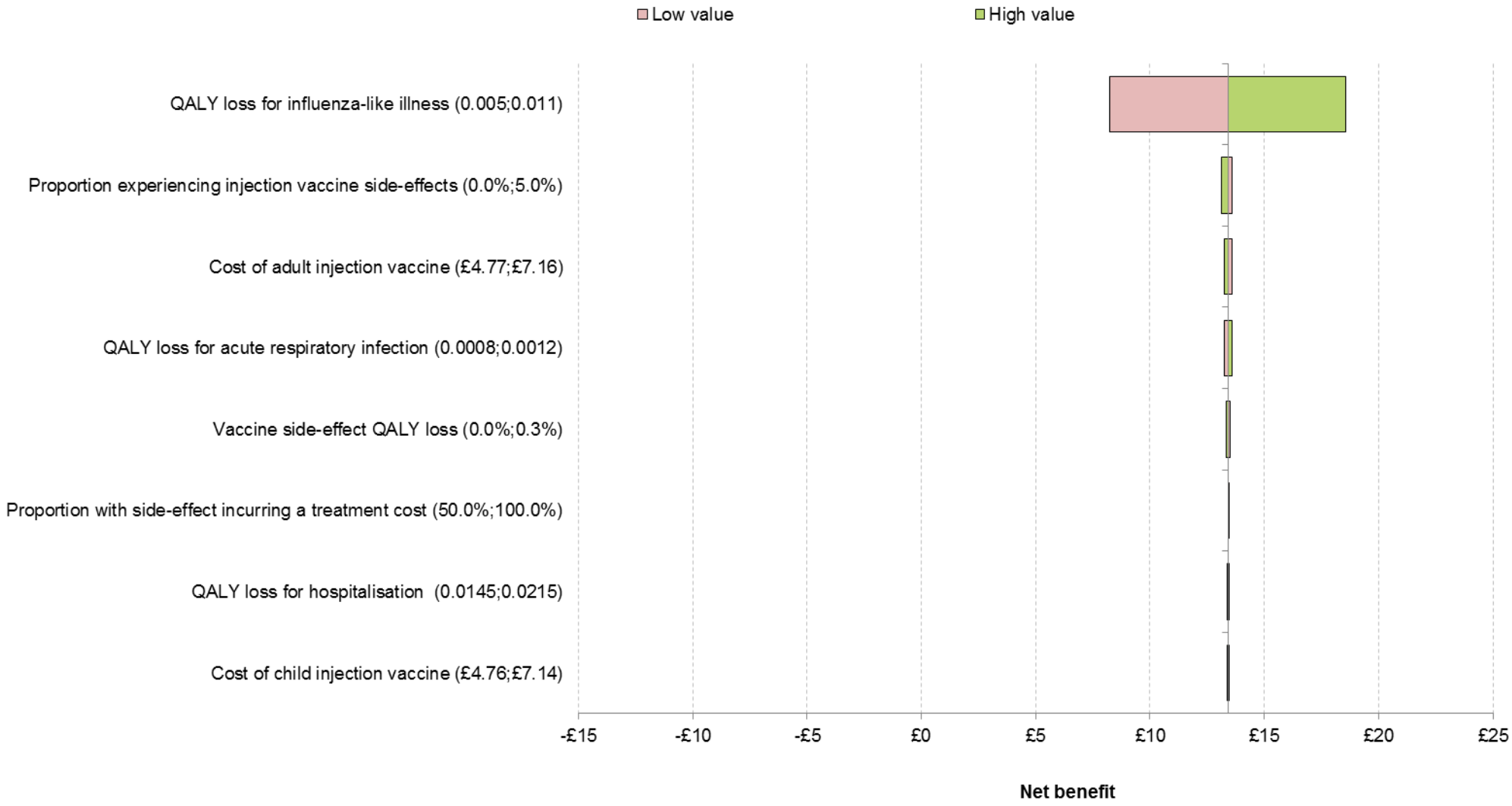
Scenario 7 (uptake by pregnant women is 5% lower than the baseline rate)



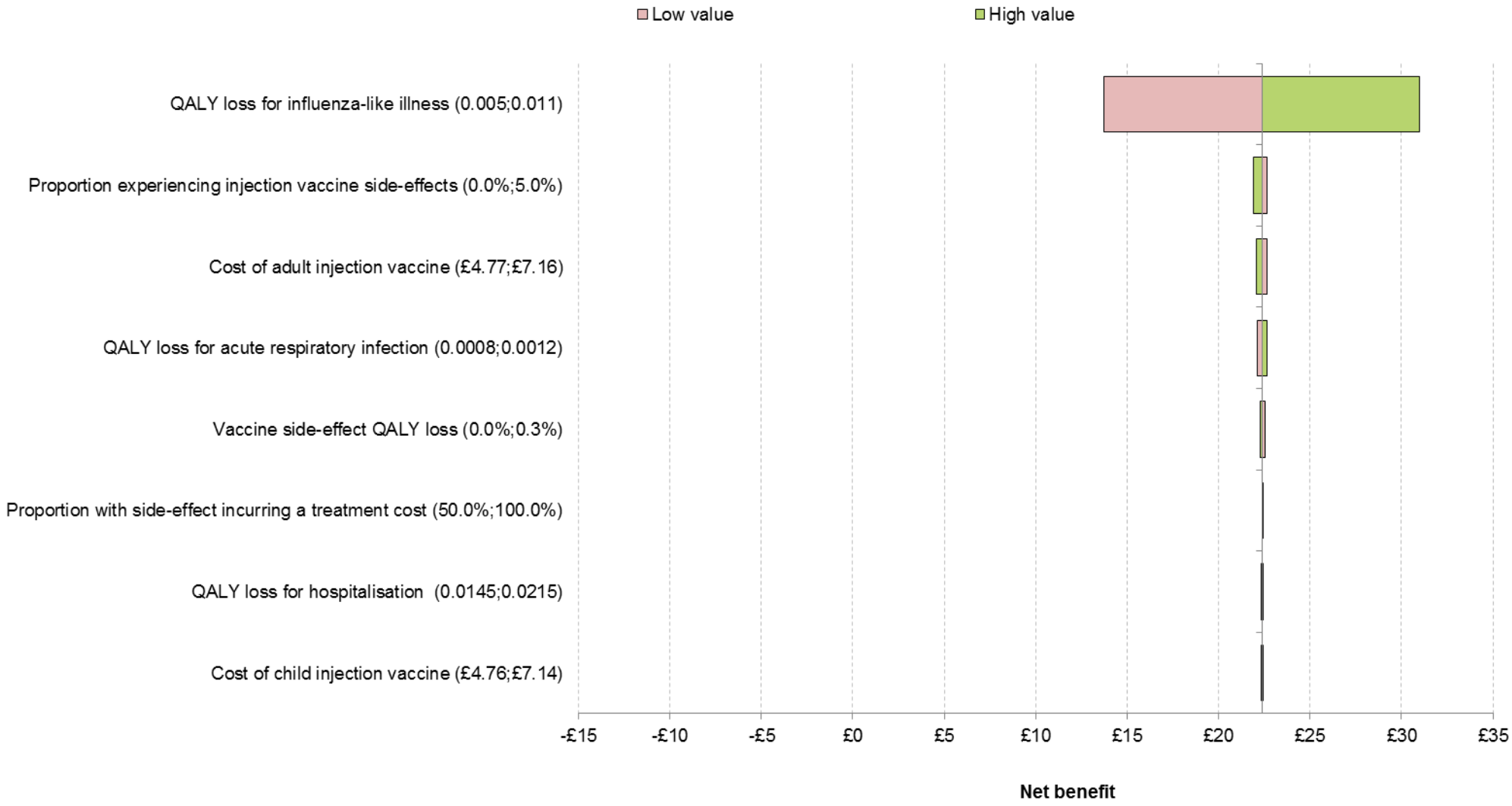
Scenario 8 (uptake by pregnant women is 5% higher than the baseline rate)



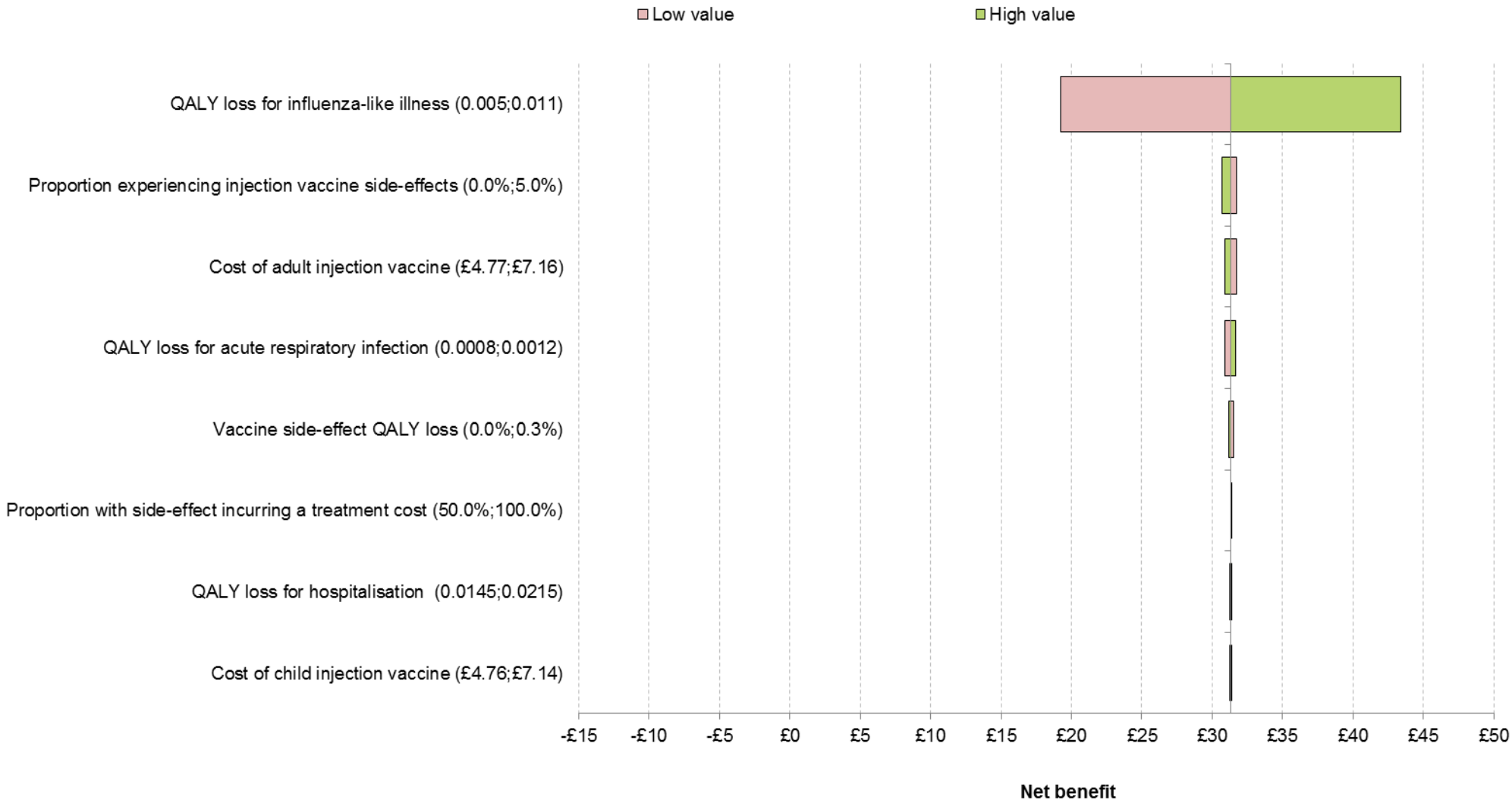
Scenario 9 (uptake by pregnant women is 15% higher than the baseline rate)



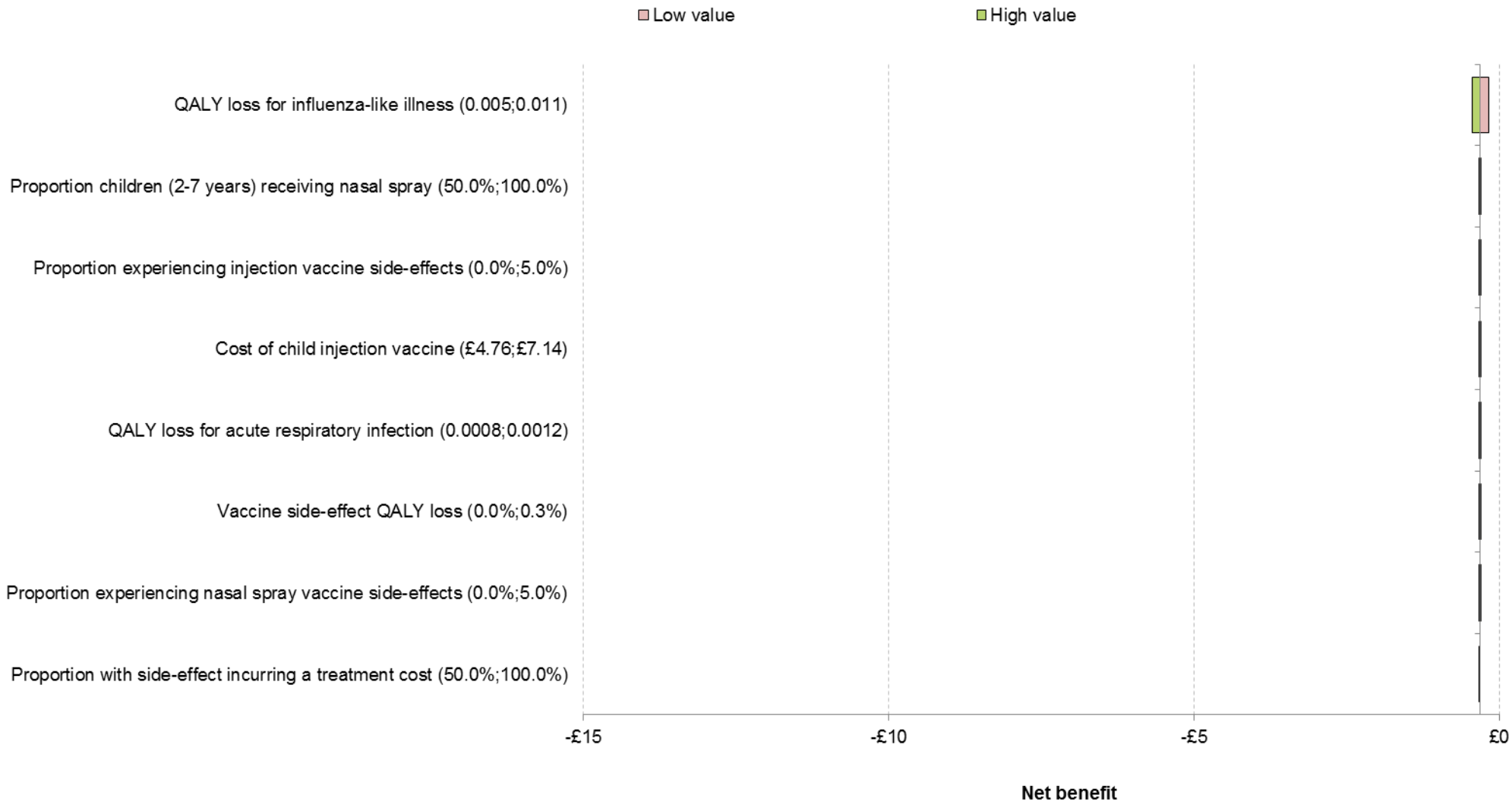
Scenario 10 (uptake by pregnant women is 25% higher than the baseline rate)



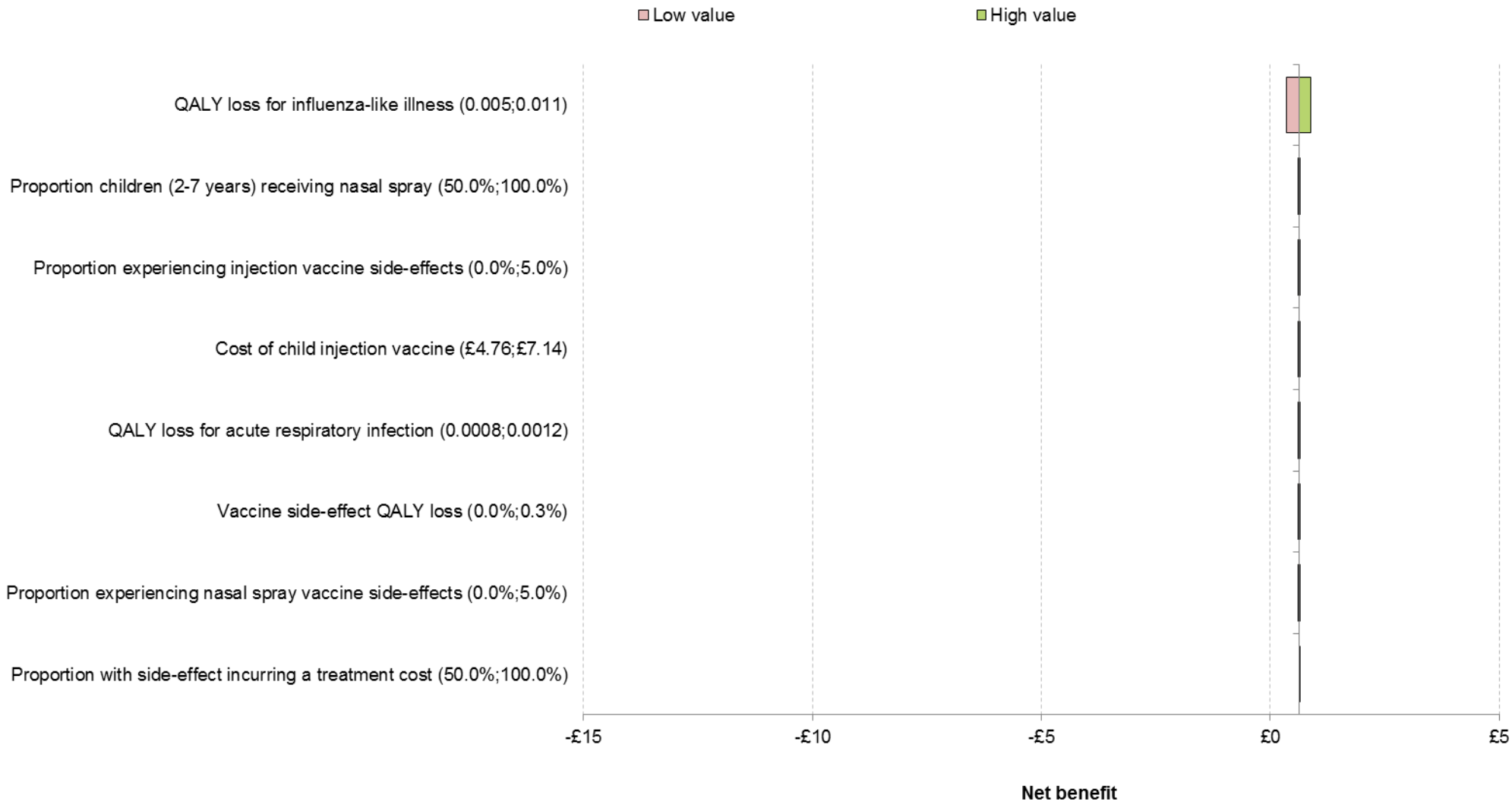
Scenario 11 (uptake by pregnant women is 35% higher than the baseline rate)



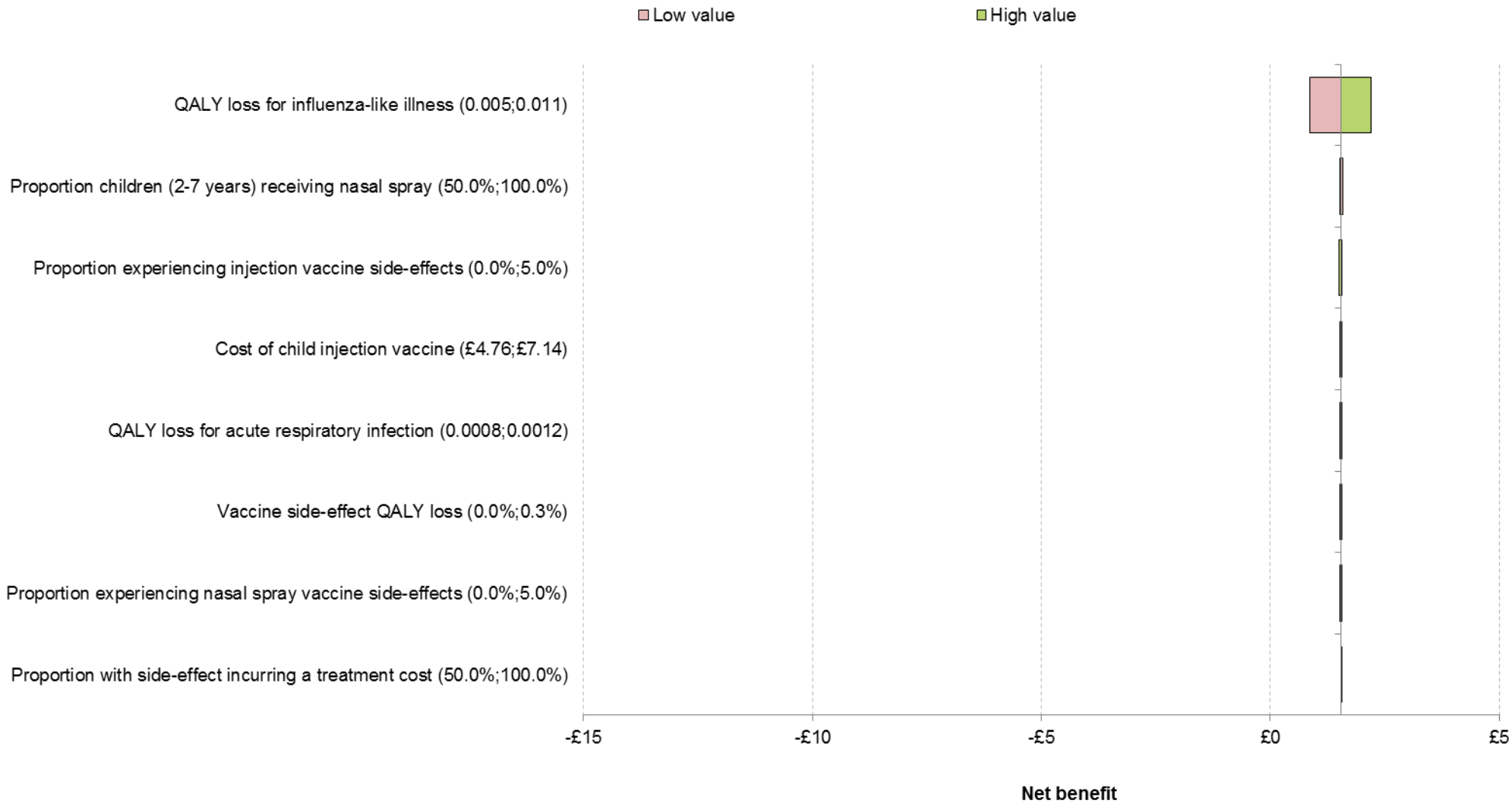
Scenario 16 (uptake in high risk children is 5% lower than the baseline rate)



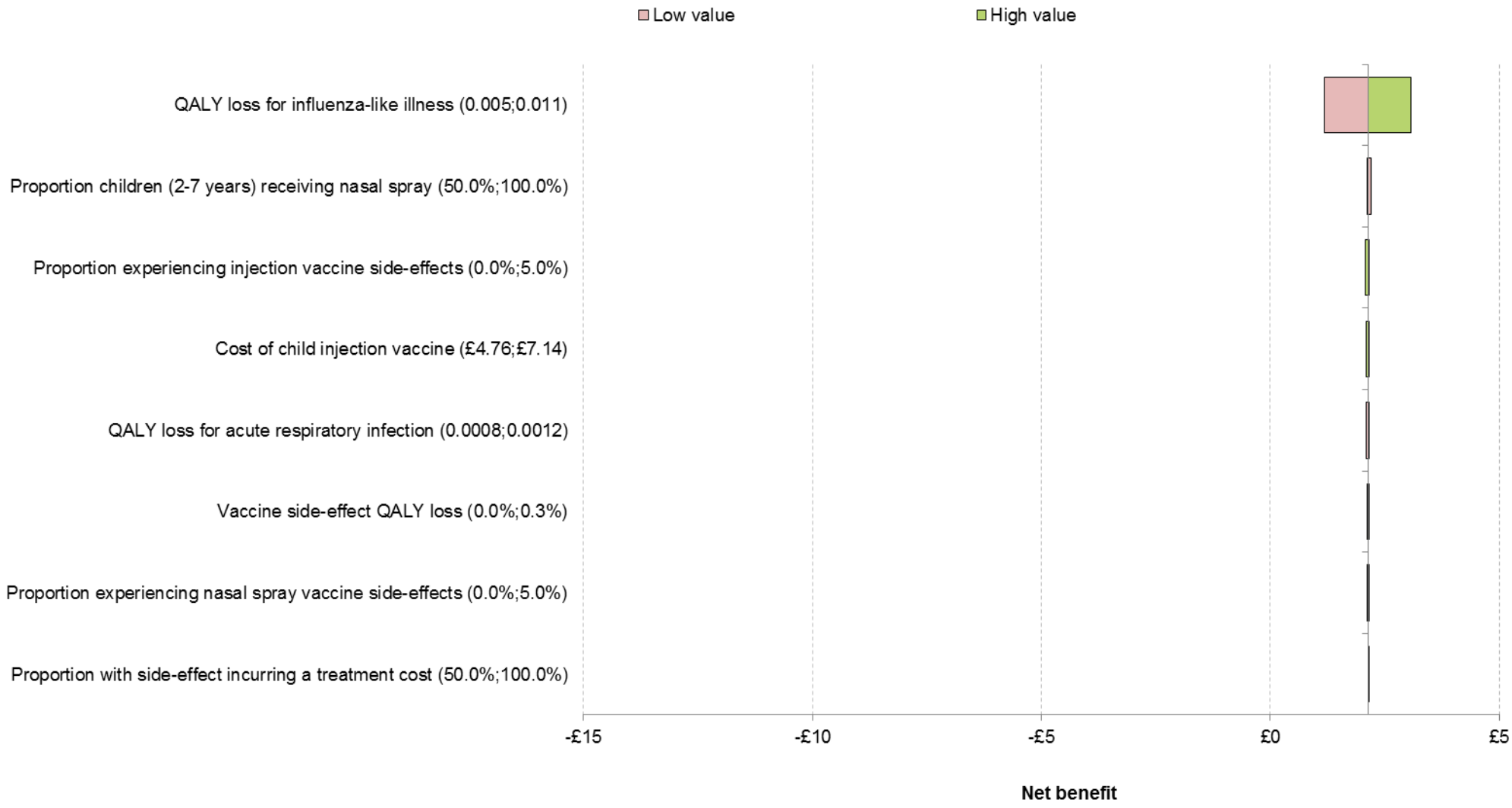
Scenario 17 (uptake in high risk children is 10% higher than the baseline rate)



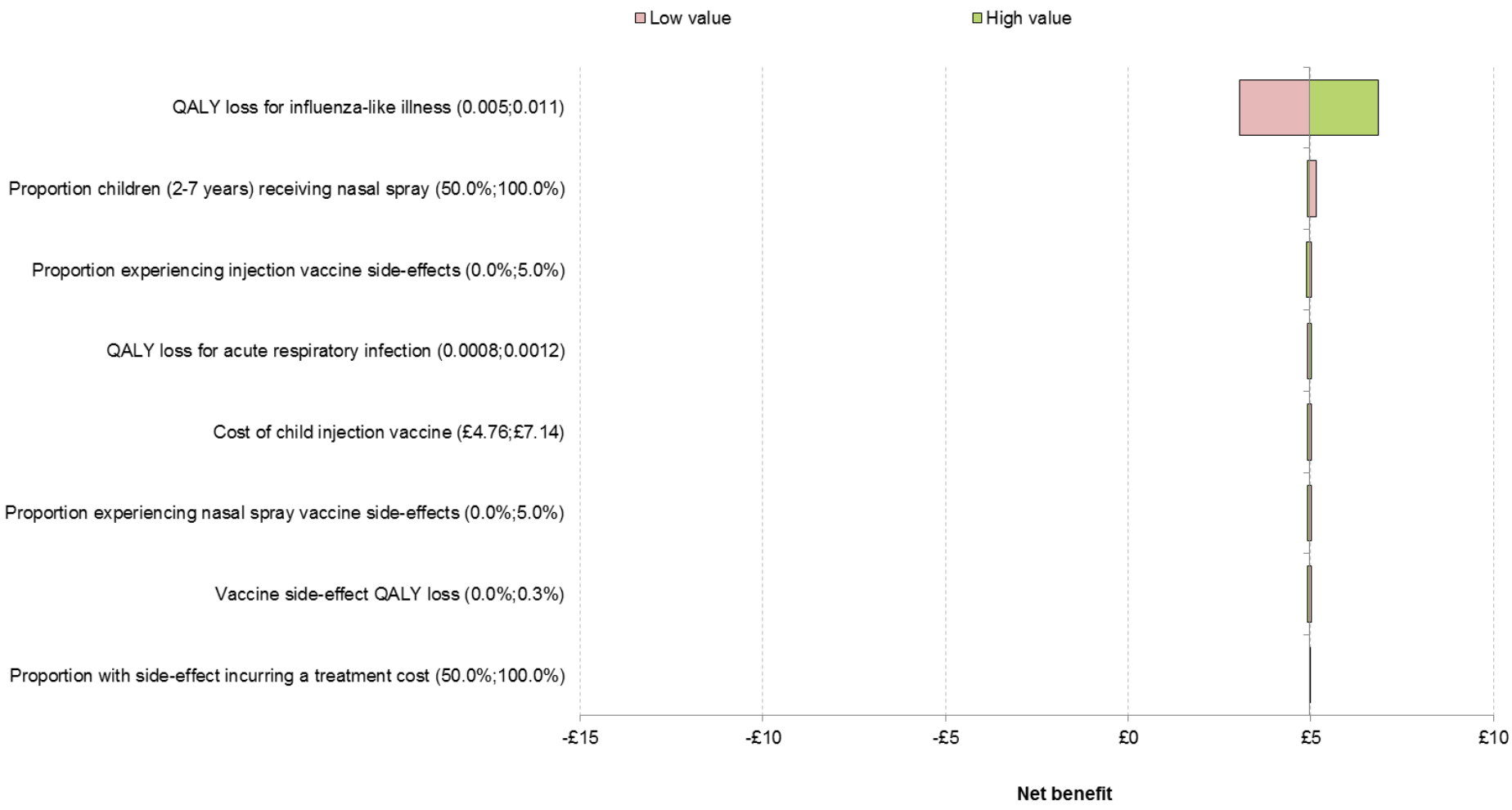
Scenario 18 (uptake in high risk children is 25% higher than the baseline rate)



Scenario 19 (uptake in high risk children is 35% higher than the baseline rate)



Scenario 20 (uptake in low risk children is 10% higher than the baseline rate)

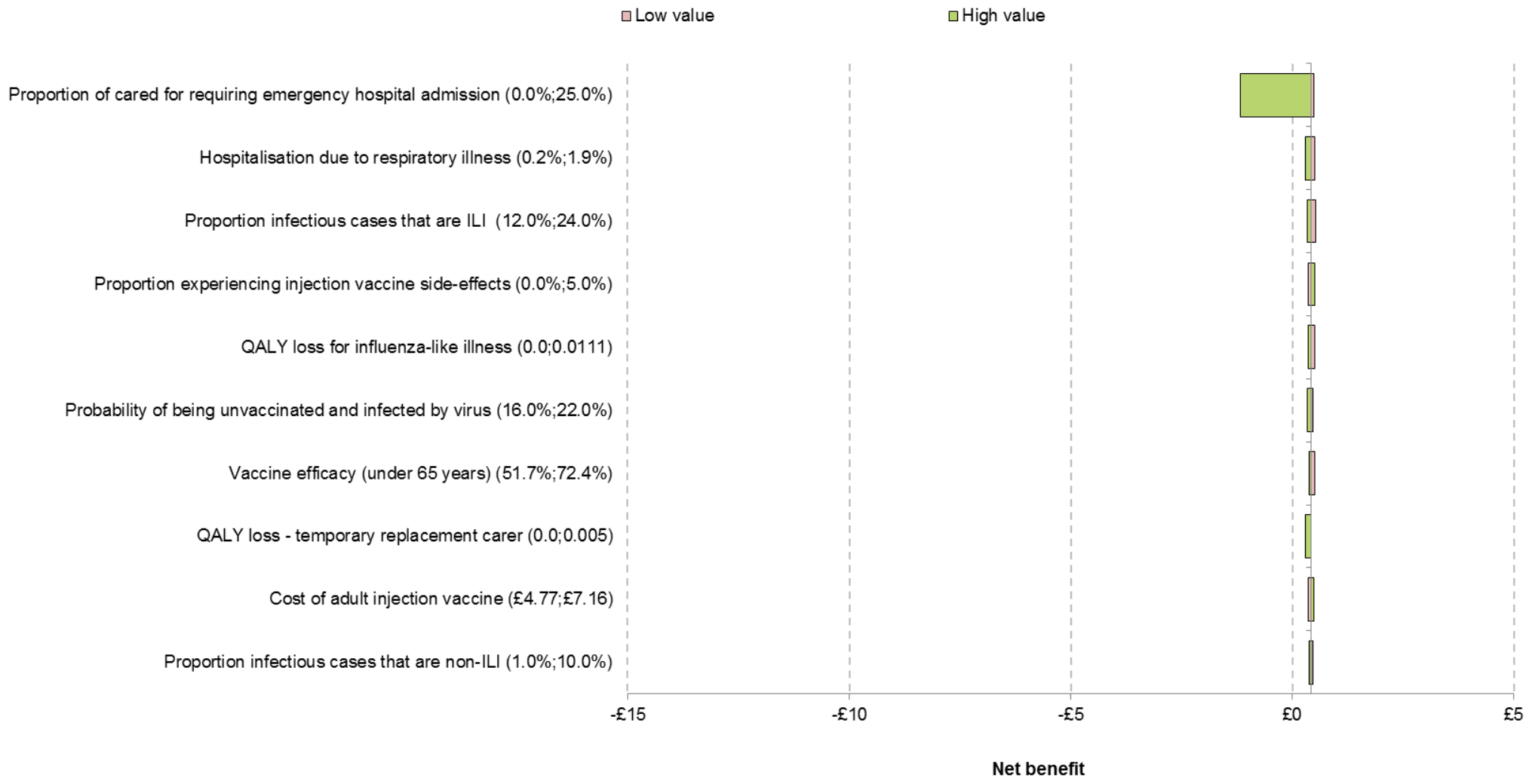


* *Please note that no bar is shown on the diagram for the average weekly carer wage as it is capped at £110, the upper limit for the tornado diagram is the base case value used in the model.*

APPENDIX I

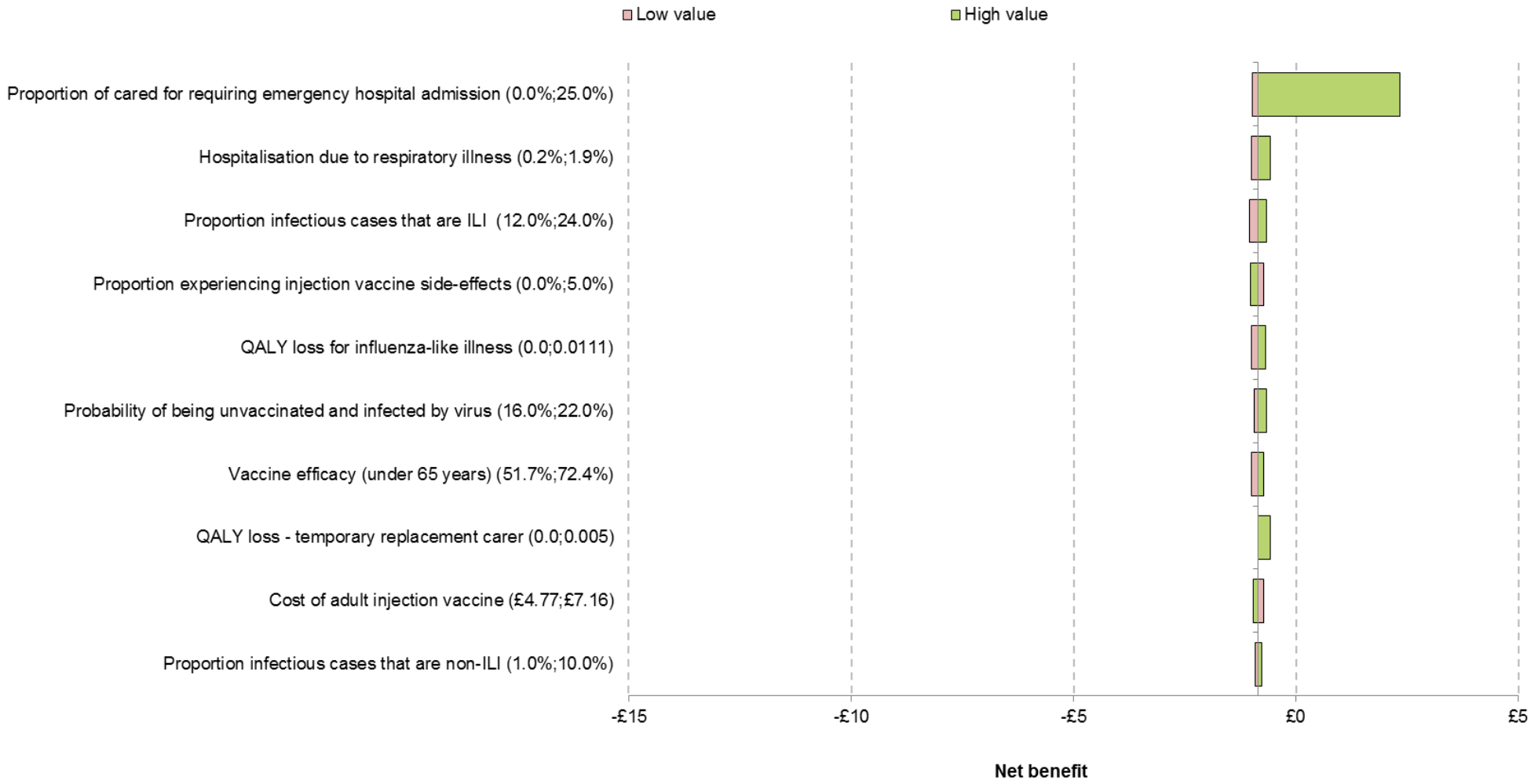
Tornado Diagrams
Carers

Scenario 2 (uptake in carers is 5% lower than the baseline rate)



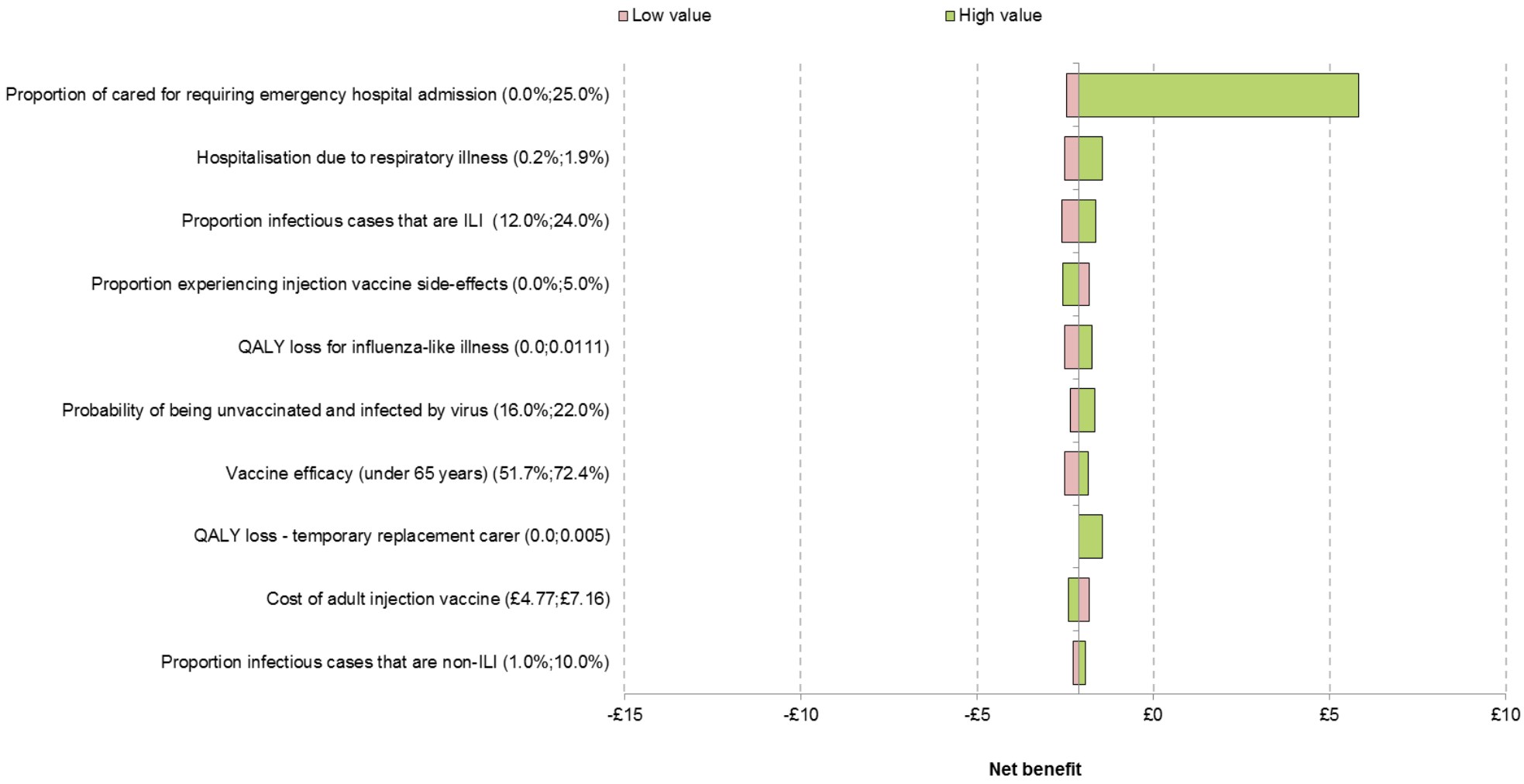
* *Please note that there is no low value bar for the QALY loss – temporary replacement carer because the QALY loss is zero in the base case.*

Scenario 3 (uptake in carers is 10% higher than the baseline rate)



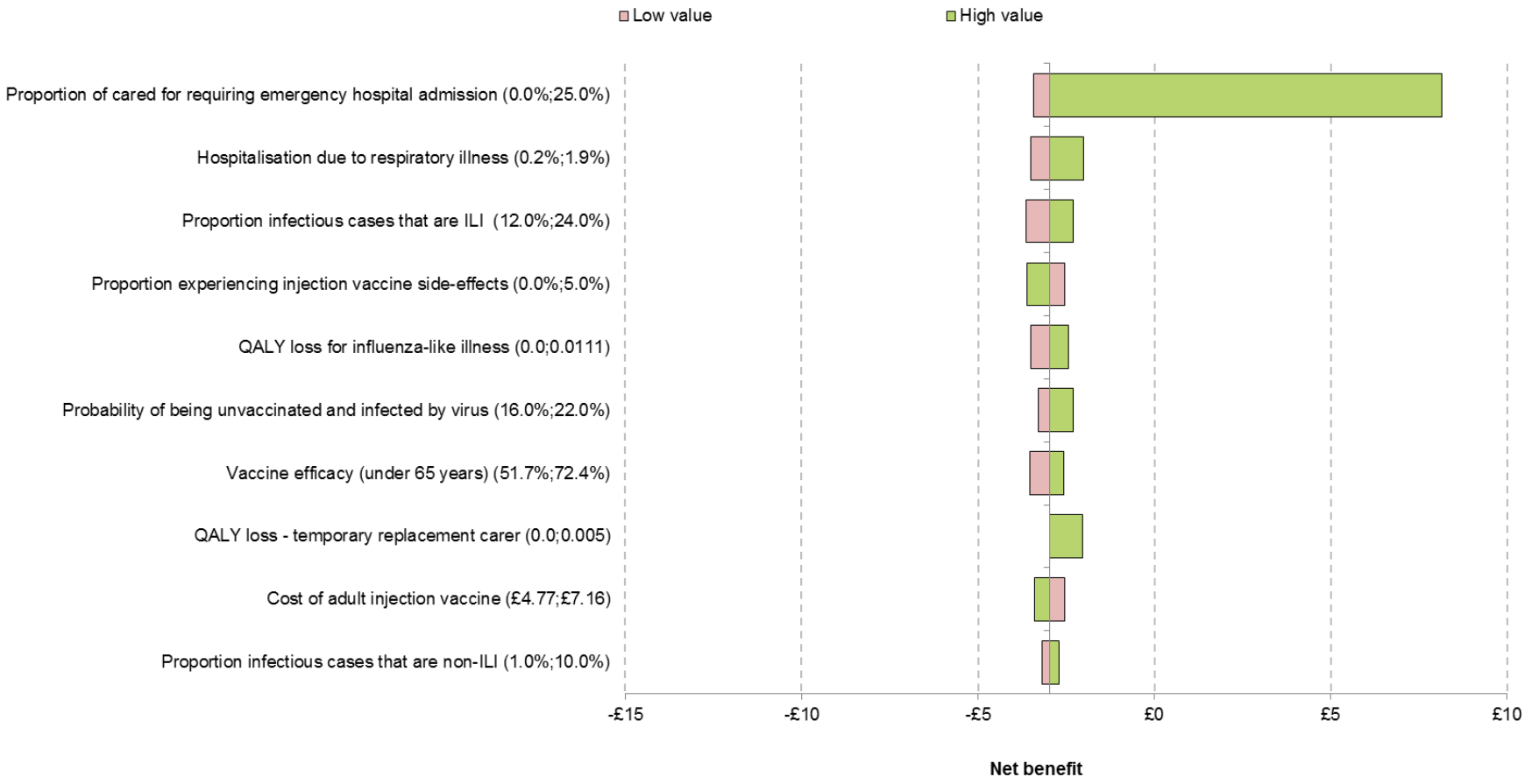
* *Please note that there is no low value bar for the QALY loss – temporary replacement carer because the QALY loss is zero in the base case.*

SCENARIO 4 (UPTAKE IN CARERS IS 25% HIGHER THAN THE BASELINE RATE)



* *Please note that there is no low value bar for the QALY loss – temporary replacement carer because the QALY loss is zero in the base case.*

Scenario 5 (uptake in carers is 35% higher than the baseline rate)

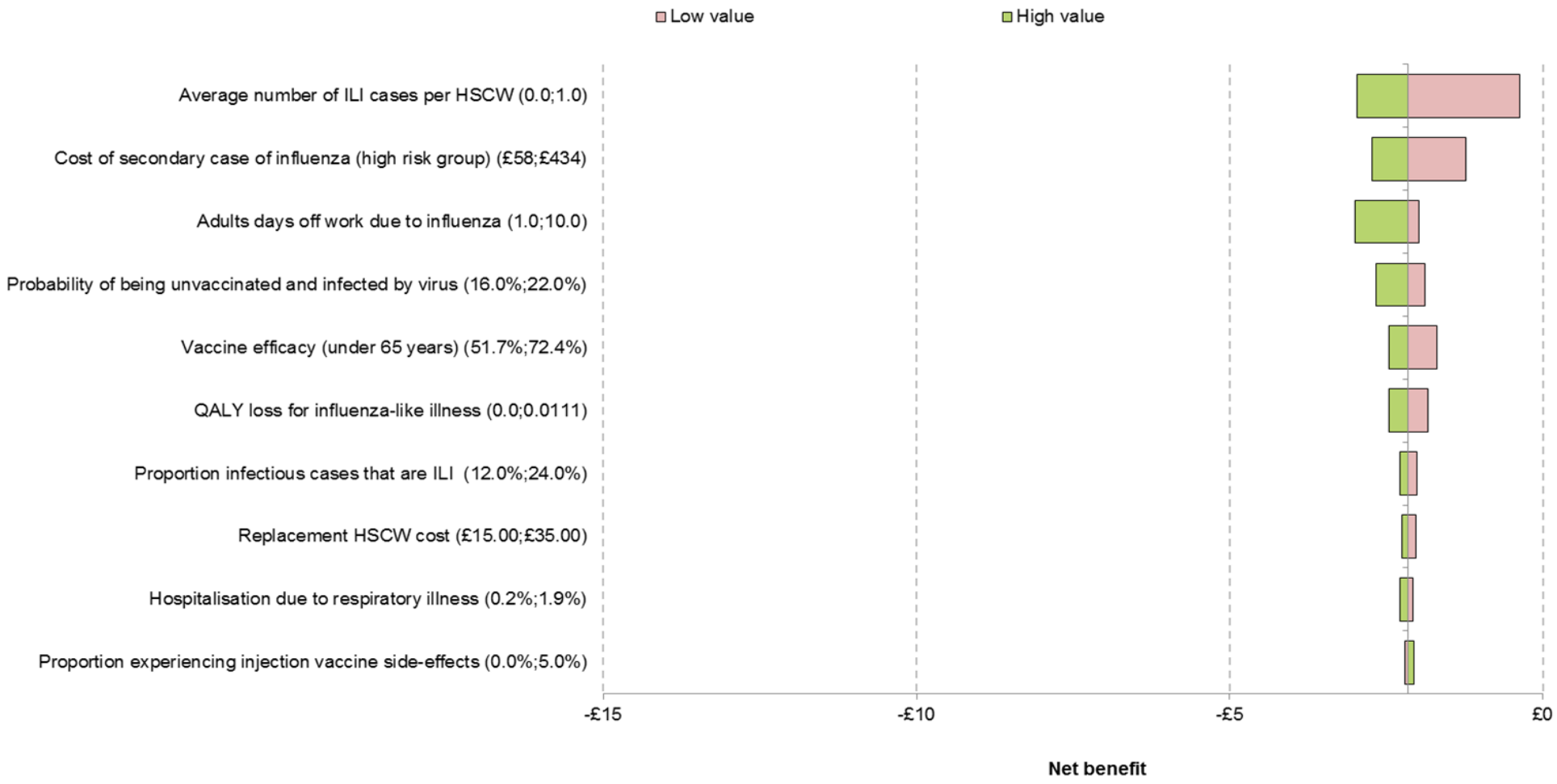


* *Please note that there is no low value bar for the QALY loss – temporary replacement carer because the QALY loss is zero in the base case.*

APPENDIX J

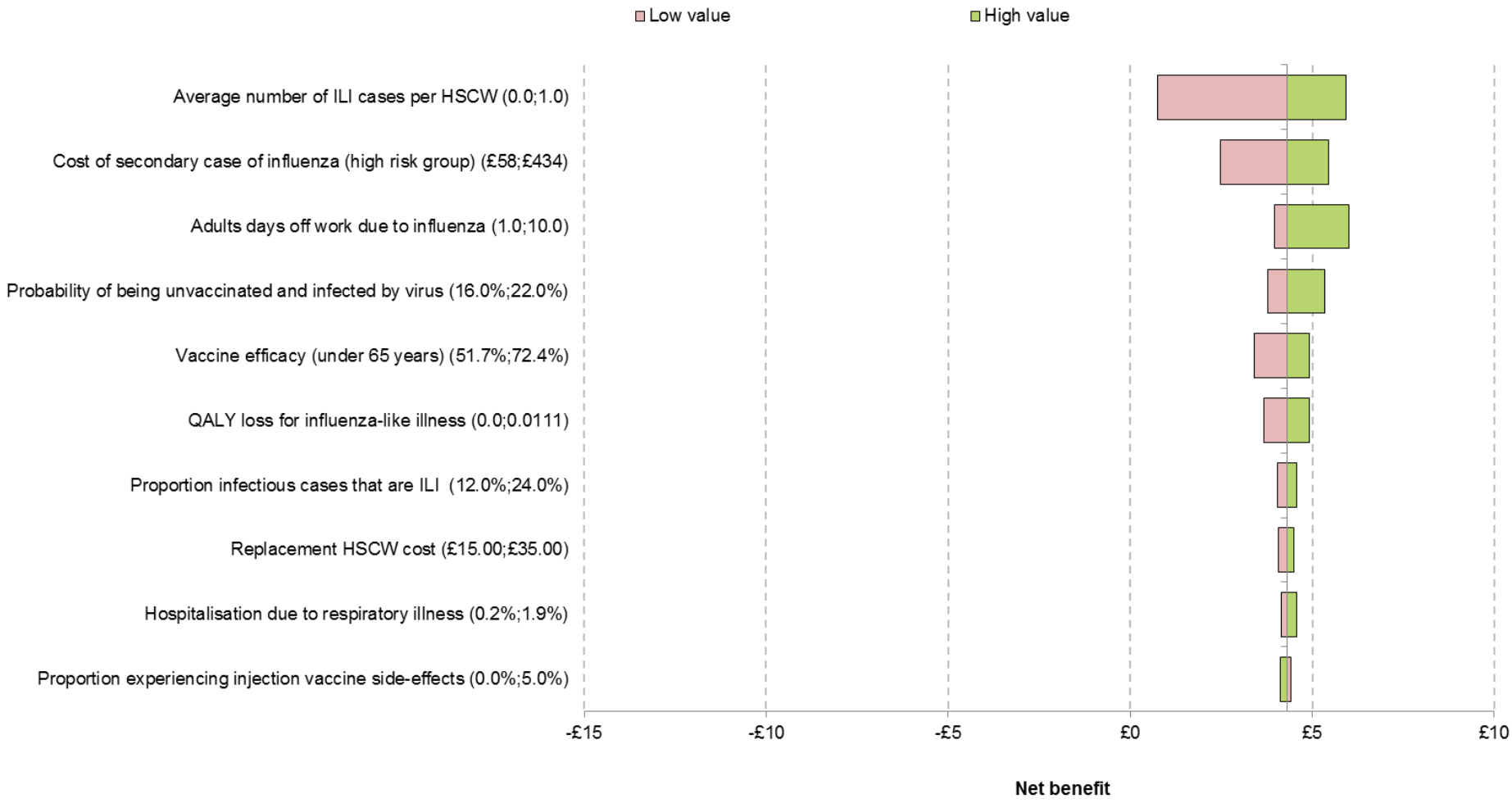
Tornado Diagrams
Health and Social Care Workers

Scenario 2 (uptake in health and social care workers is 5% lower than the baseline rate)



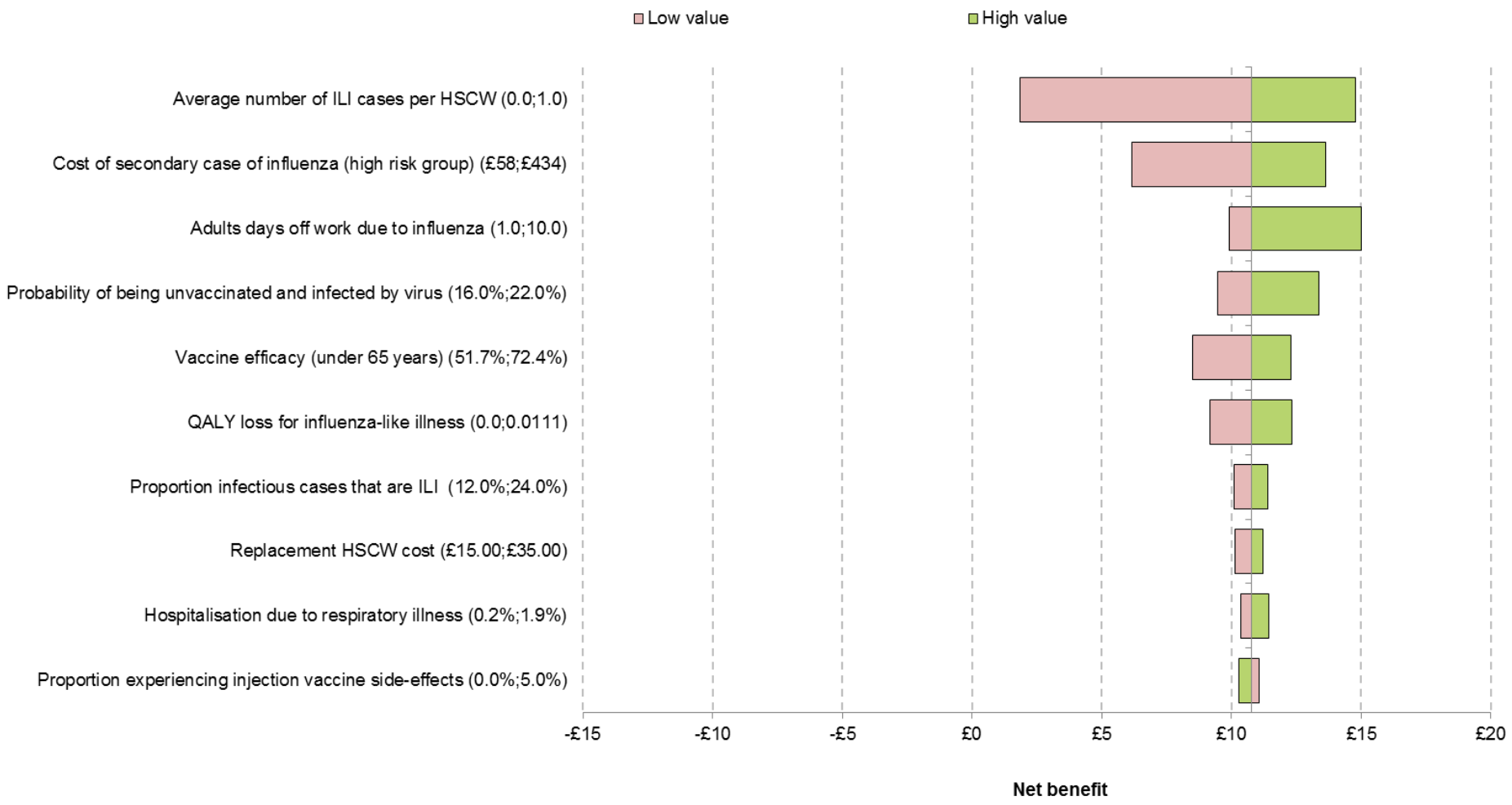
* *Please note that adult days off work due to influenza appears on the tornado diagram for the NHS and PSS perspective due to the number of days of absence impacting on the cost to the NHS to temporarily replace the absent health and social care worker.*

Scenario 3 (uptake in health and social care workers is 10% higher than the baseline rate)



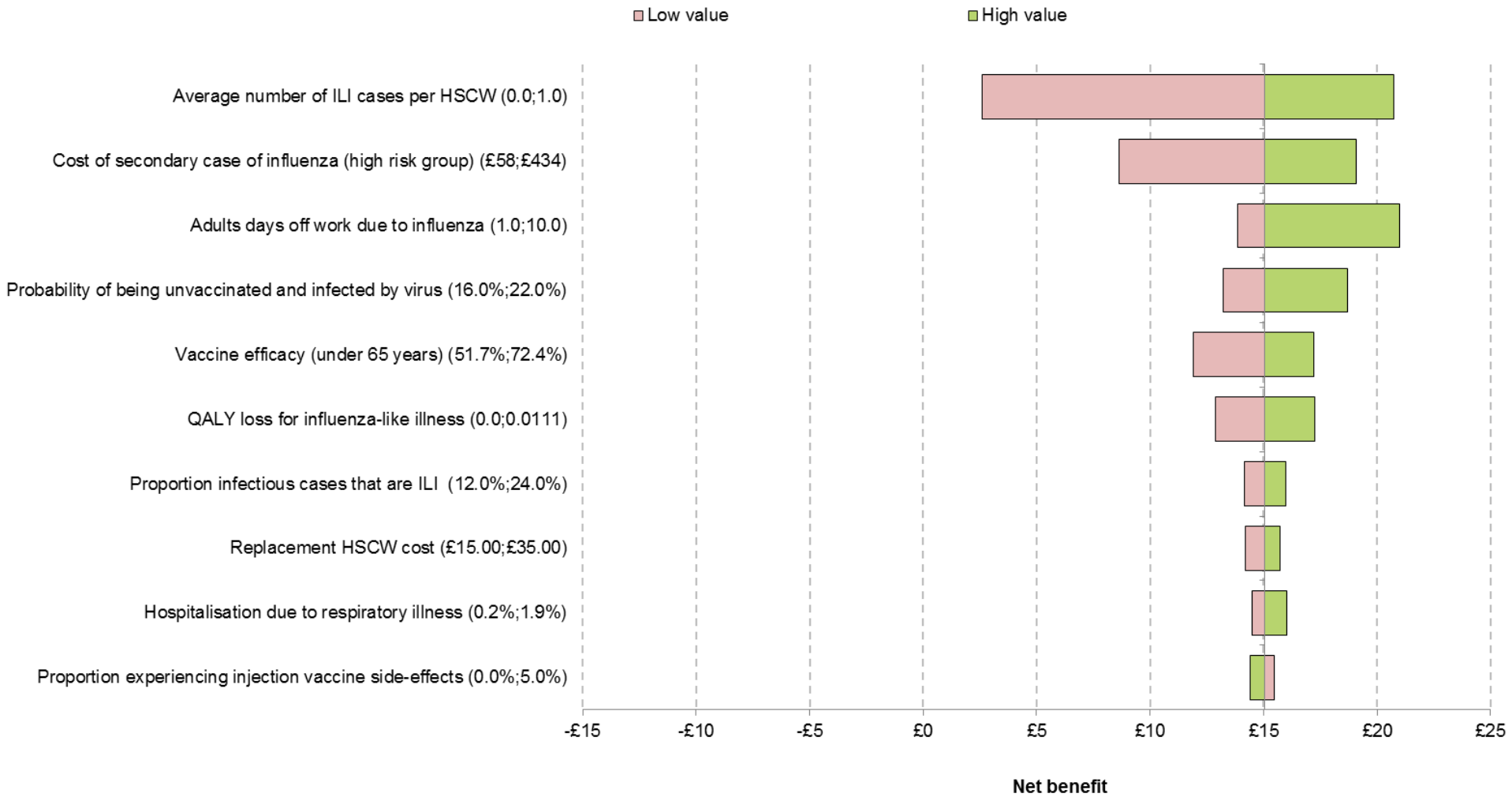
* *Please note that adult days off work due to influenza appears on the tornado diagram for the NHS and PSS perspective due to the number of days of absence impacting on the cost to the NHS to temporarily replace the absent health and social care worker.*

Scenario 4 (uptake in health and social care workers is 25% higher than the baseline rate)



* *Please note that adult days off work due to influenza appears on the tornado diagram for the NHS and PSS perspective due to the number of days of absence impacting on the cost to the NHS to temporarily replace the absent health and social care worker.*

Scenario 5 (uptake in health and social care workers is 35% higher than the baseline rate)

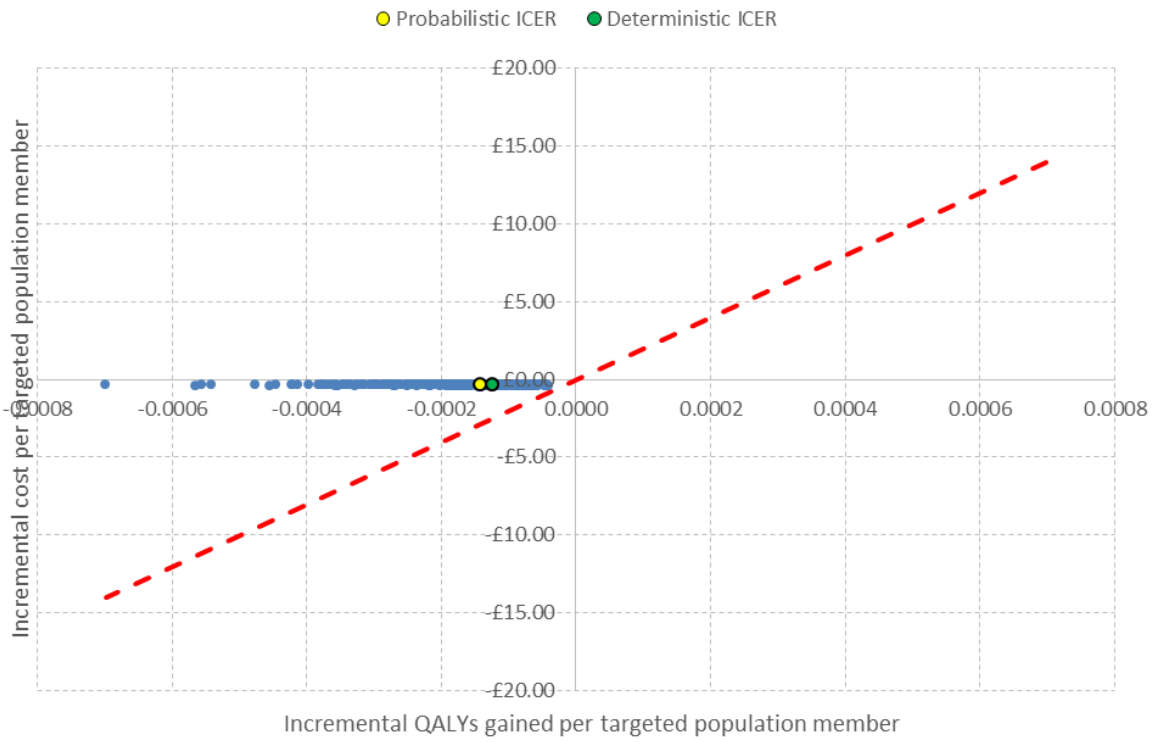


* *Please note that adult days off work due to influenza appears on the tornado diagram for the NHS and PSS perspective due to the number of days of absence impacting on the cost to the NHS to temporarily replace the absent health and social care worker*

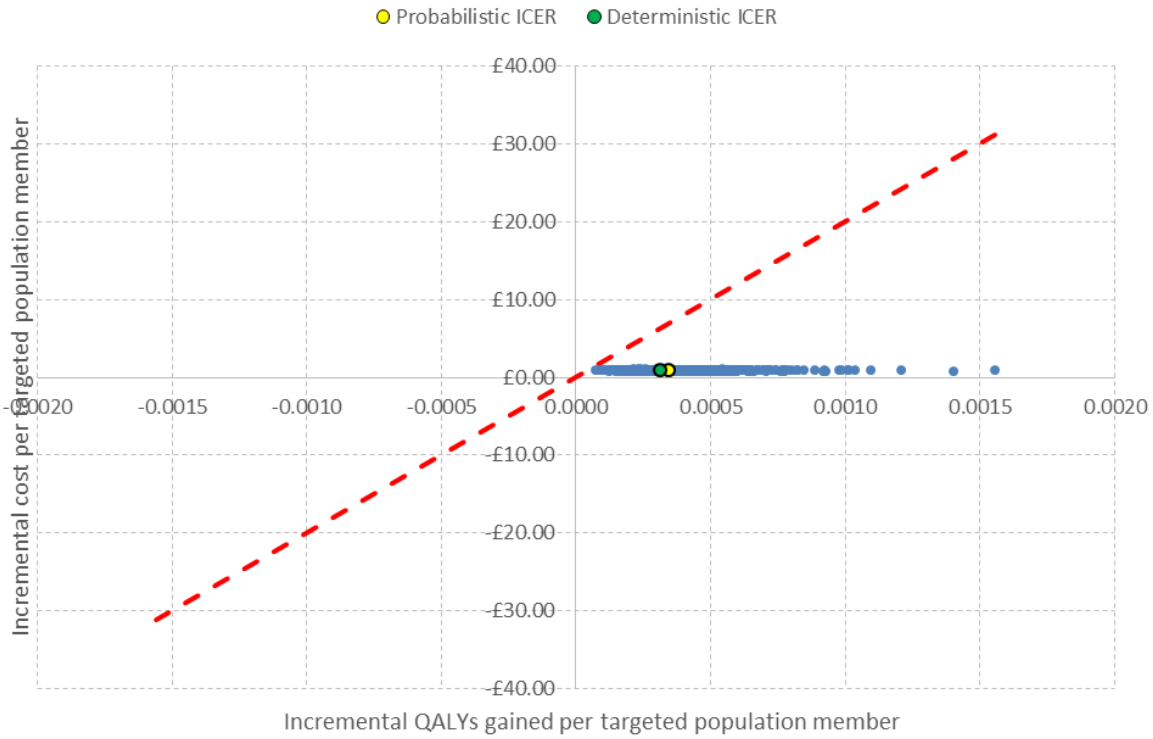
APPENDIX K

PSA Scatterplots
Children

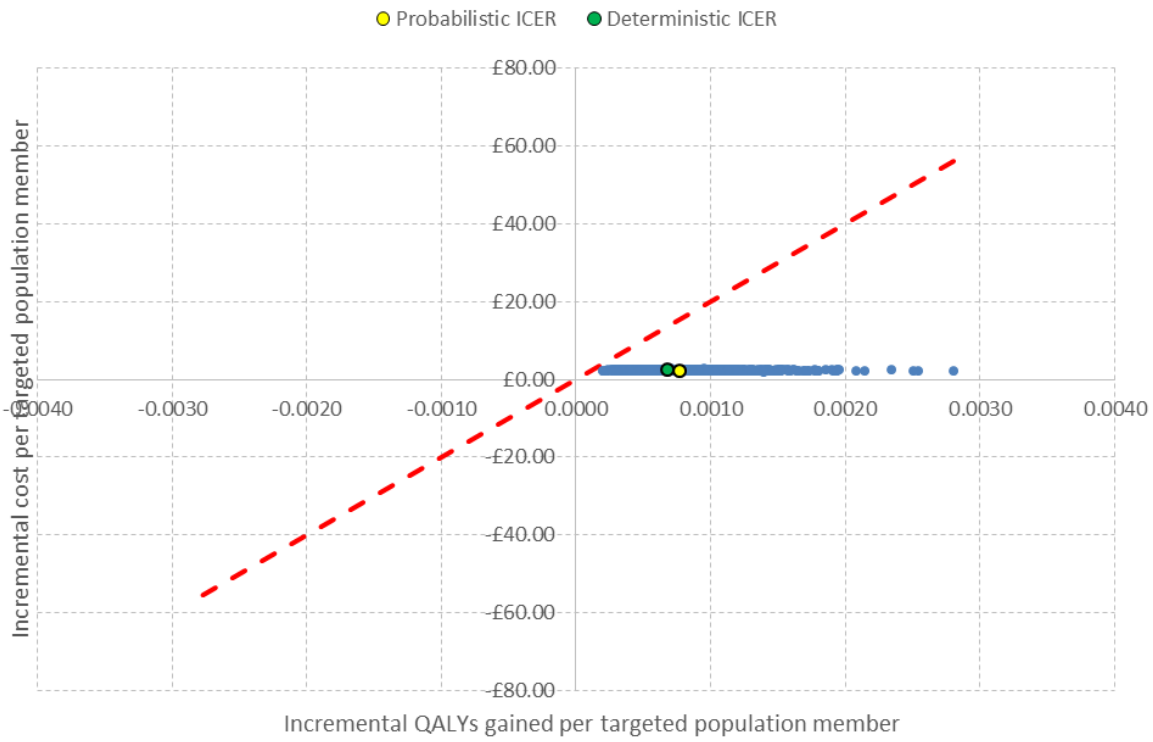
Scenario 12 (uptake in children between 2 and 17 years is 5% lower than the baseline rate)



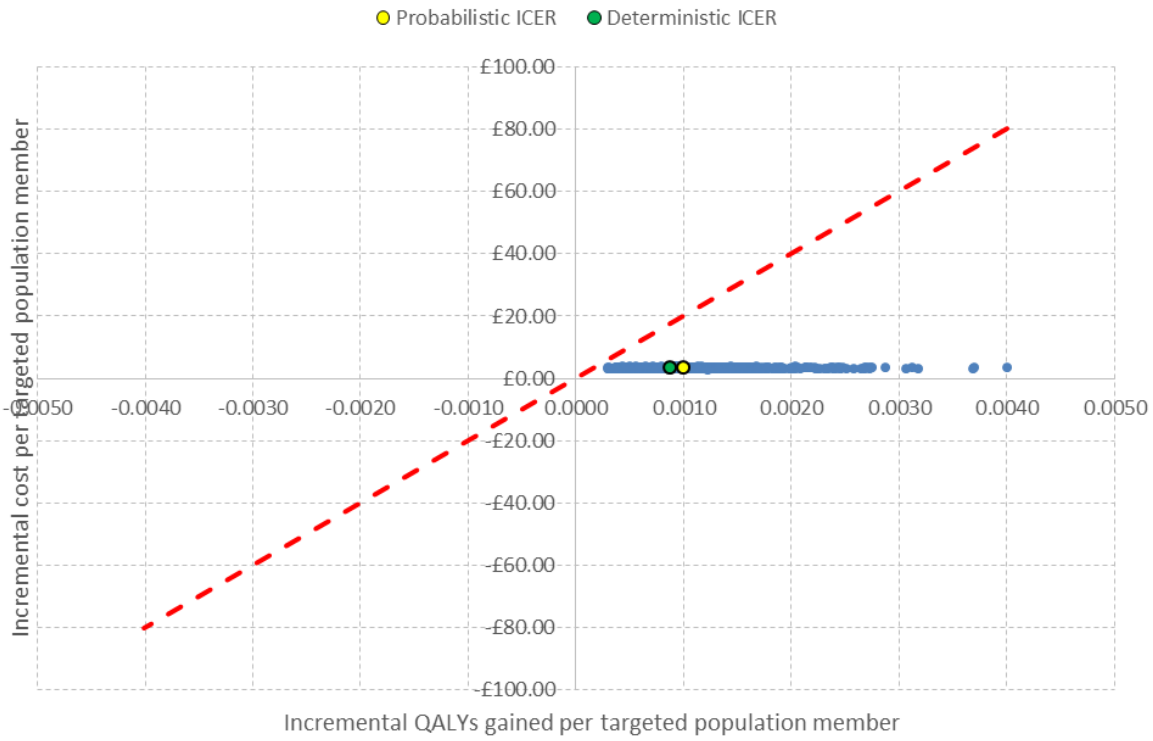
Scenario 13 (uptake in children between 2 and 17 years is 10% higher than the baseline rate)



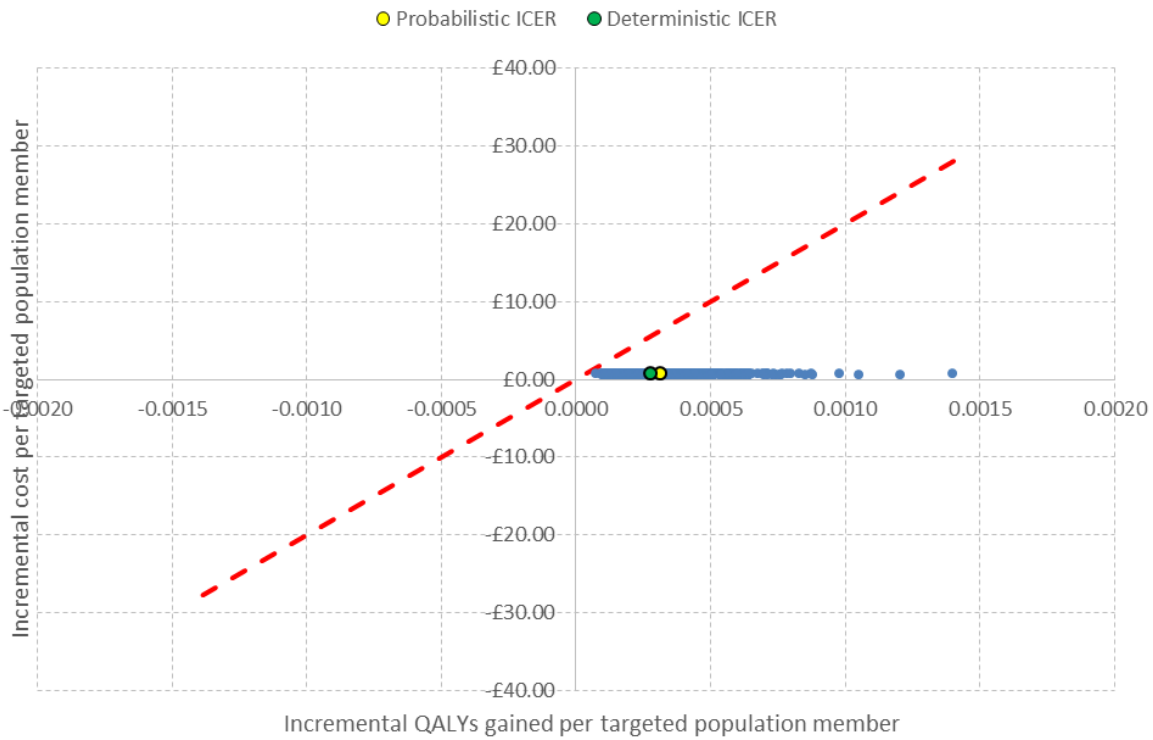
Scenario 14 (uptake in children between 2 and 17 years is 25% higher than the baseline rate)



Scenario 15 (uptake in children between 2 and 17 years is 35% higher than the baseline rate)



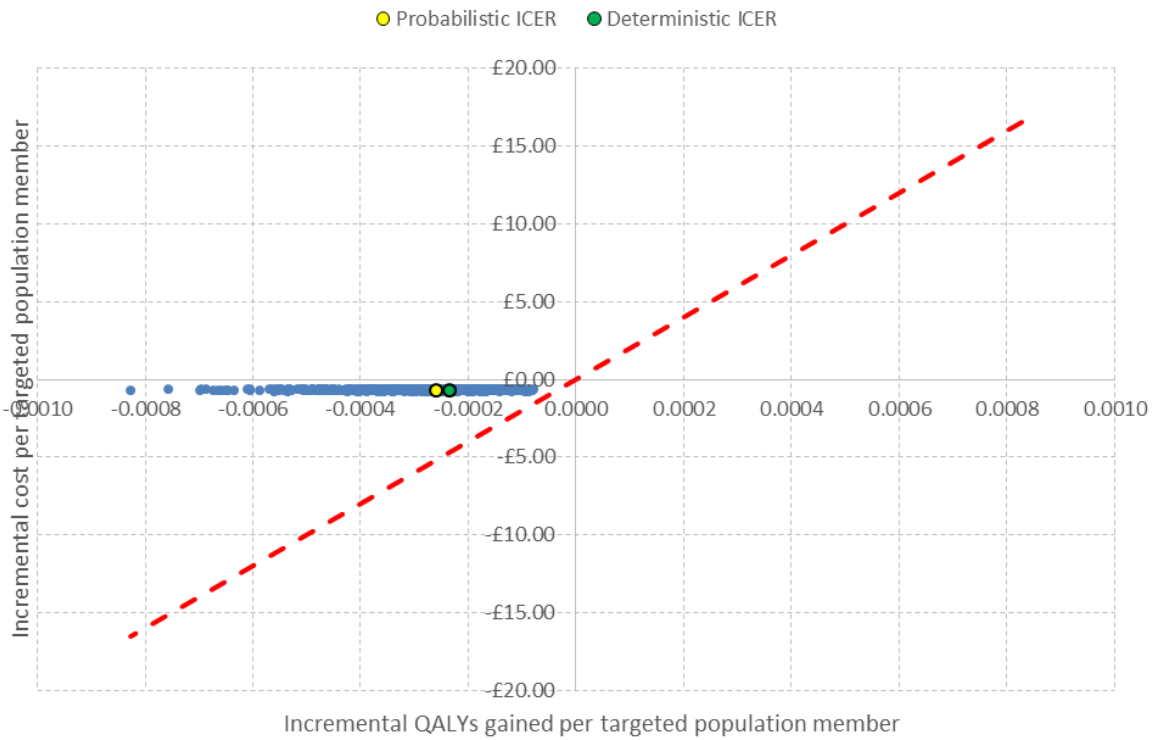
Scenario 20 (uptake in low risk children is 10% higher than the baseline rate)



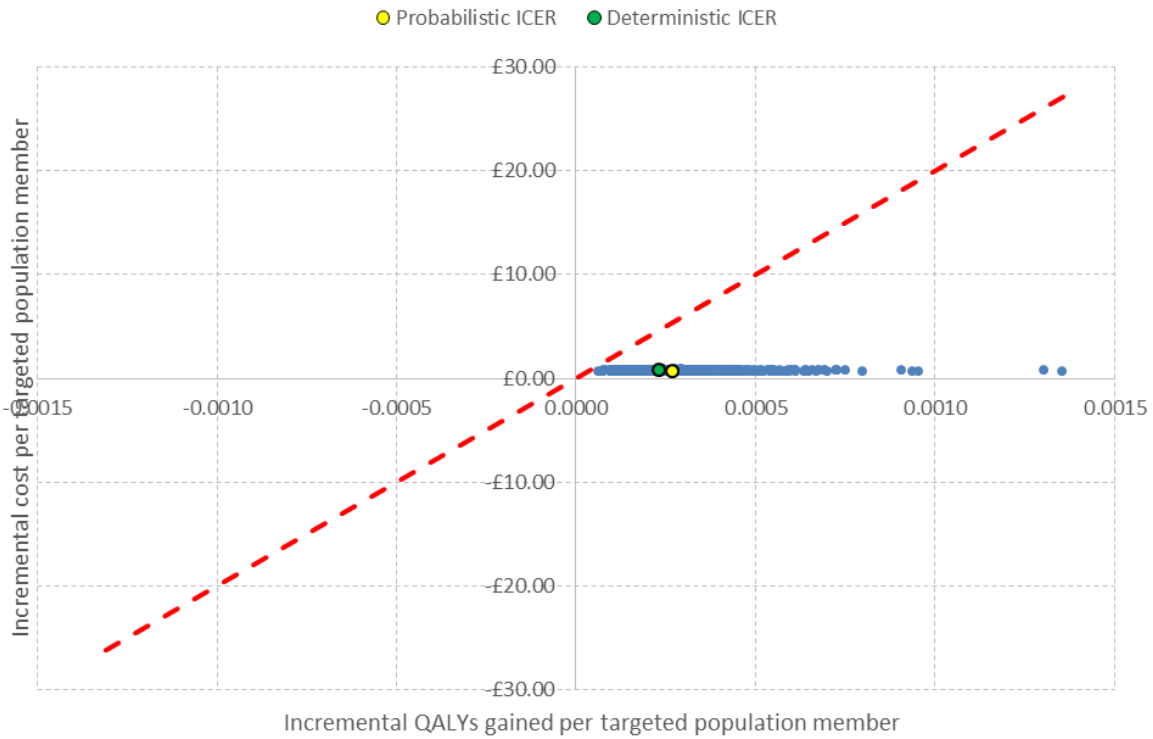
APPENDIX L

PSA Scatterplots
Clinical Risk Groups

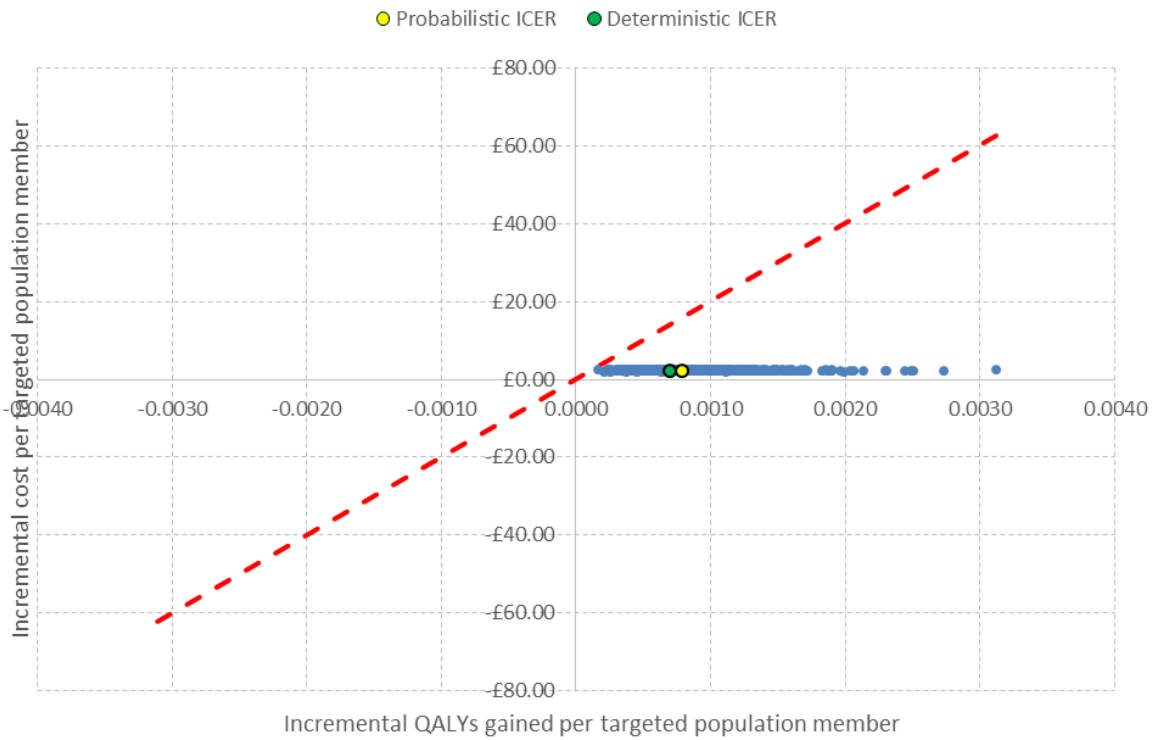
Scenario 2 (uptake by adults in a clinical risk group is 5% lower than the baseline rate)



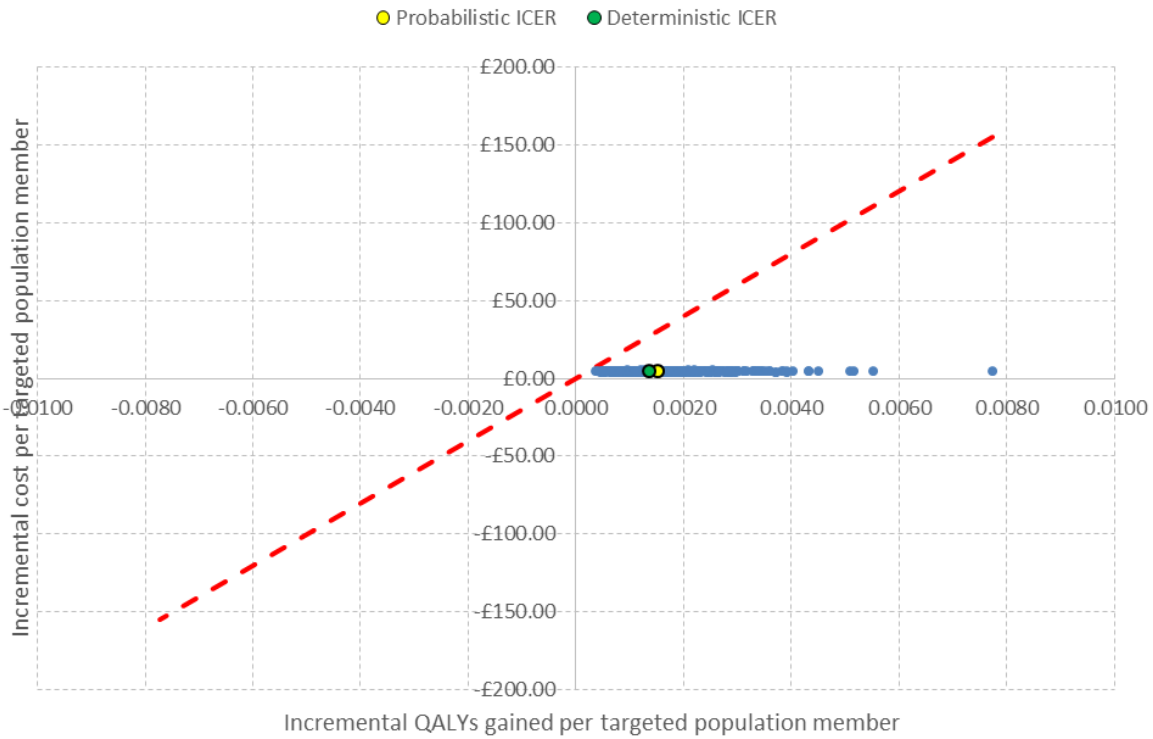
Scenario 3 (uptake by adults in a clinical risk group is 5% higher than the baseline rate)



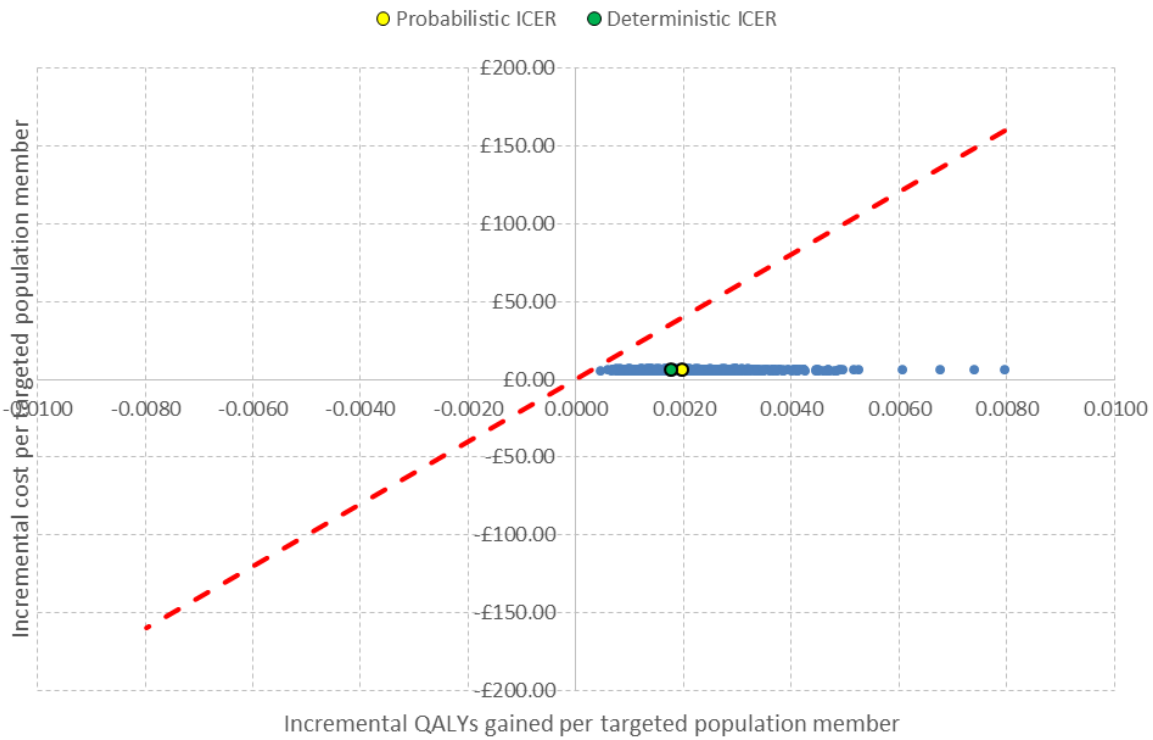
Scenario 4 (uptake by adults in a clinical risk group is 15% higher than the baseline rate)



Scenario 5 (uptake by adults in a clinical risk group is 35% higher than the baseline rate)

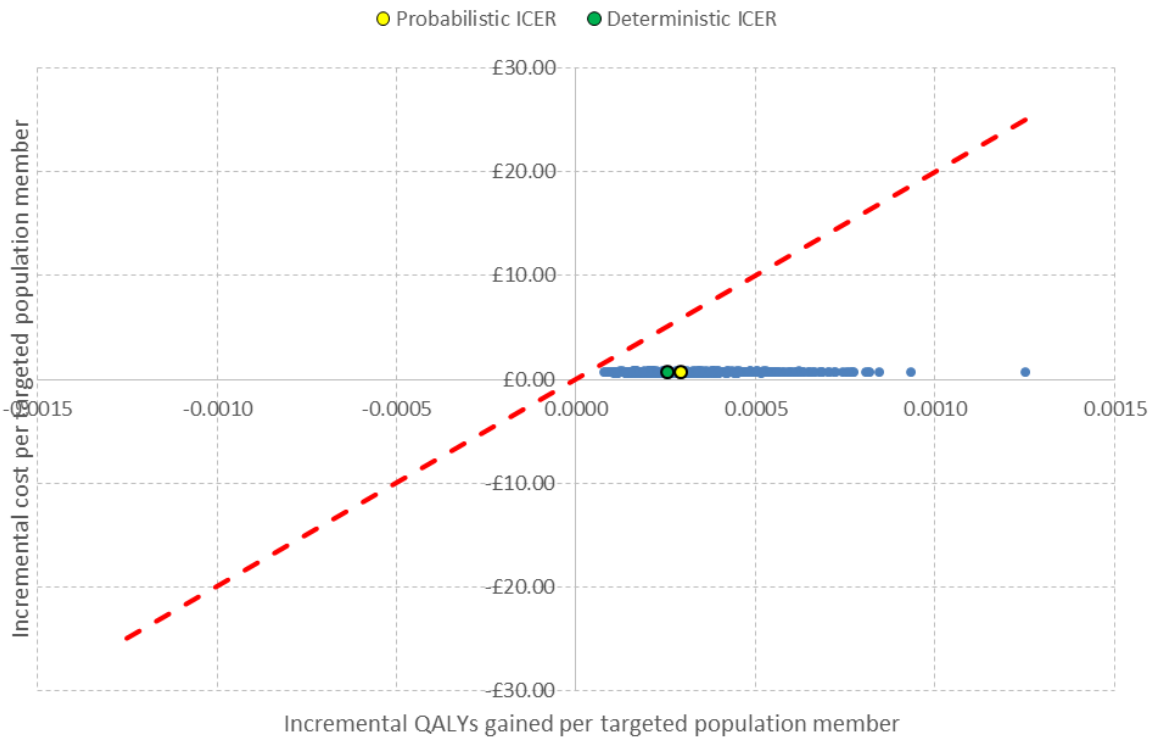


Scenario 6 (uptake by adults in a clinical risk group is 40% higher than the baseline rate)

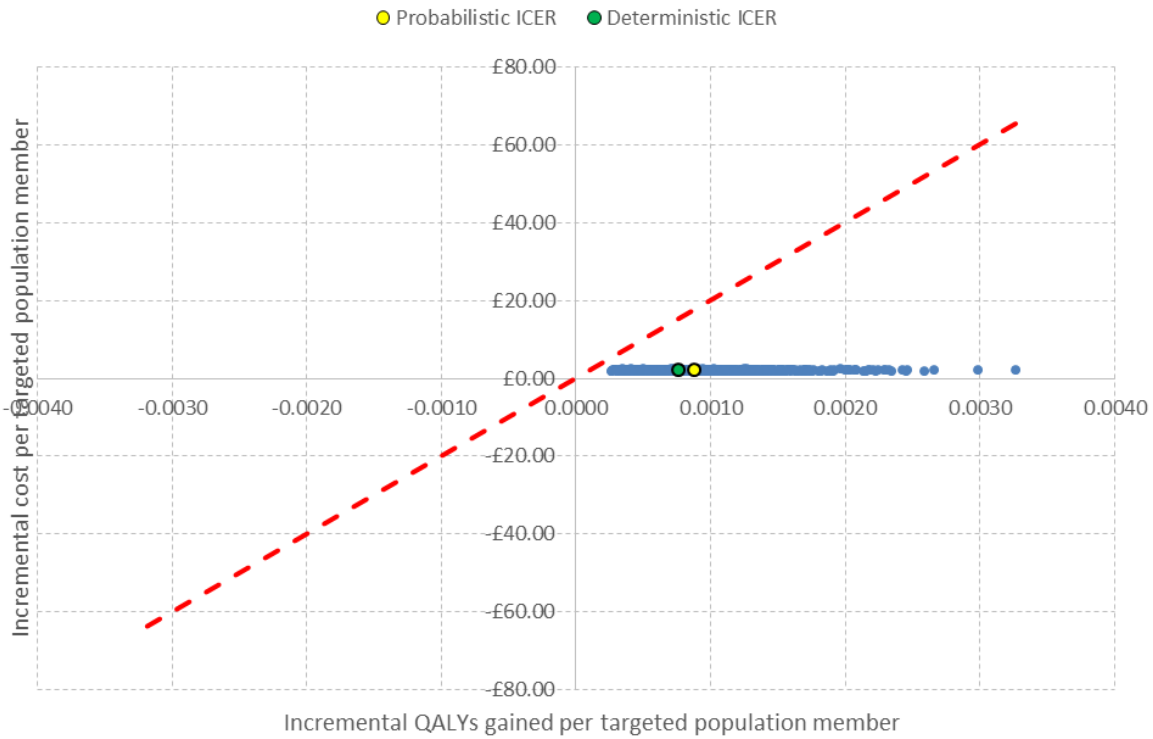


Scenario 7 (uptake by pregnant women is 5% lower than the baseline rate)

Scenario 8 (uptake by pregnant women is 5% higher than the baseline rate)

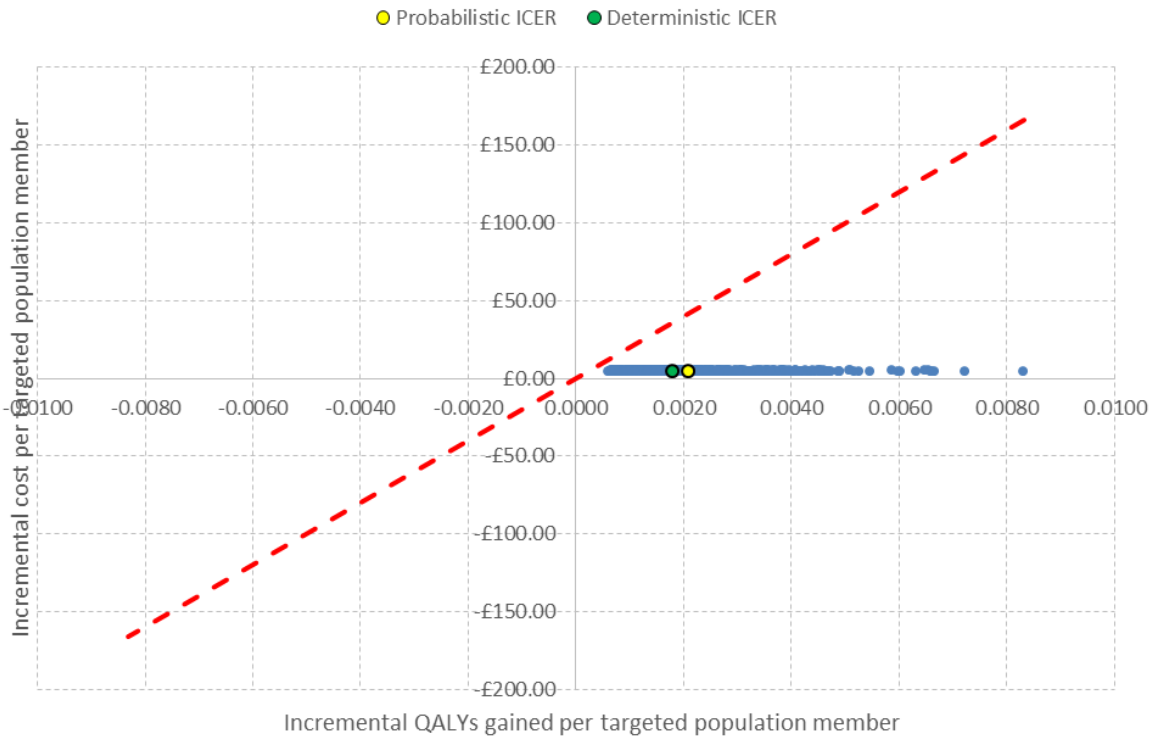


Scenario 9 (uptake by pregnant women is 15% higher than the baseline rate)

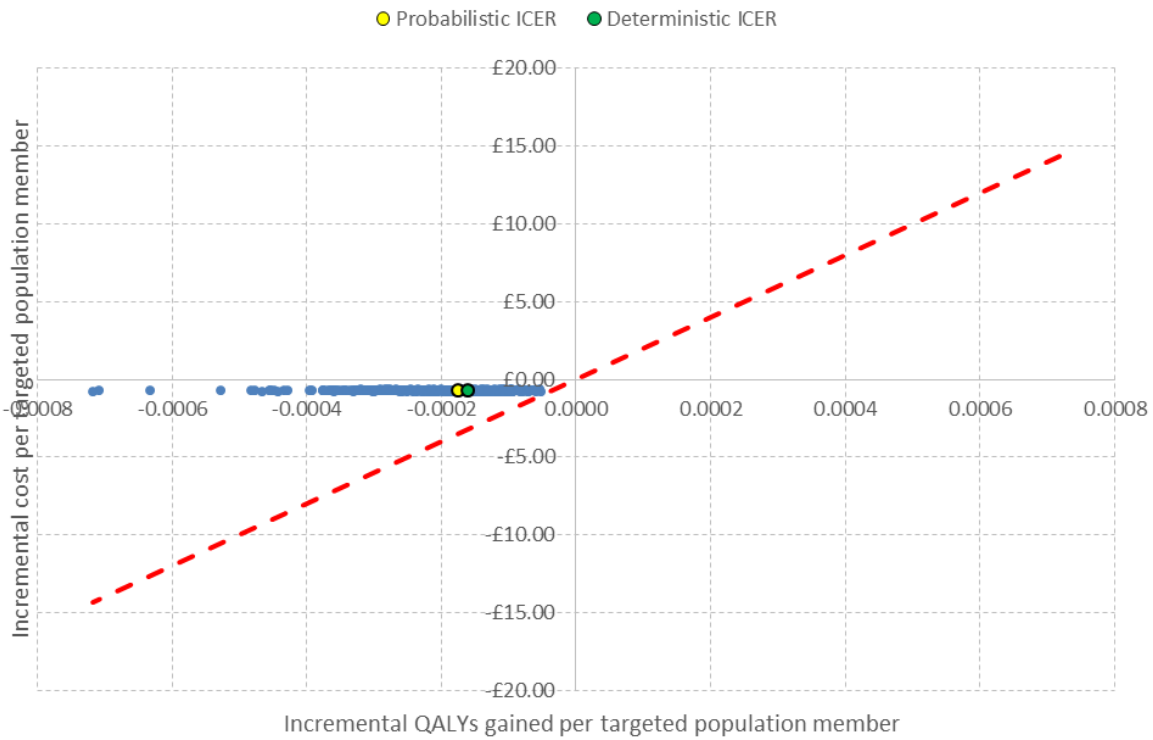


Scenario 10 (uptake by pregnant women is 25% higher than the baseline rate)

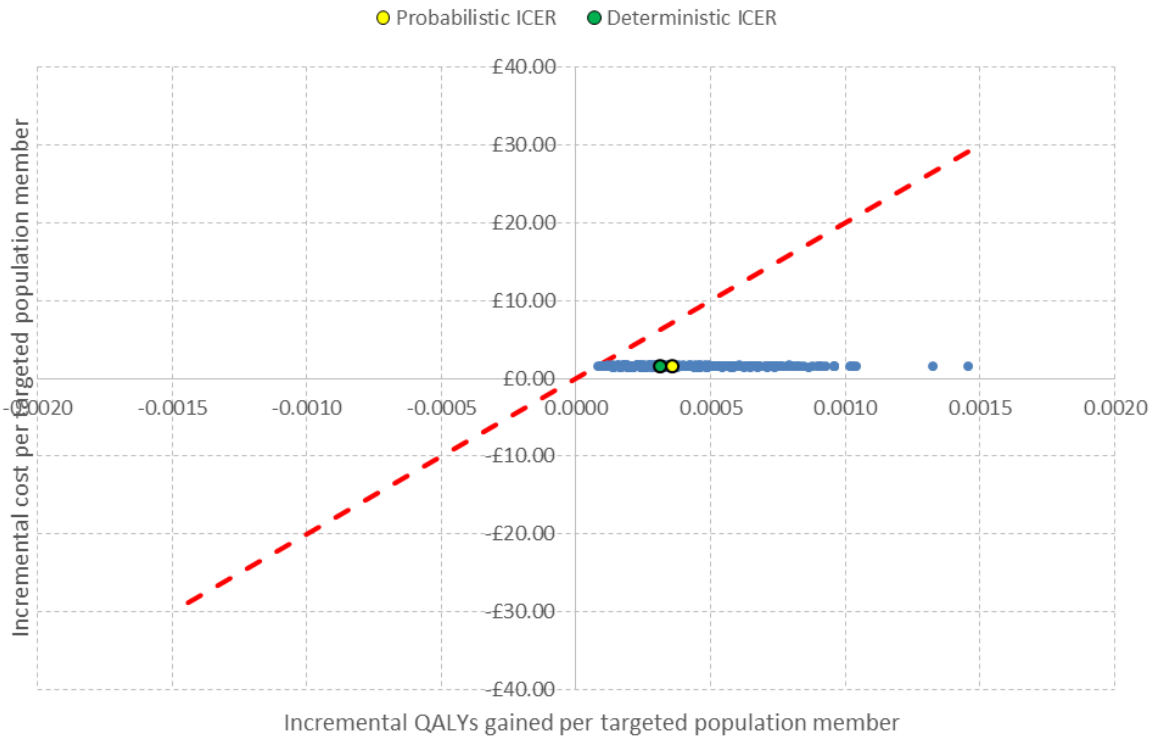
Scenario 11 (uptake by pregnant women is 35% higher than the baseline rate)



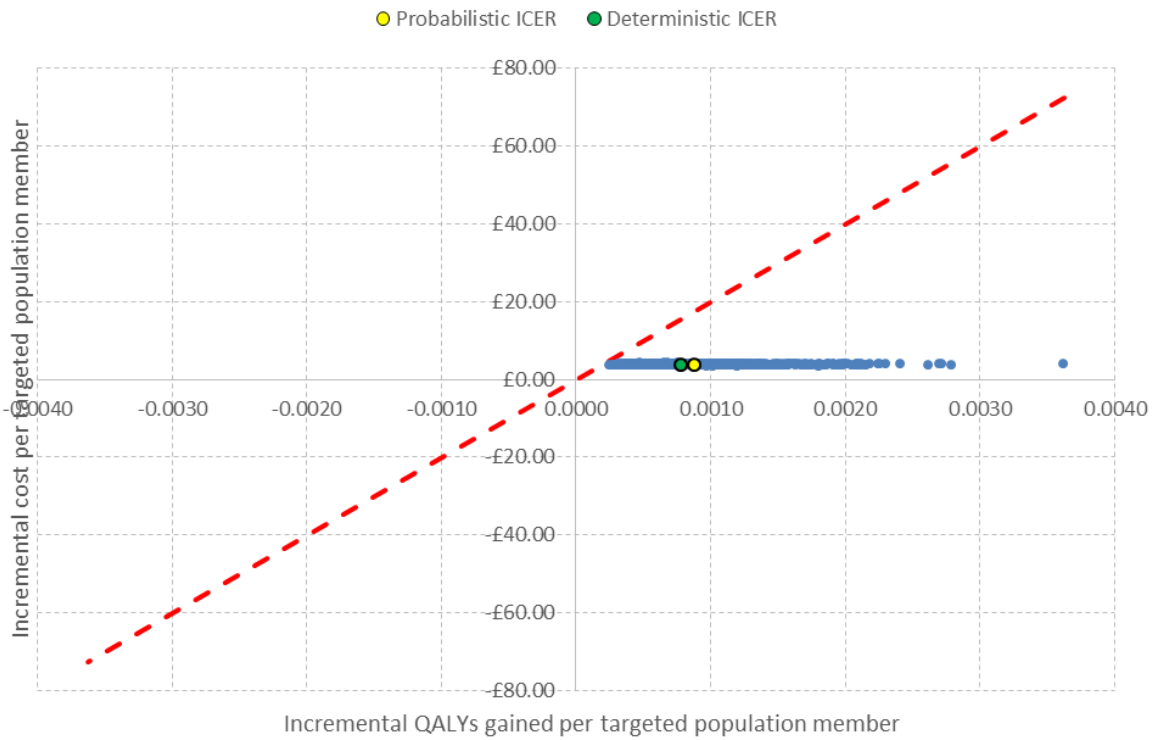
Scenario 16 (uptake in high risk children is 5% lower than the baseline rate)



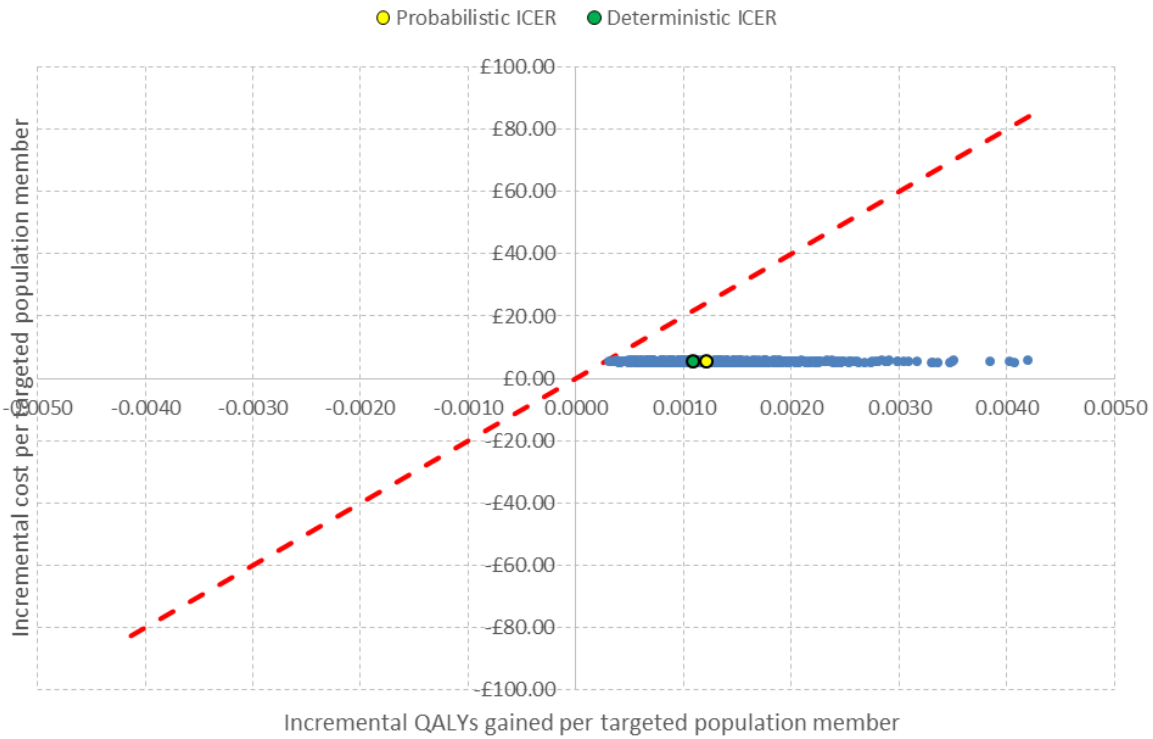
Scenario 17 (uptake in high risk children is 10% higher than the baseline rate)



Scenario 18 (uptake in high risk children is 25% higher than the baseline rate)



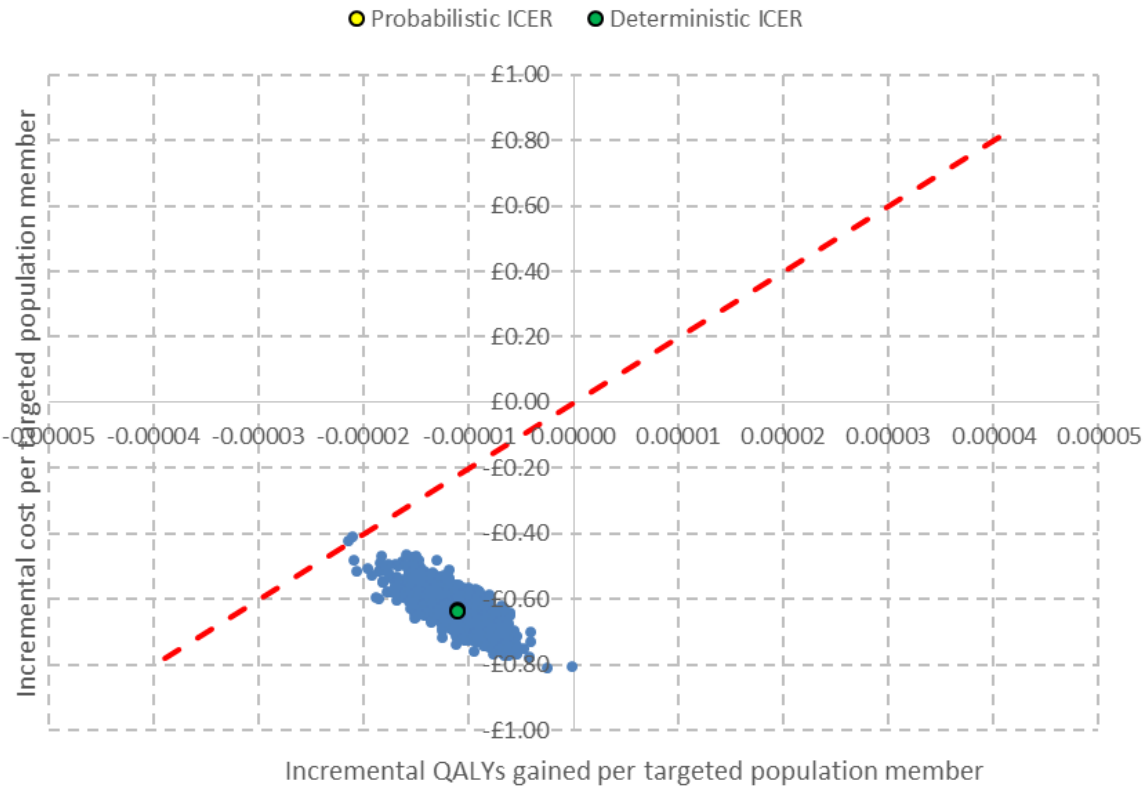
Scenario 19 (uptake in high risk children is 35% higher than the baseline rate)



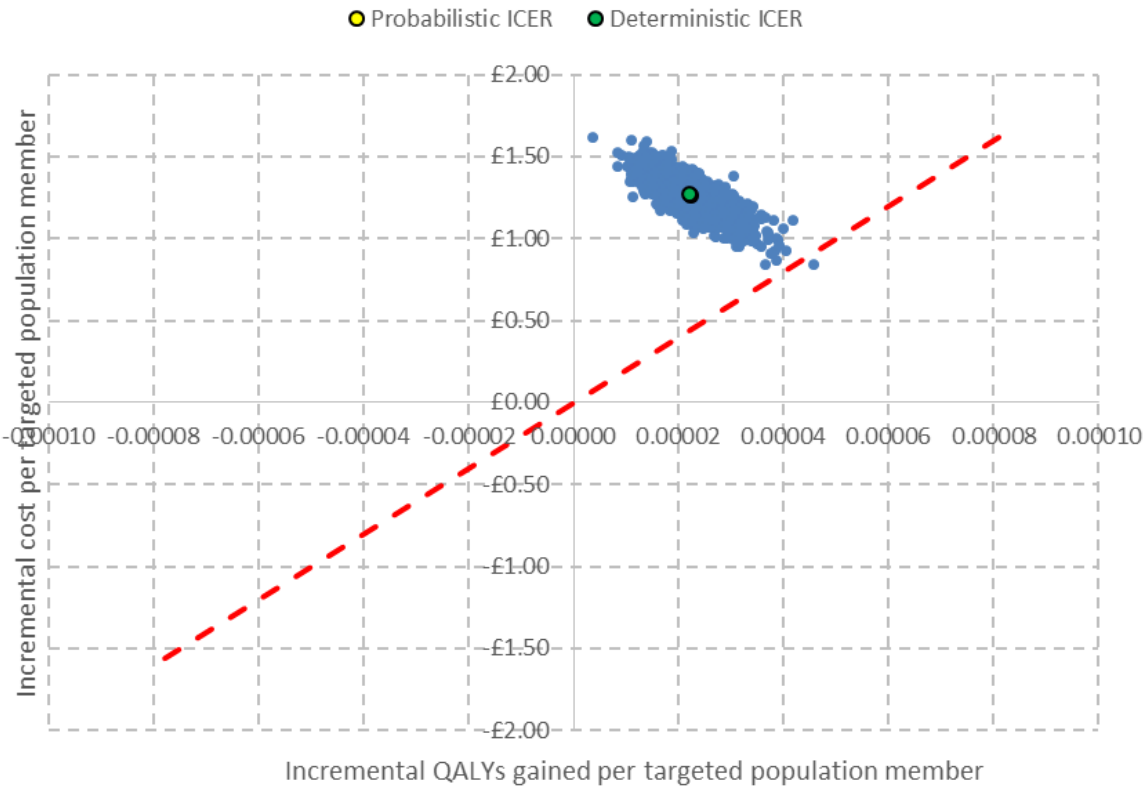
APPENDIX M

PSA Scatterplots
Carers

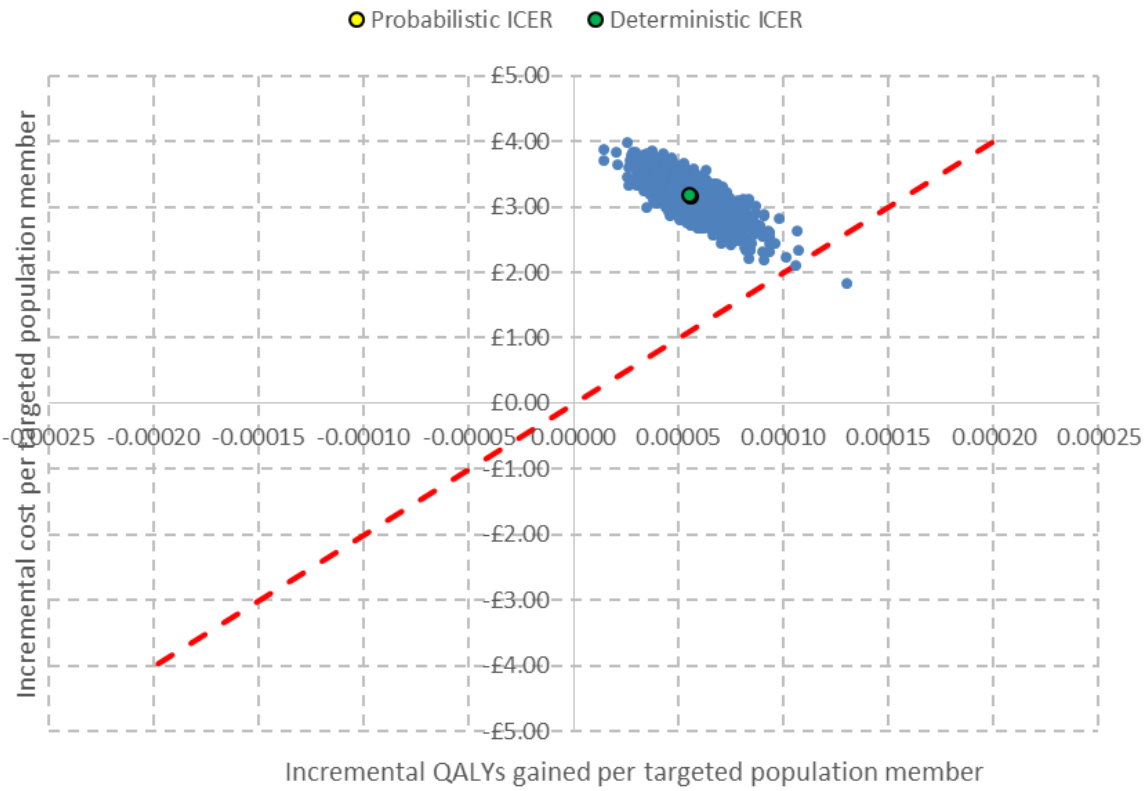
Scenario 2 (uptake in carers is 5% less than the baseline rate)



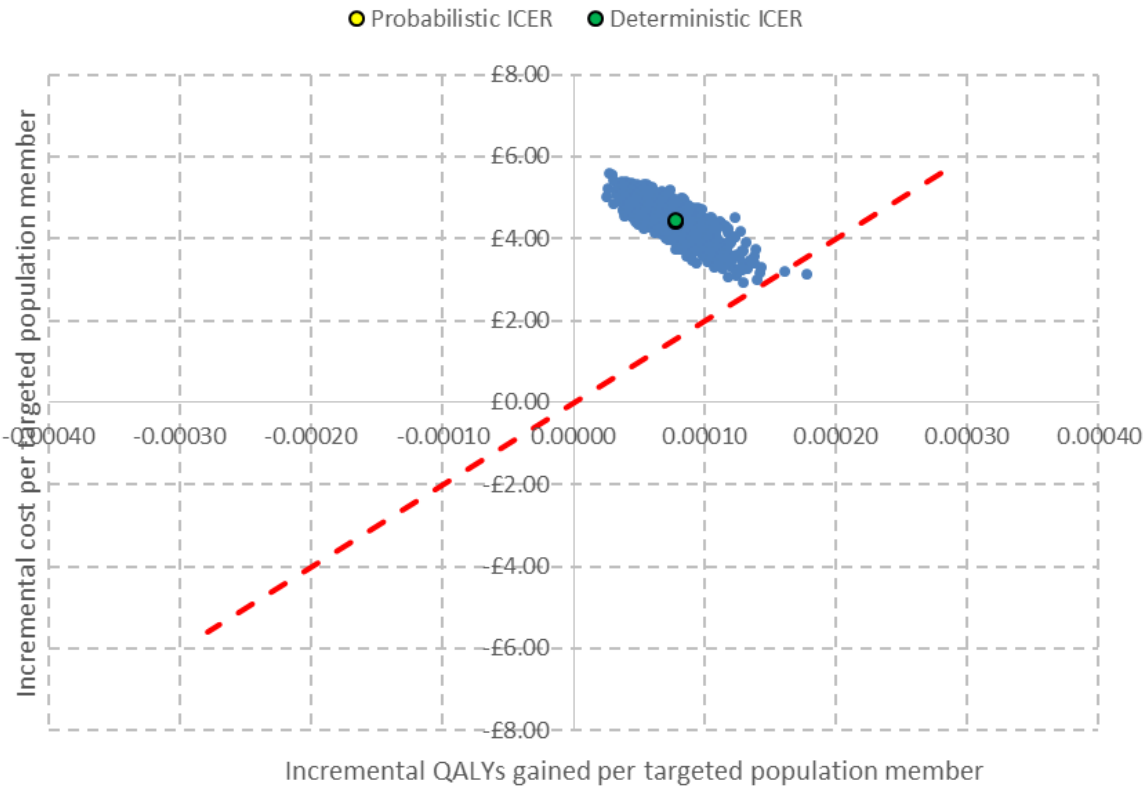
Scenario 3 (uptake in carers is 10% higher than the baseline rate)



Scenario 4 (uptake in carers is 25% higher than the baseline rate)



Scenario 5 (uptake in carers is 35% higher than the baseline rate)

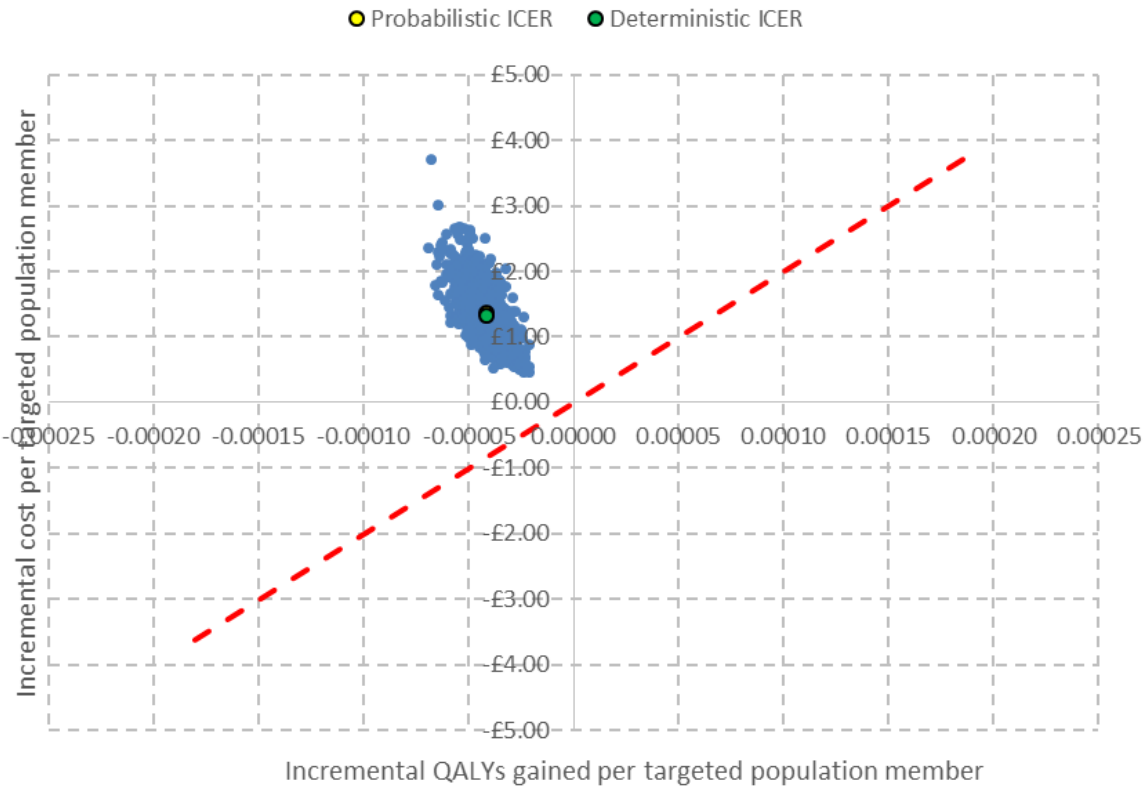


Scenario 6 (uptake in carers is 100% compared against the baseline rate)

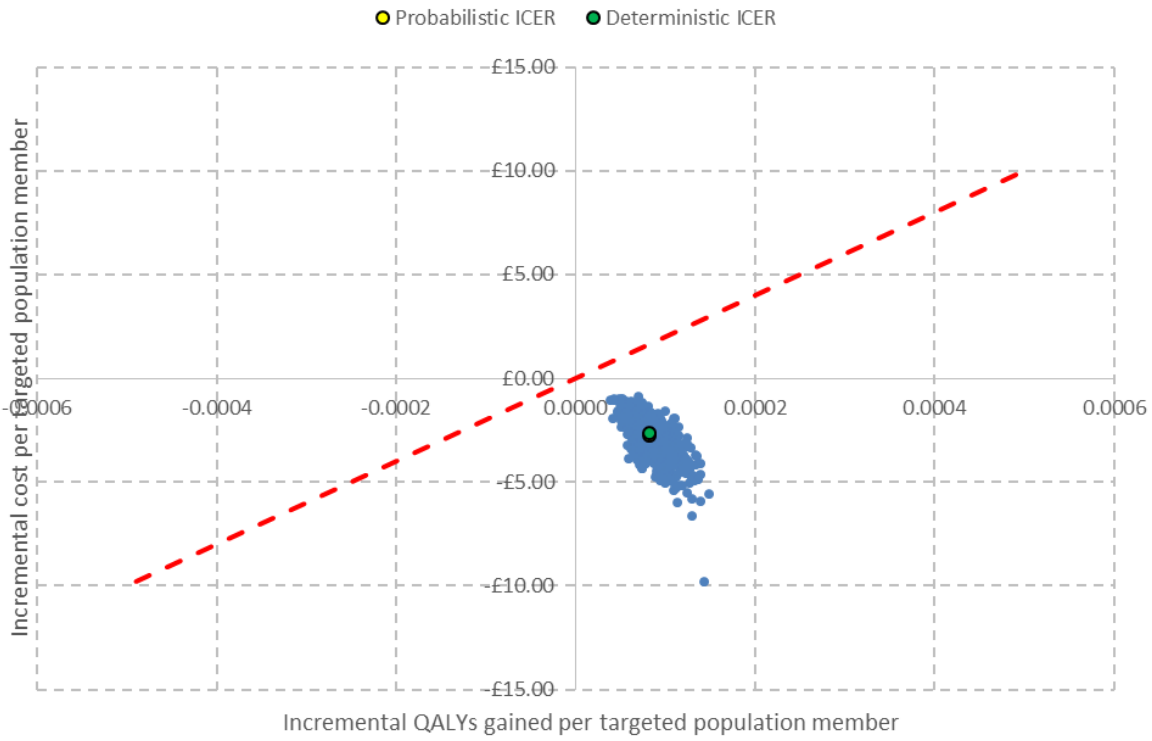
APPENDIX N

PSA Scatterplots
Health and Social Care Workers

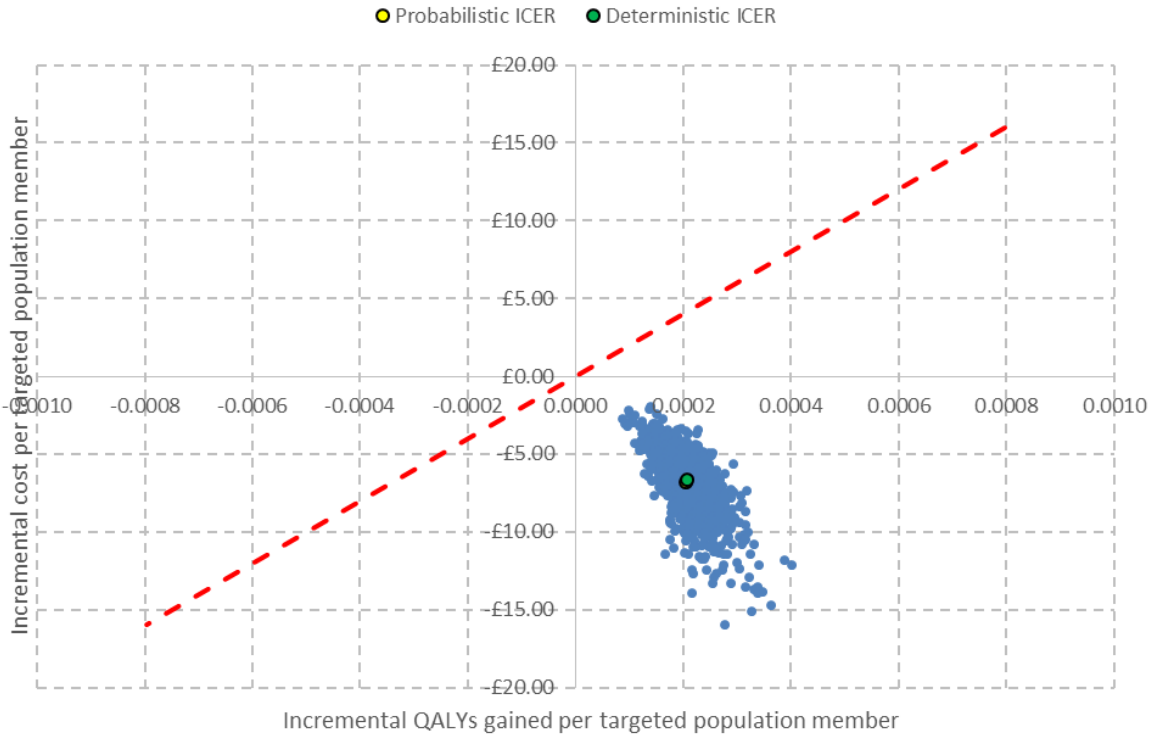
Scenario 2 (uptake in health and social care workers is 5% lower than the baseline rate)



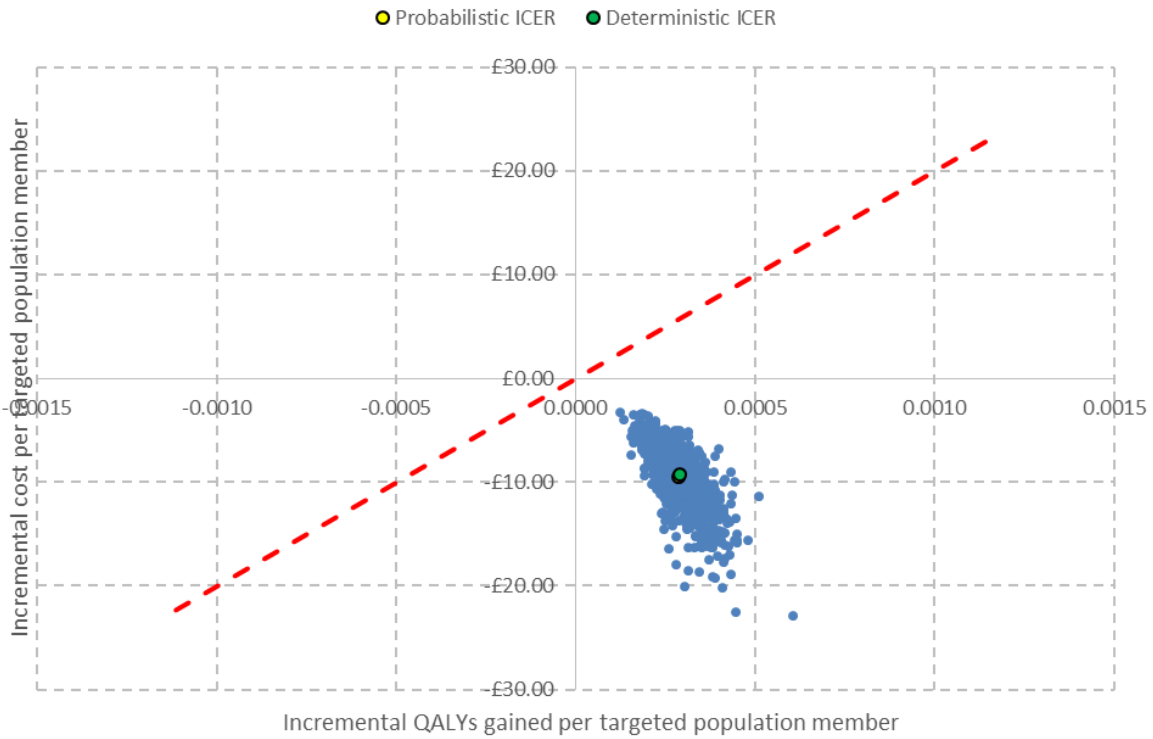
Scenario 3 (uptake in health and social care workers is 10% higher than the baseline rate)



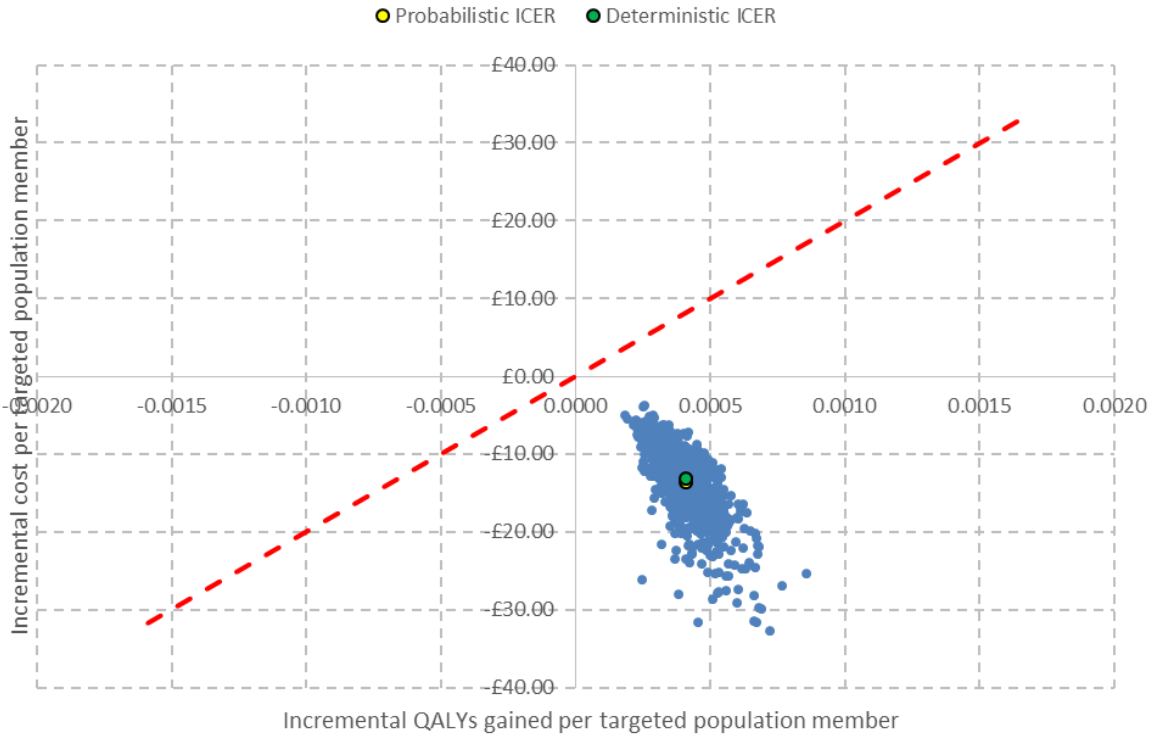
Scenario 4 (uptake in health and social care workers is 25% higher than the baseline rate)



Scenario 5 (uptake in health and social care workers is 35% higher than the baseline rate)



Scenario 6 (uptake in health and social care workers is 100% compared to the baseline rate)



APPENDIX O

One-way sensitivity analysis: cost of hospitalisation

Maximum willingness to pay for the intervention per target population member (Children)

Scenario	Cost of hospitalisation										
	£1,000	**£2,000**	**£3,000**	**£4,000**	**£5,000**	**£6,000**	**£7,000**	**£8,000**	**£9,000**	**£10,000**	**£11,000**
Scenario 12	-£2.12 (£0.00)	-£2.16 (-£0.04)	-£2.19 (-£0.08)	-£2.23 (-£0.11)	-£2.27 (-£0.15)	-£2.31 (-£0.19)	-£2.35 (-£0.23)	-£2.39 (-£0.27)	-£2.43 (-£0.31)	-£2.46 (-£0.35)	-£2.50 (-£0.38)
Scenario 13	£5.49 (£0.00)	£5.59 (£0.09)	£5.68 (£0.18)	£5.77 (£0.27)	£5.86 (£0.37)	£5.96 (£0.46)	£6.05 (£0.55)	£6.14 (£0.64)	£6.23 (£0.74)	£6.32 (£0.83)	£6.42 (£0.92)
Scenario 14	£11.47 (-£0.01)	£11.68 (£0.20)	£11.88 (£0.40)	£12.08 (£0.60)	£12.28 (£0.80)	£12.48 (£1.00)	£12.69 (£1.21)	£12.89 (£1.41)	£13.09 (£1.61)	£13.29 (£1.81)	£13.49 (£2.01)
Scenario 15	£14.25 (-£0.01)	£14.50 (£0.25)	£14.76 (£0.51)	£15.02 (£0.77)	£15.28 (£1.03)	£15.54 (£1.28)	£15.79 (£1.54)	£16.05 (£1.80)	£16.31 (£2.06)	£16.57 (£2.32)	£16.83 (£2.58)
Scenario 20	£4.95 (£0.00)	£5.03 (£0.08)	£5.12 (£0.16)	£5.20 (£0.24)	£5.28 (£0.33)	£5.36 (£0.41)	£5.44 (£0.49)	£5.53 (£0.57)	£5.61 (£0.65)	£5.69 (£0.74)	£5.77 (£0.82)

* The values in brackets indicate the difference between the maximum willingness to pay for the intervention in the sensitivity analysis and the base case value. Negative values indicate that the result for the sensitivity analysis is lower than the result for the base case.

Maximum willingness to pay for the intervention per target population member (CRG Children)

Scenario	Cost of hospitalisation										
	£1,000	**£2,000**	**£3,000**	**£4,000**	**£5,000**	**£6,000**	**£7,000**	**£8,000**	**£9,000**	**£10,000**	**£11,000**
Scenario 16	-£2.43 (£0.00)	-£2.48 (-£0.04)	-£2.52 (-£0.09)	-£2.57 (-£0.14)	-£2.62 (-£0.18)	-£2.66 (-£0.23)	-£2.71 (-£0.28)	-£2.76 (-£0.32)	-£2.80 (-£0.37)	-£2.85 (-£0.41)	-£2.89 (-£0.46)
Scenario 17	£4.83 (£0.00)	£4.92 (£0.09)	£5.02 (£0.18)	£5.11 (£0.27)	£5.20 (£0.36)	£5.29 (£0.45)	£5.38 (£0.55)	£5.47 (£0.64)	£5.56 (£0.73)	£5.65 (£0.82)	£5.75 (£0.91)
Scenario 18	£11.95 (-£0.01)	£12.18 (£0.22)	£12.40 (£0.44)	£12.63 (£0.67)	£12.85 (£0.90)	£13.08 (£1.12)	£13.31 (£1.35)	£13.53 (£1.57)	£13.76 (£1.80)	£13.98 (£2.03)	£14.21 (£2.25)
Scenario 19	£16.58 (-£0.01)	£16.89 (£0.30)	£17.20 (£0.62)	£17.52 (£0.93)	£17.83 (£1.24)	£18.14 (£1.56)	£18.46 (£1.87)	£18.77 (£2.18)	£19.08 (£2.50)	£19.40 (£2.81)	£19.71 (£3.13)

* The values in brackets indicate the difference between the maximum willingness to pay for the intervention in the sensitivity analysis and the base case value. Negative values indicate that the result for the sensitivity analysis is lower than the result for the base case.

Maximum willingness to pay for the intervention per target population member (CRG Adults)

Scenario	Cost of hospitalisation										
	£1,000	**£2,000**	**£3,000**	**£4,000**	**£5,000**	**£6,000**	**£7,000**	**£8,000**	**£9,000**	**£10,000**	**£11,000**
Scenario 2	-£3.95 (£0.00)	-£4.01 (-£0.05)	-£4.06 (-£0.10)	-£4.11 (-£0.15)	-£4.16 (-£0.21)	-£4.21 (-£0.26)	-£4.27 (-£0.31)	-£4.32 (-£0.36)	-£4.37 (-£0.41)	-£4.42 (-£0.47)	-£4.47 (-£0.52)
Scenario 3	£3.96 (£0.00)	£4.01 (£0.05)	£4.07 (£0.10)	£4.12 (£0.15)	£4.17 (£0.21)	£4.22 (£0.26)	£4.27 (£0.31)	£4.33 (£0.36)	£4.38 (£0.41)	£4.43 (£0.47)	£4.48 (£0.52)
Scenario 4	£11.87 (£0.00)	£12.02 (£0.15)	£12.18 (£0.31)	£12.33 (£0.46)	£12.49 (£0.62)	£12.64 (£0.77)	£12.80 (£0.93)	£12.95 (£1.08)	£13.11 (£1.24)	£13.27 (£1.39)	£13.42 (£1.55)
Scenario 5	£23.24 (-£0.01)	£23.54 (£0.30)	£23.85 (£0.60)	£24.15 (£0.91)	£24.46 (£1.21)	£24.76 (£1.52)	£25.07 (£1.83)	£25.38 (£2.13)	£25.68 (£2.44)	£25.99 (£2.74)	£26.29 (£3.05)
Scenario 6	£30.00 (-£0.01)	£30.40 (£0.39)	£30.80 (£0.79)	£31.20 (£1.19)	£31.60 (£1.59)	£32.00 (£1.99)	£32.40 (£2.39)	£32.80 (£2.79)	£33.20 (£3.19)	£33.60 (£3.59)	£34.00 (£3.99)

* The values in brackets indicate the difference between the maximum willingness to pay for the intervention in the sensitivity analysis and the base case value. Negative values indicate that the result for the sensitivity analysis is lower than the result for the base case.

Maximum willingness to pay for the intervention per target population member (Pregnant women)

Scenario	Cost of hospitalisation										
	£1,000	**£2,000**	**£3,000**	**£4,000**	**£5,000**	**£6,000**	**£7,000**	**£8,000**	**£9,000**	**£10,000**	**£11,000**
Scenario 7	-£4.47 (£0.00)	-£4.54 (-£0.07)	-£4.61 (-£0.15)	-£4.69 (-£0.22)	-£4.76 (-£0.29)	-£4.84 (-£0.37)	-£4.91 (-£0.44)	-£4.98 (-£0.51)	-£5.06 (-£0.59)	-£5.13 (-£0.66)	-£5.20 (-£0.74)
Scenario 8	£4.47 (£0.00)	£4.55 (£0.07)	£4.62 (£0.15)	£4.69 (£0.22)	£4.77 (£0.29)	£4.84 (£0.37)	£4.91 (£0.44)	£4.99 (£0.51)	£5.06 (£0.59)	£5.14 (£0.66)	£5.21 (£0.73)
Scenario 9	£13.40 (-£0.01)	£13.62 (£0.21)	£13.84 (£0.43)	£14.07 (£0.65)	£14.29 (£0.88)	£14.51 (£1.10)	£14.73 (£1.32)	£14.95 (£1.54)	£15.17 (£1.76)	£15.39 (£1.98)	£15.61 (£2.20)
Scenario 10	£22.36 (-£0.01)	£22.72 (£0.36)	£23.09 (£0.72)	£23.46 (£1.09)	£23.82 (£1.46)	£24.19 (£1.82)	£24.56 (£2.19)	£24.92 (£2.55)	£25.29 (£2.92)	£25.66 (£3.29)	£26.02 (£3.65)
Scenario 11	£31.30 (-£0.01)	£31.81 (£0.50)	£32.33 (£1.01)	£32.84 (£1.52)	£33.35 (£2.03)	£33.86 (£2.54)	£34.37 (£3.06)	£34.88 (£3.57)	£35.40 (£4.08)	£35.91 (£4.59)	£36.42 (£5.10)

* The values in brackets indicate the difference between the maximum willingness to pay for the intervention in the sensitivity analysis and the base case value. Negative values indicate that the result for the sensitivity analysis is lower than the result for the base case.

Maximum willingness to pay for the intervention per target population member (Carers)

Scenario	Cost of hospitalisation										
	£1,000	**£2,000**	**£3,000**	**£4,000**	**£5,000**	**£6,000**	**£7,000**	**£8,000**	**£9,000**	**£10,000**	**£11,000**
Baseline -5%	£0.42 (£0.00)	£0.33 (-£0.09)	£0.24 (-£0.18)	£0.15 (-£0.27)	£0.06 (-£0.36)	-£0.04 (-£0.45)	-£0.13 (-£0.54)	-£0.22 (-£0.63)	-£0.31 (-£0.72)	-£0.40 (-£0.81)	-£0.49 (-£0.90)
Baseline +10%	-£0.83 (-£0.01)	-£0.65 (£0.18)	-£0.47 (£0.36)	-£0.29 (£0.54)	-£0.11 (£0.72)	£0.07 (£0.90)	£0.25 (£1.08)	£0.43 (£1.26)	£0.61 (£1.44)	£0.79 (£1.62)	£0.98 (£1.80)
Baseline +25%	-£2.09 (-£0.01)	-£1.63 (£0.44)	-£1.18 (£0.89)	-£0.73 (£1.34)	-£0.28 (£1.80)	£0.18 (£2.25)	£0.63 (£2.70)	£1.08 (£3.15)	£1.53 (£3.61)	£1.99 (£4.06)	£2.44 (£4.51)
Baseline +35%	-£2.92 (-£0.02)	-£2.29 (£0.61)	-£1.65 (£1.25)	-£1.02 (£1.88)	-£0.39 (£2.52)	£0.25 (£3.15)	£0.88 (£3.78)	£1.52 (£4.42)	£2.15 (£5.05)	£2.78 (£5.68)	£3.42 (£6.32)
Uptake is 100%	-£5.22 (-£0.03)	-£4.09 (£1.10)	-£2.96 (£2.23)	-£1.82 (£3.37)	-£0.69 (£4.50)	£0.44 (£5.63)	£1.58 (£6.76)	£2.71 (£7.90)	£3.84 (£9.03)	£4.98 (£10.16)	£6.11 (£11.30)

* The values in brackets indicate the difference between the maximum willingness to pay for the intervention in the sensitivity analysis and the base case value. Negative values indicate that the result for the sensitivity analysis is lower than the result for the base case.

Maximum willingness to pay for the intervention per target population member (Health and social care workers)

Scenario	Cost of hospitalisation										
	£1,000	**£2,000**	**£3,000**	**£4,000**	**£5,000**	**£6,000**	**£7,000**	**£8,000**	**£9,000**	**£10,000**	**£11,000**
Baseline -5%	-£2.13 (£0.02)	-£2.94 (-£0.79)	-£3.76 (-£1.61)	-£4.57 (-£2.42)	-£5.39 (-£3.24)	-£6.20 (-£4.05)	-£7.02 (-£4.86)	-£7.83 (-£5.68)	-£8.64 (-£6.49)	-£9.46 (-£7.31)	-£10.27 (-£8.12)
Baseline +10%	£4.25 (-£0.05)	£5.88 (£1.58)	£7.51 (£3.21)	£9.14 (£4.84)	£10.77 (£6.47)	£12.40 (£8.10)	£14.03 (£9.73)	£15.66 (£11.36)	£17.29 (£12.99)	£18.92 (£14.62)	£20.55 (£16.25)
Baseline +25%	£10.63 (-£0.12)	£14.71 (£3.95)	£18.78 (£8.03)	£22.86 (£12.10)	£26.93 (£16.18)	£31.00 (£20.25)	£35.08 (£24.32)	£39.15 (£28.40)	£43.22 (£32.47)	£47.30 (£36.55)	£51.37 (£40.62)
Baseline +35%	£14.89 (-£0.17)	£20.59 (£5.54)	£26.29 (£11.24)	£32.00 (£16.94)	£37.70 (£22.65)	£43.40 (£28.35)	£49.11 (£34.05)	£54.81 (£39.76)	£60.51 (£45.46)	£66.22 (£51.16)	£71.92 (£56.87)
Uptake is 100%	£21.01 (-£0.24)	£29.06 (£7.81)	£37.11 (£15.86)	£45.16 (£23.91)	£53.21 (£31.96)	£61.26 (£40.01)	£69.31 (£48.06)	£77.36 (£56.11)	£85.41 (£64.16)	£93.46 (£72.21)	£101.51 (£80.26)

* The values in brackets indicate the difference between the maximum willingness to pay for the intervention in the sensitivity analysis and the base case value. Negative values indicate that the result for the sensitivity analysis is lower than the result for the base case.