Effect of needle size on immunogenicity and reactogenicity of vaccines in infants: randomised controlled trial

Linda Diggle, Jonathan J Deeks and Andrew J Pollard

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Effect of needle size on immunogenicity and reactogenicity of vaccines in infants: randomised controlled trial
Linda Diggle, Jonathan J Deeks, Andrew J Pollard

Abstract

Objectives To assess the immunogenicity of vaccines for infants and to investigate whether the incidence of reactogenicity is reduced after each immunisation dose using needles of varying lengths and gauges.

Design Randomised controlled trial.

Setting 18 general practices within two UK primary care trusts.

Participants 696 healthy infants vaccinated at 2, 3, and 4 months of age, with follow-up to 6 months of age.

Interventions Combined diphtheria, tetanus, whole cell pertussis, and Haemophilus influenzae type b vaccine and a serogroup C meningococcal glycoconjugate vaccine administered using either a wide, long needle (23 gauge/0.6 mm diameter, 25 mm), a narrow, short needle (25 gauge/0.5 mm diameter, 16 mm), or a narrow, long needle (25 gauge, 25 mm).

Main outcome measures Local and general reactions recorded by parents for three days after each dose; and diphtheria, tetanus, and H influenzae type b antibody concentrations and functional antibody against serogroup C Neisseria meningitidis 28–42 days after the third dose.

Results Local reactions to diphtheria, tetanus, whole cell pertussis, H influenzae type b vaccinations decreased significantly with wide, long needles compared with narrow, short needles. At all three doses one less infant experienced local reactions at days 1, 2, or 3 for every six to eight vaccinated. Significantly fewer infants vaccinated with the long needle experienced severe local reactions. Non-inferiority of the immune response was shown using a wide, long needle rather than a narrow, short needle for serogroup C meningococcal glycoconjugate vaccine and for diphtheria but not for H influenzae type b or tetanus, although no evidence was found of a decrease. Little difference was found between needles of the same length but different gauges in local reaction or immune response.

Conclusions Long (25 mm) needles for infant immunisations can significantly reduce vaccine reactogenicity at each dose while achieving comparable immunogenicity to that of short (16 mm) needles.

Trial registration Current Controlled Trials ISRCTN62032215.

Introduction

Within UK general practices infants are immunised at 2, 3, and 4 months of age. Although over four million injected vaccines are given to UK infants each year, evidence based guidance on needle size for intramuscular delivery is lacking. The width (gauge) of a needle is defined by hub colour. Latest Department of Health literature recommends a 25 mm blue hub (23 gauge) needle, but many practitioners prefer to use a 16 mm orange hub (25 gauge) needle. Some local policies stipulate use of the larger diameter 23 gauge needle, drawing on anecdotal evidence that this enables the vaccine to dissipate over a wider space, reducing risks of localised redness and swelling. Others advise that a 16 mm needle adequately reaches anterolateral thigh muscle when inserted at 90° and using the intramuscular delivery technique recommended by the World Health Organization, WHO, however, recommends a 25 mm needle for infant immunisations. Uncertainty has arisen because of insufficient data to define best practice.

We have shown that wider, longer needles significantly reduce the incidence of local reaction at 4 months of age. This study did not, however, determine whether reduced reactogenicity was related to a difference in gauge or length and whether the same effects would be seen at earlier immunisations, nor whether needle size affected vaccine immunogenicity. Benefits gained from a reduction in local reactogenicity would have to be balanced against any compromise of immunogenicity.

We carried out a randomised controlled trial to compare three needles of varying diameter and length (23 gauge, 25 mm; 25 gauge, 16 mm; and 25 gauge, 25 mm). We also assessed immunogenicity as well as local and general reaction rates after immunisation with combined diphtheria, pertussis, tetanus, and Haemophilus influenzae type b vaccine and a serogroup C meningococcal glycoconjugate vaccine in infants at 2, 3, and 4 months of age. The trial was designed to test whether immunogenicity using a wide, long needle is equivalent or superior to a narrow, short needle (a non-inferiority hypothesis). If the previously observed reduction in adverse events with the wider, longer needle was repeated, while achieving comparable immunogenicity, this would be sufficient to recommend best practice.

Methods

Eighteen of 35 general practices approached in the Vale of Aylesbury primary care trust, Buckinghamshire and North East Oxfordshire primary care trust agreed to recruit. Parents of infants due to receive their first immunisation between April 2002 and March 2004 were sent a letter inviting their children to participate. We excluded infants of less than 37 weeks’ gestation, those of birth weight less than 2500 g, and those undergoing treatment or with conditions that could bias the evaluation of an...
immune response. The first vaccination was at age 8-11 weeks, with subsequent vaccinations at intervals of 4-6 weeks.

**Study procedures**

Infants were allocated to a needle group according to a computer generated randomisation scheme generated by the study statistician, stratified by general practice with random variable block sizes of three, six, and nine. Allocations were concealed in sequentially numbered opaque sealed envelopes. When written parental consent had been obtained, the study nurse allocated the next sequential participant number and opened the appropriate envelope to determine to which needle size the infant had been randomised: wide, long (23 gauge, 25 mm), narrow, short (25 gauge, 16 mm), or narrow, long (25 gauge, 25 mm) needle. Infants received all immunisations through the allocated needle size.

A combined diphtheria, pertussis, tetanus, and *Haemophilus influenzae* type b vaccine (ACY-Hib DTP; Pasteur-Mérieux-MSD, Berkshire) was administered into the right anterolateral thigh, with a meningococcal C vaccine given concomitantly into the left thigh: 72% of infants received Meningitec (Wyeth Vaccines, Berkshire) at the first and second doses and 76% at the third dose, and the remainder received Menjugate (Chiron Vaccines, Liverpool).

We used the standard intramuscular injection technique as advocated for infants by WHO: the vaccine was injected into the anterolateral thigh, with the skin stretched flat between the thumb and forefinger and the needle inserted at 90° and pushed down into the muscle. Parents were not informed of the allocated needle size. As needle gauge can be identified by hub colour, parents were not informed of the significance of these differences. Parents known to be health professionals were asked not to view the injection procedure.

Study nurses instructed parents on how to complete the diary on reactions after each immunisation; parental rating of local and systemic symptoms has been validated. Parents measured the diameter of any redness, hardness, or swelling using a ruler printed in the diary. Infants’ reactions to movement of the thigh or touch of the injection site were graded on a scale of none, mild, moderate, or severe. Parents were instructed in the use of a digital thermometer to record temperature, were asked to note use of analgesics, and were asked to respond to questions on incidence of general reactions. The diaries were collected at the evening after vaccination (six hour time point) and subsequent three evenings (days 1, 2, and 3) after each immunisation, as assessed by parents. Incidence of general reactions was also recorded. We express comparisons between needle groups as relative geometric mean titres or geometric mean concentrations for immunogenicity outcomes and as risk ratios for reactogenicity outcomes.

**Outcome measures**

Primary end points were measurement of the geometric mean titres of serogroup C meningococcal glycoconjugate antibodies and geometric mean concentrations of diphtheria, tetanus, and *H influenzae* type b antibodies 28-42 days after the third vaccine dose. Secondary end points were rates of any local reaction (swelling, redness, hardness, or tenderness) at both injection sites on the evening after vaccination (six hour time point) and subsequent three evenings (days 1, 2, and 3) after each immunisation, as assessed by parents. Incidence of general reactions was also recorded. We use statistical significance using one tailed tests on log transformed data, computing the area in the left tail beyond the 10% equivalence bound. Significance was defined at the 2.5% level. We used confidence intervals calculated from the t distribution to compute the probability that an immune response was not inferior.

To distinguish whether difference in length or gauge affected local reaction rates, we made two pairwise comparisons of local reactogenicity rates between wide, long needle and narrow, short needle. We prestated an equivalence assay which would be interpreted as showing non-inferiority. We assessed statistical significance using one tailed t tests on log transformed data, computing the area in the left tail beyond the 10% equivalence bound. Significance was defined at the 5% level. Differences in systemic reaction rates between the three groups were tested using a χ² test with two degrees of freedom (or Fisher’s exact test if event rates were low).

Presuming that immunogenicity would be 20% higher with a wide, long needle than with a narrow, short needle (using results from a study of adolescents that found a 20% difference in diphtheria and tetanus antibody levels when an intramuscular injection was compared with a subcutaneous injection), we determined that 201 infants would be required per group to have 80% power of showing non-inferiority using a 10% equivalence range at a one sided 2.5% significance level, assuming that the standard deviation of the log of the serological titres was 1.0. A sample size of 201 per group would enable reductions in overall local reaction rates from 80% to 65% to be detected with 90% power.

Initially we allowed for 5% drop out or failure to obtain a blood sample rate and aimed to recruit 633 participants. We monitored the dropout rate during the study and found it to be
closer to 12%. We therefore increased recruitment to 696 infants to maintain a target of 201 evaluable participants per group.

Statistical analyses were undertaken using SPSS version 11.5 and Stata version 9.0.

Results

Of the 696 infants enrolled, 240 were randomised to the wide, long needle, 230 to the narrow, short needle, and 226 to the narrow, long needle (fig 1). No substantial differences were found between the groups at baseline for sex, birth weight, age, or weight at each vaccination (table 1). Overall, 84 infants (12%) were withdrawn from the study: 14 (2%) violated the protocol, 14 (2%) had serious local or general reactions, 5 (1%) discontinued participation during the vaccination period, 13 (2%) were lost to follow-up, and 38 (5%) had inadequate blood samples or the parents refused venepuncture. Numbers were similar across groups except for serious local reactions.

Wide, long needle versus narrow, short needle

**Immunogenicity**—The average immune response was higher with the wide, long needle compared with the narrow, short needle, although none of the differences were statistically significant (table 2). The largest increase was observed for the meningococcal C vaccine where the geometric mean titre increased by 30% (95% confidence interval −1% to 69%; P = 0.06). Significant non-inferiority of response was shown for meningococcal C and diphtheria, the lower limits of the 95% confidence interval being above the 10% equivalence bound (fig 2). Although *H influenzae* type b and tetanus did not show any evidence of immune response being compromised by use of the wide, long needle, this was not conclusively excluded as a possibility. The probability that immune response using the wide, long needle was not inferior was estimated to be 84% for *H influenzae* type b and 90% for tetanus.

**Local reactogenicity to combined vaccine**—On average 61% (388) of the infants experienced local reactions to each dose of the combined vaccine. Redness occurred in 44% (279), tenderness in 35% (221), and swelling in 18% (113). Fifty four per cent (341) showed a reaction six hours after vaccination, 46% (288) one day later, 28% (180) two days later, and 14% (87) three days later. Infants vaccinated with the wide, long rather than the narrow, short needle experienced significantly fewer local reactions for all three doses at days 1, 2, and 3 (fig 3), with relative reductions of between 22% (6% to 36%) and 54% (11% to 69%; P = 0.06). Significant non-inferiority was estimated to be 84% for *H influenzae* type b and 90% for tetanus.

Denominators differ from baseline owing to withdrawals.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Wide, long needle (n=240)</th>
<th>Narrow, short needle (n=230)</th>
<th>Narrow, long needle (n=226)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No (%) boys</td>
<td>107 (45)</td>
<td>138 (60)</td>
<td>115 (51)</td>
</tr>
<tr>
<td>Mean (SD) birth weight (g)</td>
<td>3500 (500)</td>
<td>3500 (400)</td>
<td>3600 (500)</td>
</tr>
<tr>
<td>First vaccination:</td>
<td>mean (range) age (days)</td>
<td>62 (56-77)</td>
<td>62 (56-76)</td>
</tr>
<tr>
<td></td>
<td>61 (55-76)</td>
<td>61 (55-76)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean (SD) weight (kg)</td>
<td>5.2 (0.7)</td>
<td>5.3 (0.7)</td>
</tr>
<tr>
<td></td>
<td>5.3 (0.7)</td>
<td>5.3 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Second vaccination:</td>
<td>mean (range) age (days)</td>
<td>92 (82-112)</td>
<td>91 (84-113)</td>
</tr>
<tr>
<td></td>
<td>91 (83-113)</td>
<td>91 (83-113)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean (SD) weight (kg)</td>
<td>6.0 (0.8)</td>
<td>6.0 (0.7)</td>
</tr>
<tr>
<td></td>
<td>6.1 (0.8)</td>
<td>6.1 (0.8)</td>
<td></td>
</tr>
<tr>
<td>Third vaccination:</td>
<td>mean (range) age (days)</td>
<td>122 (111-146)</td>
<td>121 (112-143)</td>
</tr>
<tr>
<td></td>
<td>121 (111-147)</td>
<td>121 (111-147)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mean (SD) weight (kg)</td>
<td>6.6 (0.8)</td>
<td>6.8 (0.8)</td>
</tr>
<tr>
<td></td>
<td>6.8 (0.8)</td>
<td>6.8 (0.8)</td>
<td></td>
</tr>
</tbody>
</table>

Denominators differ from baseline owing to withdrawals.
Research

Table 2 Vaccine immunogenicity in infants randomised to receive immunisations through one of three needle sizes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Geometric mean concentration or geometric mean titre by needle size (95% CI)</th>
<th>Ratio of geometric mean concentration or geometric mean titre (95% CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wide, long needle</td>
<td>Narrow, short needle</td>
</tr>
<tr>
<td></td>
<td>n=196</td>
<td>n=179</td>
</tr>
<tr>
<td>Meningococcal C vaccine†</td>
<td>1262 (1052 to 1514)</td>
<td>973 (799 to 1184)</td>
</tr>
<tr>
<td>SD (log)</td>
<td>1.29</td>
<td>1.28</td>
</tr>
<tr>
<td></td>
<td>n=208</td>
<td>n=194</td>
</tr>
<tr>
<td>Haemophilus influenzae type b</td>
<td>3.47 (2.82 to 4.28)</td>
<td>3.30 (2.65 to 4.12)</td>
</tr>
<tr>
<td>SD (log)</td>
<td>1.52</td>
<td>1.26</td>
</tr>
<tr>
<td></td>
<td>n=203</td>
<td>n=191</td>
</tr>
<tr>
<td>Tetanus</td>
<td>1.71 (1.51 to 1.93)</td>
<td>1.68 (1.47 to 1.93)</td>
</tr>
<tr>
<td>SD (log)</td>
<td>0.90</td>
<td>0.88</td>
</tr>
<tr>
<td></td>
<td>n=154</td>
<td>n=155</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>0.24 (0.21 to 0.28)</td>
<td>0.21 (0.18 to 0.25)</td>
</tr>
<tr>
<td>SD (log)</td>
<td>0.95</td>
<td>0.85</td>
</tr>
</tbody>
</table>

SD (log) = standard deviation of measurements on natural log scale.
*Statistically significant non-inferiority corresponds to lower limit of 95% confidence interval exceeding 0.90.
†Serogroup C meningococcal glycoconjugate vaccine.

(29% to 73%). At six hours assessment relative reductions were smaller—5% (-12% to 20%) to 11% (-1% to 21%), and not statistically significant. Overall reaction rates were dominated by the high reaction rate at six hours and showed a statistically significant reduction for the first dose only (see bmj.com). Statistically significant reductions were, however, found with the wide, long needle in reactions that were evident the second day or later with relative reductions of 31% (16% to 44%), 24% (8% to 38%), and 24% (8% to 37%) for the first, second, and third doses, respectively. The number of infants needed to vaccinate with a needle in reactions evident the second day or later (see bmj.com).

The incidence of any local reaction after each immunisation dose in the UK schedule for infants aged 2, 3, and 4 months is significantly reduced when a wide, long (25 mm) needle rather than a narrow, short (16 mm) needle is used. Although only two of the four vaccine components formally showed non-inferiority, the weight of evidence clearly favoured the wide, long needle, achieving comparable, if not superior, immunogenicity to that of the narrow, short needle. If reductions in immune response up to 25% are considered to provide clinically equivalent protection, then non-inferiority would be proved for all four components.

Systemic reactogenicity—No significant differences were found between the groups of infants with fever (axillary temperature ≥38°C) after any vaccine dose. Overall analgesic use and incidence of systemic reactions did not differ significantly between groups (table 3).

Narrow, long needle versus wide, long needle
No significant differences were found in immunogenicity between the two longer needles (table 2). Local reaction rates seemed slightly lower with the narrow needle, although differences were small and only reached statistical significance for the overall rates of reaction for the third dose of the combined vaccine (see bmj.com) and rates on day 2 for the third dose (fig 3). No difference was found in systemic reactogenicity (table 3).

Discussion
The incidence of any local reaction after each immunisation dose in the UK schedule for infants aged 2, 3, and 4 months is significantly reduced when a wide, long (25 mm) needle rather than a narrow, short (16 mm) needle is used. Although only two of the four vaccine components formally showed non-inferiority, the weight of evidence clearly favoured the wide, long needle, achieving comparable, if not superior, immunogenicity to that of the narrow, short needle. If reductions in immune response up to 25% are considered to provide clinically equivalent protection, then non-inferiority would be proved for all four components.

![Fig 2](https://example.com) Ratio of antibody levels in infants immunised using different sized needles

Fig 2 Ratio of antibody levels in infants immunised using different sized needles
This study also provides evidence that needle length, rather than gauge, is associated with reduced reactogenicity. In our previous study needle gauge had been a confounding factor. Some authors have suggested that the narrower 25 gauge needle might cause increased trauma and local reaction rates. The present study, however, provided no evidence to support this claim, with needle gauge having been a confounding factor. We suggest, as stated in our previous work, that the longer 25 needle provided a better immunological response.

Authors have suggested that the narrower 25 gauge needle might produce an injection jet under greater pressure and that this delivery provided significantly improved seroconversion. We suggest, as stated in our previous work, that the longer 25 needle provided a better immunological response.

In comparison in studies of adults, intramuscular delivery minimises adverse reactions, with intramuscular delivery of vaccines contributing towards improved immunogenicity has been described. Compared with subcutaneous tissue with its poor vascularity, slower mobilisation or processing of antigens, and lack of phagocytic or antigen-presenting cells, muscle has an abundant blood supply.

Our data cannot be directly compared with subcutaneous tissue with its poor vascularity, slower mobilisation or processing of antigens, and lack of phagocytic or antigen-presenting cells, muscle has an abundant blood supply. In comparison in studies of adults, intramuscular delivery also provides significantly improved seroconversion. We suggest, as stated in our previous work, that the longer 25 needle provided a better immunological response. Our results suggest that consideration of needle size is advisable when planning clinical trials of vaccines and we repeat calls for systematic review recommending changing to a 25 mm needle, the results were limited by the inclusion of two small studies and could not separate the effect of gauge from that of length. These latest results would add weight to any subsequent meta-analysis.

We suggest, as stated in our previous work, that the longer 25 mm needle ensures delivery into an infant's thigh muscle. Several clinical trials of vaccines in adults or adolescents have shown that intramuscular delivery minimises adverse reactions and a clear physiological rationale justifies its importance; poorer drainage channels in subcutaneous tissue and the propensity to retain injected material for longer seems to leave subcutaneous fat more susceptible to the adverse effects of vaccines. For vaccines containing aluminium adjuvant, intramuscular delivery is particularly recommended, as inadvertent subcutaneous administration of this adjuvant may increase irritation or lead to lumps and nodules at the injection site. As injection with a 16 mm needle inserted at 90° has been shown not to reach muscle in a significant number of infants aged 4 months, and as the combined diphtheria, pertussis, tetanus, and Haemophilus influenzae type b vaccine contains aluminium adjuvant, this may explain the differences in reactogenicity seen between needle lengths in our study.

Although few studies have compared infants' immune responses to vaccines using different needle lengths, the mechanism by which intramuscular delivery of vaccines contributes towards improved immunogenicity has been described. Compared with subcutaneous tissue with its poor vascularity, slower mobilisation or processing of antigens, and lack of phagocytic or antigen-presenting cells, muscle has an abundant blood supply. In comparison in studies of adults, intramuscular delivery also provides significantly improved seroconversion. We suggest, as stated in our previous work, that the longer 25 needle provided a better immunological response. Our results suggest that consideration of needle size is advisable when planning clinical trials of vaccines and we repeat calls for this variable to be reported to facilitate comparisons between trials.

After completion of this study, vaccines recommended for use in the UK immunisation schedule were changed in view of the high rates of systemic reactions attributed to vaccines containing whole cell pertussis. The combined diphtheria, pertussis, tetanus, and Haemophilus influenzae type b vaccine was replaced by a less reactogenic vaccine consisting of diphtheria, tetanus acellular pertussis, H influenzae type b, and inactivated polio (Pediacel; Sanofi Pasteur MSD). Our data cannot be directly extrapolated to this combination which is now used in the United Kingdom; however, our study implies that local reactogenicity is reduced by intramuscular delivery and there is no evidence to indicate that this would be different for other vac-
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cines. Our data support use of a longer needle for improved immunogenicity of meningococcal C vaccine, and since this vaccine is still used in the United Kingdom, the observations remain relevant.

In conclusion, data from this study are likely to be highly relevant to settings where children receive reactogenic vaccines containing diphtheria, tetanus, and whole cell pertussis. As our data are from a population of well nourished infants, our findings may not be directly transferable to populations where most diphtheria, tetanus, and whole cell pertussis vaccines are now administered—that is, in resource poor countries with less well nourished children. Nevertheless, these data support the delivery of infant immunisations into muscle rather than subcutaneous tissue, and the longer needle size increases the likelihood that this will be achieved in all populations, irrespective of variations in injection technique. With increasing parental attention focused on the safety rather than the efficacy of vaccines, simple interventions that reduce local reactions, such as longer needles, should be welcomed. Vaccine manufacturers and national policymakers should consider needle size in recommendations for infant immunisation.

We thank the participants; research nurses Karen Stone, Helen Layton, and Tessa Waterhouse for carrying out the study visits, administering immunisations, and collecting venepuncture samples; Shaminn Shah-Gallardo for distraction of infants during venepuncture; general practices of Vale of Aylesbury and Oxfordshire for running the programmes for verification of double data entry; Chief Medical Officer, Chief Nursing Officer, Chief Pharmaceutical Officer. Births and deaths in Northern Ireland were provided by Northern Ireland Statistics and Research Agency. www.orsisra.gsi.gov.uk/dep/dep161.html

Contributors: LD conceived and planned the study, recruited and trained study nurses, managed data collection, undertook initial analyses, wrote the first draft of the paper, and is guarantor for the study. JJD advised on design, produced the randomisation scheme, verified initial analyses, and undertook further analyses. AJP advised on serum analyses and supervised clinical decisions relevant to the infants. LD and JJD had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. All authors contributed to the manuscript.

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Competing interests: LD has received assistance from Wyeth Vaccines and Sanofi Pasteur MSD to attend scientific meetings. AJP acts as chief investigator for clinical trials conducted on behalf of Oxford University, sponsored by vaccine manufacturers (Sanofi-Pasteur MSD, Novartis Vaccines, GlaxoSmithKline, Sanofi-Pasteur, and Wyeth Vaccines), and has received assistance from GSK vaccines, Sanofi Pasteur MSD, Novartis Vaccines, and Wyeth Vaccines to attend scientific meetings. AJP is an inventor on a patent application in the area of meningococcal B vaccines. Industry sourced consultancies or honorariums are paid directly to an independent charity or an educational fund held by the Department of Paediatrics, University of Oxford.

Ethical approval: This study was approved by the Mid and South Buckinghamshire and Oxfordshire local research ethics committees.

Conclusions

What is already known on this topic

At age 4 months a wide, long rather than narrow, short needle for immunisation reduces local reaction

Whether this was due to needle length or gauge or could be achieved at younger immunisation ages was unknown

Effect on immunogenicity was unknown

What this study adds

Long (25 mm) needles provide the optimum immunisation at 2, 3, and 4 months of age

Needle length, not gauge, affects reactogenicity

Immunogenicity is comparable between long and short (16 mm) needles

6 Chief Medical Officer, Chief Nursing Officer, Chief Pharmaceutical Officer. Important changes to the childhood immunisation programmes. London: Department of Health, 12 Jul 2006.
14 Poirier MK, Poland GA, Jacobsen RM. Parameters potentially affecting interpretation of clinical trials conducted on behalf of Oxford University, sponsored by vaccine manufacturers (Sanofi-Pasteur MSD, Novartis Vaccines, GlaxoSmithKline, Sanofi-Pasteur, and Wyeth Vaccines), and has received assistance from GSK vaccines, Sanofi Pasteur MSD, Novartis Vaccines, and Wyeth Vaccines to attend scientific meetings. AJP is an inventor on a patent application in the area of meningococcal B vaccines. Industry sourced consultancies or honorariums are paid directly to an independent charity or an educational fund held by the Department of Paediatrics, University of Oxford.

Linda Diggie: principal research nurse

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