Epidemiol. Infect. (2016), **144**, 2087–2097. © Cambridge University Press 2016
doi:10.1017/S0950268815003325

Assessing the impact of a nurse-delivered home dried blood spot service on uptake of testing for household contacts of hepatitis B-infected pregnant women across two London trusts

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Received 4 August 2015; Final revision 1 December 2015; Accepted 22 December 2015; first published online 2 February 2016

SUMMARY

Despite national guidance recommending testing and vaccination of household contacts of hepatitis B-infected pregnant women, provision and uptake of this is sub-optimal. The aim of this study was to evaluate the use of in-home dried blood spot (DBS) testing to increase testing and vaccination of household contacts of hepatitis B-infected pregnant women as an alternative approach to conventional primary-care follow-up. The study was conducted across two London maternity trusts (North Middlesex and Newham). All hepatitis B surface antigen-positive pregnant women identified through these trusts were eligible for inclusion. The intervention of in-home DBS testing for household contacts was introduced at North Middlesex Trust from November 2010 to December 2011. Data on testing and vaccination uptake from GP records across the two trusts were compared between baseline (2009) and intervention (2010–2011) periods. In-home DBS service increased testing uptake for all ages ($P < 0{\cdot}001$) with the biggest impact seen in partners, where testing increased from 30·3% during the baseline period to 96·6% during the intervention period in North Middlesex Trust. Although impact on vaccine uptake was less marked, improvements were observed for adults. The provision of nurse-led home-based DBS may be useful in areas of high prevalence.

Key words: Control, epidemiology, hepatitis B, immunization (vaccination), public health.

INTRODUCTION

The prevalence of chronic hepatitis B virus (HBV) infection shows marked global variation. Although the UK is categorized as a low-prevalence country [1], prevalence of chronic HBV infection is heterogeneously distributed in the population, influenced by factors such as country of birth and ethnicity. This is demonstrated by the considerable geographical variation in antenatal prevalence of chronic hepatitis B infection seen, with the highest prevalence reported in London (1·02%) and the lowest in the South West (0·15%) [2]. In England and Wales, it is estimated that 96% of all new chronic infections each year are attributed to migration of individuals who acquired infection in their country of origin, often at the time of birth [3, 4].

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Control of HBV in the UK is based on a targeted approach of identifying and offering vaccination to individuals at risk [5, 6]. Since 2000, the UK has recommended universal antenatal screening for HBV to identify mothers at risk of transmitting HBV infection to their infants and to provide post-exposure prophylaxis to these infants to prevent perinatal transmission. Horizontal transmission within the household through sexual contact or contact with infected blood or other fluids is also an important route of infection and therefore all close contacts of a hepatitis B-infected pregnant woman should be tested and offered vaccination [6, 7]. Testing and vaccination of these contacts is essential in order to detect other chronically infected individuals who require appropriate treatment and to prevent onward transmission.

Despite national guidance recommending testing and vaccination of household contacts, implementation is sub-optimal. A study in 2009 found that only 60% of older children in the household of a hepatitis B-infected woman had been vaccinated and only 58% and 39% of partners were tested and vaccinated, respectively [8]. The reasons for this low uptake are unclear but it is likely that a lack of engagement and understanding of the importance of testing, both by the healthcare professional and the patient, plays a part. Access to and acceptability of the current service is also likely to influence uptake and therefore the provision of dried blood spot (DBS) testing in the home may provide one potential solution.

DBS testing is less invasive than conventional venepuncture and can be readily undertaken in the home setting. The use of DBS testing has successfully increased testing uptake for HIV and hepatitis B and C in people who inject drugs (PWID) [9, 10]. However, its use in contacts of HBV-infected individuals has not previously been investigated. This interventional before-and-after study aimed to assess the impact of a home-delivered DBS testing service on the uptake of hepatitis B testing and vaccination in household contacts of HBV-infected pregnant women identified through antenatal screening in two London hospital trusts that had some of the highest antenatal prevalence in England.

METHODS

This interventional before-and-after study was conducted across two maternity units in London that were selected based on their high antenatal HBV prevalence; North Middlesex (28·1 infections/1000 women screened) and Newham (13·2/1000 women screened) [3]. Data were collected over two periods: a baseline retrospective review from 1 January 2009 to 31 December 2009 and a prospective intervention period from 1 November 2010 to 31 December 2011. All HBsAg-positive pregnant women identified through antenatal screening at North Middlesex or Newham hospitals during the review and intervention periods were eligible for inclusion. HBsAg-positive pregnant women were excluded if (*a*) they were known to be positive prior to antenatal screening and their families had been tested and vaccinated appropriately; or (*b*) their care was transferred to a trust not participating in the intervention. The main outcomes of interest were: the proportion of newly tested, newly vaccinated and newly referred for care and treatment (if currently infected) household contacts. The two trusts had different routine pathways for follow-up of partners of HBV-positive women: Newham Trust referred partners to genitourinary medicine (GUM) clinics for testing and vaccination. All other contacts were referred to the General Practitioner (GP). In North Middlesex children were seen in community paediatric clinics while adults were referred to the GP. Data was collected for ethnicity of the cases; however, due to data quality issues individuals were assigned to one of four broad ethnic groups. Asian/Asian British, Black/Black British, White/White other, and Mixed/Other.

Retrospective review

During the baseline period, a retrospective review was carried out of GP records of pregnant women identified through the Enhanced Surveillance of Antenatal Hepatitis B (ESAHB) database managed by Public Health England (PHE) staff, which collects individual-level information on hepatitis B infection in the pregnant women population for London, and their household contacts [3], in the two sites (North Middlesex and Newham). Once case identification had occurred, the relevant GP was sent a letter explaining the purpose of the review and a questionnaire requesting further information on the case and their household contacts. This included demographic information including age, ethnicity and country of birth as well as previous testing dates and information on referral of the case. For household contacts information was sought on age, relationship to the case, and history of testing and vaccination. Where testing had taken place, the HBV status was requested. To

improve the response rate and data completeness, further follow-up was undertaken by phone and fax as well as visits to the surgeries. Missing referral data for cases were supplemented with information from hospital records and patients' notes (this was also the case for contacts who were positive). At the North Middlesex site, missing childhood vaccination information was sought from community paediatric clinic records where all children were referred for hepatitis B vaccination. In Newham, missing information for partners of the infected woman was sought from the relevant GUM clinic. Further missing information on testing histories for both cases and contacts was supplemented by querying the national sentinel surveillance of testing for blood-borne viruses (SSBBV) database [11], matching on NHS number which is a unique patient identifier given to everyone registered with the NHS.

Prospective study

North Middlesex acted as the prospective intervention arm and Newham acted as the prospective comparison arm where service provision remained unchanged from the baseline review period. In the intervention group, women whose household contacts were eligible for home DBS testing were identified by weekly meetings with the trust's antenatal screening coordinator and study nurse. The single study nurse made direct contact with the case to arrange an appointment with the family at their home for screening and vaccination of contacts. At the time of the visit, a study questionnaire, which collected the same information as the retrospective review, was completed, written consent obtained for DBS, and DBS samples taken from all household contacts present who had not previously been tested or vaccinated. Follow-up arrangements were made to obtain samples from those not at home at the time of the visit. The first dose of vaccine was administered by the study nurse to all contacts aged $\leqslant$16 years. Those aged >16 years were referred to their GP in line with local commissioning arrangements. Missing information was sought as in the retrospective review period.

The processes in place in the maternity units were compared across all groups, within trust, and between trusts, to ensure that any temporal changes that occurred in the follow-up and guidance provided to these individuals could be identified, in order to ensure that any benefit from the intervention was attributed correctly.

Where household contacts were HBV positive they were classified as either having a resolved infection (HBsAg negative, anti-HBc positive) or a current infection (HBsAg positive, anti-HBc positive). Where a GP indicated that an individual had HBV infection it was assumed that this was a current infection.

Sequencing analysis was only undertaken for the intervention arm of the study as there were available DBS samples from the household contacts. Using these, a matching exercise was undertaken to match these samples to available index case samples in the same household with the aim of investigating possible household transmission using sequencing analysis.

Laboratory testing

DBS testing

DBS samples were tested at the Virus Reference Department, PHE Colindale, where modified commercial tests were used, both for anti-HBc and HBsAg detection. These modifications were developed in this laboratory by optimizing each stage of the process, including standardization of the elution of the DBS. Each DBS was first tested for anti-HBc employing an optimized protocol based on the Bio-Rad anti-HBc EIA (Bio-Rad, USA); this method had previously been shown to have a sensitivity of 98·8% (81/82) and a specificity of 99·6% (276/277) (Professor J. Parry, personal communication). DBS that were anti-HBc reactive were tested for the presence of HBsAg using a modified DiaSorin/Murex HBsAg assay protocol (DiaSorin S.p.A, Italy) whose sensitivity and specificity were approaching 100%. Validation testing on DBS prepared from 99 HBsAg-positive individuals found all to be reactive, consistent with a clinical sensitivity approaching 100%. False reactions are rare but, to avoid these, a secondary HBsAg confirmatory (neutralization) test was employed on all HBsAg screen-reactive specimens. HBsAg-positive samples were also tested for HBV DNA.

DNA extraction and sequencing analysis

Case samples were extracted on the Roche Magna Pure 96 automated extraction system as previously described [12]. In addition, DBS were eluted in animal tissue lysis buffer (Qiagen, USA) and proteinase K (Qiagen). Each spot was processed in the presence of murine CMV (mCMV) which acted as an internal control. The DBS eluates were extracted on the Qiagen QIAsymphony

automated extraction system using the Cellfree200 V5 DSP protocol and QIAsymphony DSP Virus/Pathogen Mini kit (Qiagen).

HBV DNA viral load was determined using an in-house Taqman assay and sequence analysis carried out on samples with a HBV DNA viral load of $\geqslant 1{\cdot}0 \times 10^3$ IU/ml [13]. Genotype analysis was undertaken through sequence and phylogenetic analysis across the HBsAg region [12] Additional mutational analysis focused on the identification of mutations associated with the alteration of HBsAg antigenicity, antiviral resistance as well as pre-core and basal core promoter mutations [12].

Statistical analysis

The reported ethnicities were combined into four distinct groups given the small numbers in each individual category. Individuals were grouped as Asian/Asian British, Black/Black British, White/White other or Mixed/Other. When considering contacts of cases in households the data have a hierarchical structure. Where possible data were summarized at a household-level to simplify the analysis so that households became the unit of interest. This was done by creating a binary variable to classify a house as tested or not tested dependent on at least one person in that household being tested. Similar variables were created for vaccination (at least one dose), any positive (resolved or current infection), and any referred current infection. To assess the differences between groups in the type of contact (age, sex, child/adult) in order to account for the hierarchical data structure (contacts nested in cases) random-effects models were fitted in Stata v. 12 (StataCorp., USA). Where individual-level analysis was possible this was also done.

RESULTS

The number of women identified within each trust during the retrospective and prospective periods was similar; however, Newham had a higher number of women diagnosed antenatally (124 and 122 women, respectively) than North Middlesex (57 and 58 women, respectively) (Table 1). The median age of cases in each group was similar varying from 26 years (North Middlesex prospective group) to 28 years (Newham prospective group), with similar age ranges and a combined age range across all groups aged 14–42 years. The proportions across the four ethnicity groupings varied across all trusts ($P = 0{\cdot}05$). When comparing individual groups, North Middlesex and Newham retrospective groups differed significantly ($P = 0{\cdot}008$) with North Middlesex having a lower proportion of Asian/Asian British (10·5% *vs.* 25·4%) and a higher proportion of White/White other ethnicities (40·4% *vs.* 21·3%) than Newham. The level of fluent English spoken was lowest in the Newham prospective group (43·5%), although inexplicably there is a large amount of missing data for this variable in this group. Population mobility was high, with at least 29% of each group having been registered at $\geqslant 3$ addresses between 1 January 2009 and 31 December 2012.

Despite the differences between all groups for ethnicity, HBeAg status and English level, these variables were not confounders or significantly associated with the outcomes of interest (tested, vaccinated, positivity, referral) when included in the multivariable model. Therefore, results of univariate analyses are presented.

The number of cases where household contacts were known varied significantly across all groups ($P < 0{\cdot}001$) (Table 2). In the North Middlesex prospective group 100% of household contacts were identified compared to 71·9% and 73·4% in the North Middlesex and Newham retrospective groups, respectively and 55·7% in the Newham prospective group ($P < 0{\cdot}001$). The North Middlesex prospective group also had the highest number of mean contacts with 2·91 contacts per case; the Newham retrospective group had the lowest with 1·87 contacts per case identified. There was a higher proportion of males in all groups, while the Newham prospective group had the highest median age (21 years). The distribution of relationships varied significantly across the groups ($P = 0{\cdot}005$) with more children identified in the North Middlesex groups.

Households in the North Middlesex prospective group were significantly more likely to have had $\geqslant 1$ contact tested (96·6% tested) than in the North Middlesex retrospective ($P < 0{\cdot}001$) and Newham prospective groups ($P < 0{\cdot}001$), while there was no difference between retrospective and prospective periods at Newham ($P = 1{\cdot}000$) or between North Middlesex and Newham in the retrospective period ($P = 0{\cdot}086$). The North Middlesex prospective group also had a higher proportion of households where $\geqslant 1$ contact was vaccinated (74·1%) than the other groups ($P < 0{\cdot}001$). A much higher proportion of individual contacts were tested in the North Middlesex prospective group than all other groups, with the lowest proportion tested in the Newham prospective group.

Table 1. *Case demographic information for all groups*

Variable		Group 1 (North Middlesex retrospective)	Group 2 [North Middlesex prospective (DBS)]	Group 3 (Newham retrospective)	Group 4 (Newham prospective)	*P* value				
						All groups	1 *vs.* 2	3 *vs.* 4	1 *vs.* 3	2 *vs.* 4
No. of women	*N*	57	58	124	122					
Age, years	Age known (*n*)	56	58	123	122					
	Median (range)	27 (16–40)	26 (14–40)	27 (16–47)	28 (19–42)	0·341*	0·544*	0·431*	0·305*	0·227*
Ethnicity (%)	Asian/Asian British	6 (10·5)	13 (23·2)	31 (25·4)	33 (27·1)	0·052†	0·159†	0·591†	0·008†	0·648†
	Black/African/ Caribbean/Black British	26 (45·6)	20 (35·7)	61 (50·0)	53 (43·4)					
	White/White other	23 (40·4)	17 (30·4)	26 (21·3)	31 (25·4)					
	Mixed/Other	2 (3·5)	6 (10·7)	4 (3·3)	5 (4·1)					
	Unknown	0	2	2	0					
Previous screen (%)	Yes	31 (68·9)	33 (60·0)	43 (100·0)	46 (97·9)	–‡	–‡	–‡	–‡	–‡
	No	14 (31·1)	22 (40·0)	0 (0·0)	1 (2·1)					
	Unknown	12	3	81	75					
HBeAg status (%)	Negative	45 (91·8)	49 (87·5)	113 (94·2)	104 (86·0)	0·157§	0·537§	0·051§	0·732§	1·000§
	Positive	4 (8·2)	7 (12·5)	7 (5·8)	17 (14·0)					
	Unknown	8	2	4	1					
English level (%)	⩽Basic	22 (40·0)	19 (33·3)	41 (33·3)	48 (56·5)	–‡	0·557§	–‡	0·401§	–‡
	Fluent	33 (60·0)	38 (66·7)	82 (66·7)	37 (43·5)					
	Unknown	2	1	1	37					
No. of homes since 2009 (%)	1	12 (23·1)	17 (30·9)	34 (28·6)	43 (35·8)	0·210§	0·572§	0·356§	0·217§	0·330§
	2	20 (38·5)	21 (38·2)	30 (25·2)	32 (26·7)					
	⩾3	20 (38·5)	17 (30·9)	55 (46·2)	45 (37·5)					
	Unknown	5	3	5	2					
No. of GPs since 2009 (%)	1	25 (48·1)	26 (47·3)	43 (36·1)	57 (47·5)	0·257§	0·309§	0·129§	0·339§	0·711§
	2	14 (26·9)	21 (38·2)	42 (35·3)	40 (33·3)					
	⩾3	13 (25·0)	8 (14·5)	34 (28·6)	23 (19·2)					
	Unknown	5	3	5	2					

* Kruskal–Wallis test.
† Fisher's exact test – Mixed/other were excluded.
‡ *P* values not calculated as levels of missing data was >20%.
§ Fisher's exact test.

Table 2. *Contact information for all groups, and follow-up status*

Variable		Group 1 (North Middlesex retrospective)	Group 2 [North Middlesex prospective (DBS)]	Group 3 (Newham retrospective)	Group 4 (Newham prospective)	*P* value				
						All groups	1 *vs.* 2	3 *vs.* 4	1 *vs.* 3	2 *vs.* 4
Case households where contacts were identified (%)	Yes	41 (71·9)	58 (100·0)	91 (73·4)	68 (55·7)	<0·001*	<0·001*	0·005*	0·858*	<0·001*
	No	16 (28·1)	0 (0·0)	33 (26·6)	54 (44·3)					
Contacts	*N*	92	169	170	163					
	Mean (range)	2·24 (0–13)	2·91 (1–8)	1·87 (0–8)	2·40 (0–10)					
Age, years	Age known (*n*)	86	165	116	143					
	Median (range)	9 (0–49)	12 (0–54)	13 (0–73)	21 (0–65)	0·028†	0·074†	0·268†	0·066†	0·104†
Gender (%)	Female	31 (34·8)	59 (35·1)	48 (28·2)	48 (29·6)	0·463‡	0·963‡	0·774‡	0·274‡	0·287‡
	Male	58 (65·2)	109 (64·9)	122 (71·8)	114 (70·4)					
	Unknown	3	1	0	1					
Relationship (%)	Child	54 (59·3)	90 (53·3)	65 (38·2)	63 (39·1)	0·005§	0·453§	0·677§	0·001§	0·062§
	Partner	33 (36·3)	56 (33·1)	81 (47·6)	39 (24·2)	0·003¶	0·454¶	0·001¶	0·216¶	0·001¶
	Other adult	4 (4·4)	23 (13·6)	24 (14·1)	59 (36·7)					
	Unknown	1	0	0	2					
Any household tested#	*n*/*N* (%)	23/37 (62·1)	56/58 (96·6)	36/91 (39·6)	26/66 (39·4)	<0·001*	<0·001*	1·000*	0·086*	<0·001*
Any household vaccinated#	*n*/*N* (%)	20/40 (50·0)	40/54 (74·1)	32/91 (35·2)	24/66 (36·4)	<0·001*	0·019*	1·000*	0·124*	<0·001*
Number tested (by relationship)	Child	31/54 (57·4)	90/90 (100·0)	42/65 (64·6)	20/63 (31·7)					
	Partner	10/33 (30·3)	54/56 (96·4)	24/81 (29·6)	9/39 (23·1)					
	Other adult	1/4 (25·0)	23/23 (100·0)	6/24 (25·0)	18/59 (30·5)					

* Fisher's exact test.

† Wald test from random-effects model.

‡ Wald test from random-effects model – Unknown excluded.

§ Wald test from random-effects model, comparing child *vs.* adult (partner and other adult).

¶ Wald test from random-effects model, comparing partner *vs.* other adult.

Denominators vary depending on data availability.

For the North Middlesex prospective group, there were no individuals with unknown testing status and just two individuals who were not tested (Table 3). By comparison across all the other groups, there were 61 individuals whose test status was unknown and 261 individuals who were not tested. In particular, the partners in Newham appeared to have very poor testing uptake (29·6% and 23·1% tested for the retrospective and prospective groups, respectively). When considering the proportion of total contacts vaccinated, children and other adult contacts in the prospective group had a much higher uptake in North Middlesex than in Newham, although uptake in partners was similar. The proportion of children who tested negative, who were vaccinated, was similar in both North Middlesex and Newham; however, the absence of an observable difference may be due to the small numbers of children with a known test result – particularly in Newham. Due to the small numbers of contacts with documented referrals it was not possible to comment on any differences across the groups.

Sequencing analysis (North Middlesex study only)

Of the 58 index cases identified, 52 (89·7%) had samples available for testing. All 52 (100%) of these samples were HBV DNA positive. Genotype determination was possible for 41 (78·8%) of the index cases. The predominant genotype was genotype D with 18 (44·0%) index cases falling into this group, followed by genotype E (19·5%) and genotype C (14·6%). Genotypes A and B were uncommon with five (12·2%) and four (9·8%) respectively. When considering genotype in relation to ethnicity, genotype D was predominantly 'White – Other' (67%), while genotypes B and C were mainly 'Chinese' ethnicity with 100% and 83% respectively, and genotypes A and E were mostly of 'Black/Black British African' ethnicity with 80% and 88%, respectively (Table 4).

Pre-core and basal core promoter mutations were noted in 50% and 7% of sequenced samples, respectively. A small proportion (14%) of samples harboured both pre-core and basal core promoter mutations. The described mutations associated with HBV antiviral resistance were not observed in any of the samples from the cases and household contacts. Of interest, analysis across the HBsAg region indicated 18 of the case samples and one of the household contacts to bear amino acid changes occurring between codons 120–150.

Sequence comparison analysis was only possible in four matched cases and contacts. While 20 household contacts were identified as having a current infection, four (45%) had no sample available and five had withdrawn consent for further testing. Moreover, of the remaining 11 contacts, samples were unavailable for one of the matching index cases. While all 10 (100·0%) samples from the index case and seven (70·0%) of the household contact samples had detectable HBV DNA, viral load levels were too low in three samples [one (10·0%) case and two (20·0%) contacts] to undertake HBV sequence analysis.

Contacts where sequence comparison was possible were: partner ($n = 1$), siblings ($n = 2$) and daughter ($n = 1$). Identical HBV genotypes were noted in the cases and their contacts. Analysis at the nucleotide level indicated the sequences from the contacts to be between 95·8–98·3% and 94·7–96·1% similar to corresponding case sequences across the HBsAg/pol and basal core/pre-core/core regions, respectively.

DISCUSSION

Providing a home-delivered DBS testing service greatly improves testing uptake for household contacts of HBV-infected pregnant women, with 96·6% of households having at least one contact tested. A greater increase in testing was observed in partners and other adults compared to children. Vaccination uptake was also greater in 'other adults' in the intervention group. This success is likely to reflect the accessibility and convenience of a home testing service for these families, avoiding the need to attend primary- or secondary-care services. Furthermore, the availability of evening and weekend visits by the nurse added to the convenience for working families with 98·8% of all eligible individuals tested. Although the data should be interpreted with caution due to the small numbers of infected contacts detected and missing information, the change in service arrangements did not appear to improve referral rates. A lack of current infections along with case/contact matching and low DNA levels meant that sequence comparison was only possible for four cases and four contacts. While the genotype of the virus was identical between cases and contacts, it remained difficult to comment on HBV transmission within households. With comparison data indicating low sequence homology it is plausible that many of household contacts did not acquire infection from the case, but from other sources in their country of origin. This hypothesis is supported by the fact that three of the four contacts were born outside the UK (the fourth contact's country of

Table 3. *Number of household contacts tested by relationship status to the case and their outcomes depending on the results of this testing*

Variable	Group 1 (North Middlesex retrospective)	Group 2 [North Middlesex prospective (DBS)]	Group 3 (Newham retrospective)	Group 4 (Newham prospective)	Total
No. of contacts					
Child	54	90	65	63	272
Partner	33	56	81	39	209
Other adult	4	23	24	59	110
Test results					
Child					
Negative (%)	23 (42·6)	85 (94·4)	15 (23·1)	8 (12·7)	131 (48·2)
Positive [current] (%)	0 (0·0)	5 [3], (5·6 [3·3])	4 [4], (6·2 [6·2])	1 [1], (1·6 [1·6])	10 [8], (3·7 [2·9])
Unknown (%)	8 (14·8)	0 (0·0)	23 (35·4)	11 (17·5)	42 (15·4)
Not tested	23 (42·6)	0 (0·0)	23 (35·4)	43 (68·3)	89 (32·7)
Partner					
Negative (%)	6 (18·2)	19 (33·9)	8 (9·9)	5 (7·9)	38 (18·2)
Positive [current] (%)	1 [1], (3·0 [3·0])	35 [12], (62·5 [21·4])	6 [6], (7·4 [7·4])	2 [2], (5·1 [5·1])	44 [21], (21·1 [10·0])
Unknown (%)	3 (9·1)	0 (0·0)	10 (12·3)	2 (5·1)	15 (7·2)
Not tested	21 (63·6)	2 (3·57)	57 (70·4)	30 (76·9)	110 (52·6)
Other adult					
Negative (%)	1 (25·0)	10 (43·5)	2 (8·3)	10 (16·9)	23 (20·9)
Positive [current] (%)	0 (0·0)	13 [5], (56·5 [21·7])	2 [2], (8·3 [8·3])	5 [5], (8·5 [8·5])	20 [12], (18·2 [10·9])
Unknown (%)	0 (0·0)	0 (0·0)	2 (8·3)	3 (5·1)	5 (4·5)
Not tested	3 (75·0)	0 (0·0)	18 (75·0)	41 (69·5)	62 (56·4)
If negative then vaccinated?					
Child (%)	22 (95·7)	75 (88·2)	14 (93·3)	6 (75)	117 (89·3)
Partner (%)	2 (33·3)	7 (36·8)	4 (50·0)	5 (100·0)	18 (47·3)
Other adult (%)	0 (0·0)	7 (70·0)	1 (50·0)	3 (30·0)	11 (47·8)
No. vaccinated of total contacts					
Child (%)	22 (40·7)	75 (83·3)	14 (21·5)	6 (9·5)	117 (43·0)
Partner (%)	2 (6·1)	7 (12·5)	4 (4·9)	5 (12·8)	18 (8·6)
Other adult (%)	0 (0·0)	7 (30·4)	1 (4·2)	3 (5·1)	11 (10·0)
If current infection, referred?					
Child (%)	n.a.	2 (66·7)	4/4 (100·0)	1/1 (100·0)	7/8 (87·5)
Partner (%)	0 (0·0)	2 (16·7)	2/6 (33·3)	1/2 (50·0)	5/21 (23·8)
Other adult (%)	n.a.	4 (80·0)	1/2 (50·0)	4/5 (80·0)	9/12 (75·0)
No. referred of total contacts					
Child (%)	0 (0·0)	2 (2·2)	4 (6·2)	1 (1·6)	7 (2·6)
Partner (%)	0 (0·0)	2 (3·6)	2 (2·5)	1 (2·6)	5 (2·4)
Other adult (%)	0 (0·0)	4 (17·4)	1 (4·2)	1 (1·7)	9 (8·2)

n.a., Not applicable.

Table 4. *Genotype distribution in the index case ethnic groups [North Middlesex Prospective (DBS) group only]*

Genotype	Count	Asian/Asian British – Other Asian	Black/Black British – African	Chinese	White – Other	Other	Unknown
A	5		4 (80%)		1 (20%)		
B	4			4 (100%)			
C	6	1 (17%)		5 (83%)			
D	18	1 (6%)	1 (6%)		12 (67%)	4 (22%)	
E	8		7 (88%)				1 (13%)

birth was unknown). The sequence and genotype analysis demonstrated the complexity and diversity of viruses in this population of women and indicated that some of this diversity in the form of viruses harbouring amino acid changes that alter HBsAg antigenicity may impact on the effectiveness of immunization.

This intervention brought to light challenges surrounding data sharing, communication and the commissioning of services. Poor data flow between primary and secondary care resulted in multiple data sources needing to be reviewed which was both time- and resource-intensive. Despite these efforts we acknowledge that the levels of missing data is a limitation, in particular the unexplainable high levels (37) of missing data in the Newham prospective arm regarding fluency of English. To facilitate the optimal management of both cases and their contacts, it is important that GPs have the complete medical records for their patients. We found particularly poor data transfer from GUM clinics, despite having established data-sharing agreements. This meant that data for the majority of partners in the Newham group were not recorded. Given the high levels of positive contacts in partners in the North Middlesex prospective group there is a clear need to document test uptake and HBV status of these individuals in Newham for individual patient management. We recommend that testing of contacts should not be commissioned in GUM clinics unless results are made available to the GP.

This is the first study to assess the use of a nurse-delivered in-home DBS service for household contacts of HBV-positive women. The DBS approach outlined here is resource-intensive, and therefore may not be appropriate in lower prevalence areas. A combined approach of a nurse-led clinic/home approach may be more affordable without compromising access to services for hard-to-reach groups. An alternative approach that has been investigated is self-administered DBS which achieved a testing uptake of 77% in one study [14]. Although this approach achieved a lower uptake than in the North Middlesex intervention group, this may be offset by reduced staffing costs. Self-testing in the community, using either oral fluid testing or DBS warrants further economic evaluation.

Our findings suggest that the greatest improvements in testing and vaccination associated with a home-delivered DBS testing service is for adults. This may be because existing pathways are working more effectively to follow-up and vaccinate children born to hepatitis B-infected women. The introduction of universal antenatal testing and the publication of a number of national guidelines including the 'Hepatitis B antenatal screening and newborn immunization programme: best practice guidance 2011' [15], and the NICE public health guidance [7], may have contributed to the clear pathways for managing these high-risk children. However, local variations and a lack of clarity around the commissioning arrangements for managing adult household contacts needs to be addressed. Our findings also suggest that the main barriers to testing are around the acceptability of venepuncture, which would be expected to be a particular barrier in children, and the inconvenience of having to attend a health service setting. The less pronounced impact on adult vaccinations is likely to reflect the commissioning arrangements in place where adults (including partners) were referred back to their GP or to GUM clinics for vaccination, and again highlights the barrier introduced by otherwise healthy adults having to visit a healthcare setting.

For the non-intervention groups it was not possible to identify all household contacts and even where contacts were identified a large number remained untested. Making an assumption that average household size, type of contact and proportion infected are the same as in the intervention group, it is possible that an additional 11 children, and 210 infected adults could potentially be undiagnosed. Given what is known about the low levels of HBV indigenous

transmission in the UK, it is likely that most of the adults will have been infected in childhood overseas and may therefore have chronic infection. HBV-infected individuals have a 5-year cumulative incidence of developing cirrhosis of between 8% and 20% and, once cirrhosis is established, the annual incidence of HBV-related hepatocellular carcinoma is between 2% and 5%. [16] This undiagnosed burden may represent a significant burden and future cost [17] to the NHS. With new treatments for chronic hepatitis B recommended by NICE now available [18], service pathways need to be optimized to improve access to diagnosis and assessment. This study shows that home-based sampling, in this case using DBS, can increase testing and vaccination uptake, and also demonstrates the need to further investigate household transmission, particularly in households with more than one HBV-positive individual. A compelling case could be made for offering nurse-administered home-based testing and vaccinations for at-risk individuals in areas with high prevalence. Increasing testing and vaccination in at-risk groups may contribute to the broader aims of reducing premature mortality from liver disease and reducing inequalities, as set out by the Department of Health in the Public Health Outcomes Framework [19]. The challenge that remains is to ensure commissioning supports clear care pathways from testing to diagnosis and referral to specialist care so that people diagnosed with hepatitis B have timely access to treatments which can halt progression of chronic liver disease to cirrhosis and hepatocellular cancer.

ACKNOWLEDGEMENTS

The authors thank Nick Andrews at PHE Colindale for assistance with and advice on statistical methodology and analysis. Thanks are also due to Andrew Fox-Lewis and Kobika Sritharan at North Middlesex University Hospital for their assistance in data collation, and to Natalie Wing Yu To who was at the time with Health Protection Agency (now Public Health England). The authors also thank all the staff at the various GP practices across Newham and North Middlesex where data was sought, along with their colleagues at North Middlesex University Hospital and Newham Hospital, and the staff in the Immunisation, Hepatitis and Blood Safety Department and the Virus Reference Department at PHE. Finally the authors express their gratitude to the study participants in North Middlesex.

This study was funded through a GILEAD fellowship grant in 2010 awarded to Gayatri Amirthalingam (née Manikkavasagan).

DECLARATION OF INTEREST

None.

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