

## Modelling cost effectiveness of meningococcal serogroup C conjugate vaccination campaign in England and Wales

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### Abstract

**Objectives** To assess the cost effectiveness of a meningococcal serogroup C conjugate vaccination campaign in 0-17 year olds.

**Design** Cost effectiveness analysis from the perspective of the healthcare provider.

**Setting** England and Wales.

**Main outcome measure** Cost per life year saved.

**Results** In 1998-9, immediately before the introduction of meningococcal C vaccination, the burden of serogroup C disease was considerable, with an estimated 1137 cases in people aged 0-17 years and at least 72 deaths. The vaccination campaign is estimated to have cost between £126m (\$180m, €207m) and £241m (\$343m, €395m), depending on the price of the vaccine. Under base case assumptions the cost per life year saved from the vaccination campaign is estimated to be £6259 (\$8919, €10 264). School based vaccination was more cost effective than general practice based vaccination because of lower delivery costs. Immunisation of infants aged under 1 year was the least cost effective component of the campaign because, although this maximises the life years gained, the three dose schedule required is more expensive than other methods of delivery. Estimates of the cost per life year saved were sensitive to assumptions on the future incidence of disease and the case fatality ratio.

**Conclusions** Meningococcal C vaccination is likely to be more cost effective in all age groups when the incidence of disease is high. It is also more cost effective when given to children aged 1-4 (by general practitioners) and to children and young people aged 5-17 years at school than when administered to infants under 12 months of age or youths aged 16-17 years who are not at school.

### Introduction

In November 1999 the UK Department of Health incorporated meningococcal serogroup C conjugate vaccine into routine infant immunisation and launched a national campaign offering vaccine to everyone aged under 18 years.<sup>1</sup> The vaccine provided a new opportunity for primary prevention of meningococcal disease because, unlike the older polysaccharide vaccines, it is immunogenic in infants and primes for memory.<sup>2</sup>

We considered the cost effectiveness of the UK vaccination campaign in terms of the cost per life year saved from the perspective of the healthcare provider (the NHS). We considered only costs and savings accruing to the NHS compared with the life years saved. We ignored private costs and private benefits, except loss of life.

### Methods

We compared the cost effectiveness of the meningococcal C vaccine campaign with the previous strategy, when there was no national vaccination programme and cases were treated as they arose, with control measures implemented in the event of an outbreak.<sup>3</sup> We compared the cost effectiveness of different components of the UK vaccination strategy (such as routine versus catch up, school based versus general practitioner based immunisation).

### Cohort model

We constructed a model to estimate the direct impact of the campaign by following an imaginary vaccine campaign cohort over a lifetime. This comprised 18 birth cohorts of people aged 0-17 who were offered vaccine in the first year of the campaign. We assumed there were 658 800 individuals in each cohort at birth, which is the average size of birth cohorts over the past 18 years. We calculated the number of cases of serogroup C meningococcal disease per year by multiplying the estimated incidence by the number of susceptible individuals.

### Sensitivity analysis

The base case scenario was considered to be the most likely set of parameters. However, because of uncertainty surrounding these estimates we explored a range of values. Firstly, we varied one parameter at a time within its given range in a univariate sensitivity analysis. Secondly, we performed a multivariate sensitivity analysis, under six different scenarios of disease burden, using Monte Carlo simulation.

### Costs and discounting

We measured all costs in pounds sterling at 2000 prices, with costs estimated from previous years inflated using the hospital and community health services pay and prices index. Future costs and benefits were discounted back to their present value, with the assumption that all costs and benefits occurred at the

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end of the year. In the base case we used a 3% discount rate for both costs and benefits.<sup>4</sup>

### Estimating model parameters

In the base case we derived future incidence of serogroup C disease from 1998-9 estimates because this was the period immediately before the introduction of the vaccine. The incidence of notified and laboratory confirmed meningococcal disease in the United Kingdom had increased every year from 1995, and the proportion of cases attributable to serogroup C increased from 25% to almost 40%<sup>5</sup> because of the introduction and spread of a virulent clone (C2a, electrophoretic type 15) over this time period. We obtained data on serogroup and age from 1989-99 from the meningococcal reference unit of the Public Health Laboratory Service. We adjusted these data for underascertainment.

Deaths from meningococcal disease are registered with the Office for National Statistics. Not all cases are confirmed by a laboratory and not all deaths will be registered to codes specific to meningococcal disease. Because of this uncertainty we used a range of estimates in the sensitivity analysis.

We assumed that in all cases of meningococcal disease patients were admitted to hospital. We estimated the average length of stay in hospital for specific ages from hospital episode statistics between 1997-8 and 1998-9 and the proportion of cases admitted to an intensive care unit and the length of stay from 1998-9 data. We obtained details of the cost of an intensive care bed per day from NHS reference costs ([www.doh.gov.uk/nhsexec/refcosts.htm](http://www.doh.gov.uk/nhsexec/refcosts.htm)) and the cost of a bed day (non-intensive care) from *Unit Costs of Health and Social Care 2000*.<sup>6</sup> We assumed that all patients had two outpatient appointments at an average cost of £246. These costs were varied in the sensitivity analysis between +/-20% of the base case.

Survivors of meningococcal disease can have a range of long term sequelae, most commonly hearing impairment, skin scarring, amputation, and neurological disorders. In developed countries 3-15% of survivors are estimated to have sequelae,<sup>7-10</sup> with 7% assumed in the base case. We assumed that 10% of survivors with sequelae would require lifetime institutionalised full time care (£21 500 per year).<sup>6</sup> Survivors with less severe sequelae were assumed to require additional health services at an average cost of £500 (£100 to £1000 in the sensitivity analysis) per year.

Wider public health action is recommended after two or more confirmed or probable cases of meningococcal disease probably caused by the same serogroup within an institution.<sup>11</sup> The primary quantifiable costs are from vaccination with serogroup C polysaccharide (about £7 a dose), chemoprophylaxis (about £3 a dose), and swabbing of contacts considered at risk (about (£10), with staff costs approximated at £1 per procedure. The average costs of outbreak control was estimated from 1996 and 1997 data, with direct health costs of £245 550 per year assumed. Because the number and size of outbreaks cannot be predicted we varied the cost of outbreak control between +/-20% in the sensitivity analysis. For more details see the full version of the paper on [bmj.com](http://bmj.com). We assumed that outbreaks would not occur after the start of the vaccination programme.

### Vaccination programme

The UK vaccine schedule recommends three doses for infants aged under 4 months, two doses for infants aged 5-12 months, and one dose for children and young people aged 1-17 years.<sup>12</sup> On the basis of the list price of the vaccine we assumed the cost per dose to be between £8 and £18 (£12 in the base case). The total cost of the television advertising and leaflet campaign run by the Health Education Authority was £3.5m. By September 2000, 4764 suspected reactions (including headaches, fever, rash, dizziness, faints, seizures) had been reported to the Medicines Control Agency.<sup>13</sup> We assumed that each child with a reported adverse event was seen by a general practitioner at a cost of £18 per consultation<sup>6</sup> and that those with anaphylactoid reactions were admitted to hospital at a cost of £310.<sup>6</sup>

For each child vaccinated at school the Department of Health paid a fee of £1 to the relevant NHS trust or health authority to cover the cost of nursing, administration, and consumables. General practitioners received item of service payments of £6.25 per dose of vaccine or £4.30 for all but the last dose in a series if more than one dose was required. These payments may not accurately reflect the opportunity cost of the campaign. This was investigated in the sensitivity analysis. We assumed vaccine wastage was 10% in the base case.

Early reports in the United Kingdom suggest an efficacy of 92% (95% confidence interval 65% to 98%) for toddlers (aged < 2 years) and 97% (77% to 99%) for teenagers.<sup>14</sup> In the base case we assumed vaccine efficacy to be 95% in 2-12 year olds, with toddlers and teenagers as above. We assumed coverage to be 89% in under 1 year olds, 82% in 1-4 year olds,<sup>15</sup> 87% in 5-13 year olds, 83% in 14-15 year olds, and 65% in 16-17 year olds in full time education. In 16-17 year olds not in education we estimated coverage to be 50%.

## Results

In the late 1990s the burden of serogroup C meningococcal disease was considerable, with an estimated 1519 cases in 1998-9, of which 1137 occurred in people aged 0-17 years. There were 72 deaths due to laboratory confirmed serogroup C disease in this age group. After adjustment for underascertainment this figure could be as high as 107 deaths. In the absence of a meningococcal C vaccination programme, the annual costs of treating and controlling acute serogroup C disease in 0-17 year olds is estimated to be around £3.87m. Inclusion of the costs of treating long term sequelae increases this to £9.6m (table 1).

The vaccination programme should substantially reduce the future burden of disease and associated costs (table 2). The campaign is estimated to prevent 7880 cases and 845 deaths, resulting in nearly 23 000 discounted life years saved over the lifetime of the vaccine campaign cohort, given base case assumptions (table 2). This is estimated to avoid costs of about £29m present value (base case) in treatment and control. The total cost of vaccinating the campaign cohort was estimated at £172m at £12/dose (base case), ranging from £126m at £8 a dose to £241m at £18 a dose.

We estimated the cost per life year saved of the entire programme to be £6259. The school based campaign is more cost effective than the general

**Table 1** Units and costs of treating and controlling cases of serogroup C meningococcal disease in 0-17 year olds that arise in one year (base case)

Parameter	Before vaccine		After vaccine	
	Units	Cost (£)	Units	Cost (£)
Cases	1137		248	
Deaths	85		21	
Inpatient stay in intensive care	1127 bed days	1 347 900	263 bed days	282 300
Inpatient stay on ward	6522 bed days	2 021 900	1486 bed days	460 700
Outpatient follow up	2104 appointments	258 800	496 appointments	61 000
Outbreak costs	11 outbreaks per year	245 550	0 outbreaks	0
Total costs of treating acute meningococcal disease		3 874 250		804 000
Long term costs of treating sequelae*	66 mild	983 000	14 mild	211 500
	7 severe	4 708 500	2 severe	1 010 500
Total costs of treating all cases that arise in one year		9 565 750		2 026 000

\*Present value of cost of treating cases that arise in one year for the rest of their lifetime, discounted at 3%.

**Table 2** Cost per life year saved of meningitis C vaccination programme, discounted to present value (3%)

Component of campaign	Delivery method (No of doses)	Population (millions)	Cases avoided	Deaths avoided	Life years saved	Cost of vaccine campaign (£m)*	Total cost savings (£m)	Net cost (£m)	Cost per case avoided	Cost per life year saved
0-4 months	GP (3)	0.275	365	30	832	13.4	1.2	12.2	33 326	14 630
5-11 months	GP (2)	0.384	512	42	1165	12.8	1.7	11.1	21 624	9 493
1-4 years	GP (1)	2.621	2422	212	5879	42.6	8.3	34.3	14 138	5 826
5-17 years	School (1)	7.857	4432	539	14 354	96.7	17.3	79.4	17 907	5 529
16-17 year olds not in education	GP (1)	0.654	149	22	569	6.6	0.7	5.9	39 341	10 291
Overall UK campaign 0-17 years	GP and school	11.791	7880	845	22 799	172.0	29.2	142.8	18 112	6 259
<b>Alternative strategy (not implemented)</b>										
12 months	GP (1)	0.659	698	55	1658	10.6	2.4	8.3	11 878	5 003

\*Cost of Health Education Authority advertising campaign distributed according to population size in each age group.

practitioner based campaign, primarily because of the lower delivery costs per person. Although early vaccination maximises life years saved, routine vaccination at 2, 3, and 4 months is the least cost effective because the cost of giving three doses is substantially higher. In terms of continued routine vaccination, vaccinating children with one dose at 1 year is more cost effective than vaccinating infants at 2, 3, and 4 months. However, delaying vaccination could result in up to 200 potentially preventable cases of serogroup C meningococcal disease in infants under 1 year.

The sensitivity analyses show that the most striking changes in the cost per life year saved occurred when the assumptions about incidence of disease and case fatality ratios were changed (figure). The results were also sensitive to changes in vaccine cost per dose and vaccine efficacy. The cost per life year saved is fairly insensitive to changes in the parameters with the most uncertainty, such as the cost of treating long term sequelae. The choice of discount rate is critical to the outcome. Adopting the UK Treasury recommended discount rate reduces the cost per life year saved to less than £4000. In the multivariate sensitivity analysis we fixed the discount rate at 3% and compared different scenarios for risk of disease and mortality (figure).

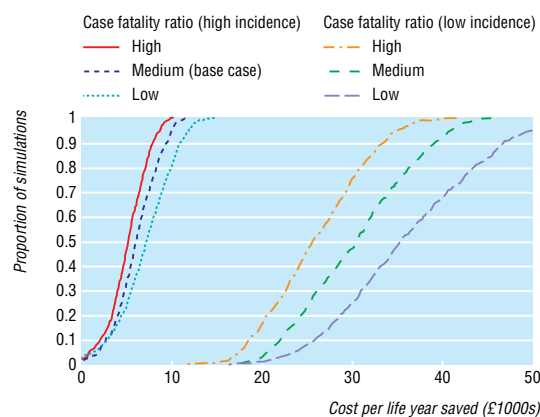
In the base case (high incidence, medium case fatality ratio) 95% of the model simulations resulted in a cost per life year saved of less than £10 000. If we assumed a high case fatality ratio and high incidence then 33% of results were below £5000 per life year saved. If the incidence in the cohort is low then cost per life year saved is greatly increased with 25%, 53%, and 75% of simulations resulting in a cost per life year

saved of more than £30 000 for high, medium, and low case fatality ratios respectively.

## Discussion

The meningococcal C vaccination campaign has rapidly and substantially reduced the incidence of serogroup C meningococcal disease in the targeted age groups.<sup>14</sup> Modelling of the cost effectiveness of the campaign supports the introduction of the vaccine.

The sensitivity analyses show that assumptions on the incidence of disease are critical in determining the cost effectiveness of the campaign. This incidence can-



Cost per life year saved estimated from multivariate sensitivity analysis

### What is already known on this topic

The burden of group C meningococcal disease in England and Wales in the late 1990s was considerable

In November 1999 the United Kingdom was the first country to introduce mass vaccination against group C meningococcal disease

There are no published economic evaluations of the vaccination campaign

### What this study adds

This economic evaluation supports the introduction of the meningococcal C vaccine

School based vaccination is more cost effective than routine vaccination of infants because delivery costs are lower and fewer doses are required

not be predicted, especially given the variation in and instability of prevalent meningococcal strains. However, disease surveillance since the start of the campaign indicates that incidence of serogroup C disease has continued to increase in people aged 20-25 years, suggesting that in the absence of vaccination the incidence of the disease may have also continued to increase in those aged 0-17 years. This would have resulted in the vaccine campaign being more cost effective than we have estimated.

This analysis ignores gains in quality of life, principally because of a lack of information. Furthermore, we did not incorporate effects of herd immunity into the model because of uncertainty over the transmission dynamics of *Neisseria meningitidis*. The experience with *Haemophilus influenzae* type b (Hib) conjugate vaccination in the United Kingdom<sup>16</sup> (and elsewhere) suggests that conjugate vaccination reduces carriage. If meningococcal C vaccination reduces transmission of serogroup C meningococci, the risk of infection for those who have not been vaccinated would decline.

The net effect of these omissions would be that the campaign was probably more cost effective than is presented here.

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## On becoming 79

Somewhere on the path of my medical education I had been told about the aches and pains of old age. I had made a conscious decision, as part of my determination to avoid ageism in my work, to ignore what I had been told in the interest of avoiding missing an important diagnosis in an elderly patient who produced vague symptoms. But, now I have entered the final year of my eighth decade, I have to concede that I do have aches and pains that do not feature in any textbook I have read. I am reminded that in my paediatric lectures at medical school I was told that teething in babies was symptomless (on the grounds that it was a normal process which could not produce symptoms), but in practice I was convinced many babies seemed distressed during dentition, having excessive salivation and flushed cheeks.

I hasten to say that I am not complaining (either in the ordinary or medical sense) but am merely curious about the nature of the feelings. If I wiggle my toes I seem to feel the tendons slide rather ungraciously through their sheaths; my calves seem to ache as I get into bed, and this sensation is not

relieved by taking paracetamol. But perhaps the most intriguing sensation is the perception that I know at any given time how much energy I have to call on.

My late, dearly loved, aunt was the herald of this phenomenon. She attended my son's wedding (at which she danced) on the eve of her 80th birthday, and so enjoyed parties on two successive days. We took her home the day after her birthday. In going through her papers after her death, I came across her diary. The entry on the day after she returned home was one word: "Tired." The entry on the following day was "Very tired." I now know the feelings first hand.

Now it may be that my clinical skills have so atrophied that I am sick without realising it, but I don't feel ill. Perhaps I need to take more exercise or, worse, am developing a syndrome that I am not clever enough to diagnose. But until some doctor comes to my rescue, I think I am just getting old.

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