ORIGINAL ARTICLE VIROLOGY

Impact of free on-site vaccine and/or healthcare workers training on hepatitis B vaccination acceptability in high-risk subjects: a pre-post cluster randomized study

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Abstract

Despite recommendations for adults at high-risk of hepatitis B virus (HBV) infection, HBV vaccine uptake remains low in this population. A pre-post randomized cluster study was conducted to evaluate the impact of on-site free HBV vaccine availability and/or healthcare worker training on HBV vaccination acceptability in high-risk adults consulting in 12 free and anonymous HIV and hepatitis B/C testing centres (FATC). The FATC were randomly allocated into three groups receiving a different intervention: training on HBV epidemiology, risk factors and vaccination (Group A), free vaccination in the FATC (Group B), both interventions (Group C). The main outcomes were the increase in HBV vaccination acceptability (receipt of at least one dose of vaccine) and vaccine coverage (receipt of at least two doses of vaccine) after intervention. Respectively, 872 and 809 HBV-seronegative adults at high-risk for HBV infection were included in the pre- and post-intervention assessments. HBV vaccination acceptability increased from 14.0% to 75.6% ($p < 0.001$) in Group B and from 17.1% to 85.8% ($p < 0.001$) in Group C and HBV vaccine coverage increased from 9.4% to 48.8% ($p < 0.001$) in Group B and from 11.2% to 41.0% ($p < 0.001$) in Group C. The association of training and free on-site vaccine availability was more effective than free on-site vaccine availability alone to increase vaccination acceptability (ratio 1.14; from 1.02 to 1.26; p 0.017). No effect of training alone was observed. These results support the policy of making HBV vaccine available in health structures attended by high-risk individuals. Updating healthcare workers' knowledge on HBV virus and its prevention brings an additional benefit to vaccination acceptability.

Keywords: hepatitis B virus vaccine, intervention study, training, vaccination strategies, vaccine acceptability, vaccine coverage
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The ANRS-FORMVAC Study Group members are listed in Appendix 1.

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Introduction

France is located in an area of low endemicity for hepatitis B virus (HBV) infection (0.65% in the adult population), yet hepatitis B remains a public health problem [1–3]. In line with the WHO recommendations [4], the French HBV vaccination policy in the general population includes the routine vaccination of infants/children before they reach 15 years of age and adolescents/adults at high-risk of HBV

infection [5]. HBV vaccine coverage is much lower in France than reported in other European countries [6–8]. Several studies have shown that a concern surrounding HBV vaccine safety had a significant impact both on the motivation of practitioners to offer the vaccine and on the acceptability of vaccination [9–11]. The French Ministry of Health has therefore recently embarked on a policy of strengthening the promotion of HBV vaccination for individuals at high-risk for HBV infection [12].

The free and anonymous HIV and hepatitis B and C testing centres (FATC) were set up by the French Health authorities to facilitate access to anonymous, confidential and free HIV testing. Since 1999, their role was extended to encompass the screening and prevention of hepatitis B and C infections.

The aim of the present study was to evaluate the impact of two public health interventions and their combination to improve HBV vaccination acceptability and vaccine coverage in subjects at risk for hepatitis B who are seen in FATC. As those interventions were implemented at the level of the FATC, a cluster design whereby the FATC were randomized to receive a different intervention was used.

Materials and Methods

Participants

In the pre-intervention phase, FATC were randomly selected from the national FATC activity database. FATC were excluded if they did not screen HBV infection, saw fewer than 1400 subjects per year or already proposed on-site HBV vaccination (Fig. 1). FATC were asked not to change their current practices regarding HBV screening and vaccination during the pre-intervention assessment phase. At the end of the pre-intervention phase, the FATC were randomly assigned to each of the three intervention groups: training of healthcare workers on HBV infection and its prevention (Group A), free HBV vaccine administration in the FATC (Group B) or both interventions (Group C).

In participating FATC, in both phases, all men and women aged ≥18 years, with an HIV-negative test, with no immunity against HBV (i.e. negative for HBV surface antigen (HBsAg), anti-HBs and anti-HBc antibodies testing performed in the FATC) and at high risk for HBV infection were consecutively enrolled if they agreed to participate. Patients at high-risk for hepatitis B infection were defined according to the list of individuals targeted by the hepatitis B vaccination recommendations, mainly persons who have sex with multiple partners, injecting drug users, travellers to countries of intermediate or high HBV endemicity and close contacts of chronic carriers of HBsAg [5]. Written informed consent was obtained from each subject. The protocol was conducted in accordance with the Declaration of Helsinki and French law for biomedical research and was approved by the French Data Protection Agency (CNIL) and by the 'Ile-de-France 3' Ethics Committee (Paris, France).

Interventions

For healthcare worker training on HBV infection and its prevention, one referral physician and one referral nurse were designated from each FATC of groups A and C and received a 1-day training outside the FATC in a specialized healthcare centre committed to the prevention of HIV infection and other sexually transmitted infections, including hepatitis B and C, substance abuse and risk behaviours in young people (Regional Centre for Information and Prevention of Aids; CRIPS Ile-de-France, Paris, France). The training team included a clinician, an epidemiologist and a health education officer, all specialized in hepatitis B infection and control. The main topics addressed during the training included general information about hepatitis B, risk factors of HBV infection and at-risk populations, missions of FATC, serological markers of hepatitis B and their interpretation, HBV vaccination and the controversy over its safety. In addition, a 2-h on-site training that focused on key messages to motivate patients targeted by HBV vaccination was performed on-site for all healthcare worker in each FATC of Groups A and C by two clinicians specialized in hepatitis B infection and control.

Objectives

We aimed to compare the effectiveness of improving the acceptability of HBV vaccination by making the vaccine available in the FATC, with that of increasing the capacity of health staff to motivate the patients through a refresher training. The third group, where both interventions were implemented at the level of the FATC, aimed to test the potential synergy between the two interventions.

Outcomes

The primary and secondary outcomes were the increase, between the two phases, in the proportion of subjects that received at least one dose (vaccination acceptability) or two doses (vaccine coverage) of HBV vaccine.

Vaccination acceptability and vaccine coverage were assessed, before and after intervention, following a similar methodology. During the initial visit (visit V1), the physician completed a case-report form for all subjects (willing or not to participate in the study). The physician was free to prescribe HBV vaccination and propose to the subjects that they

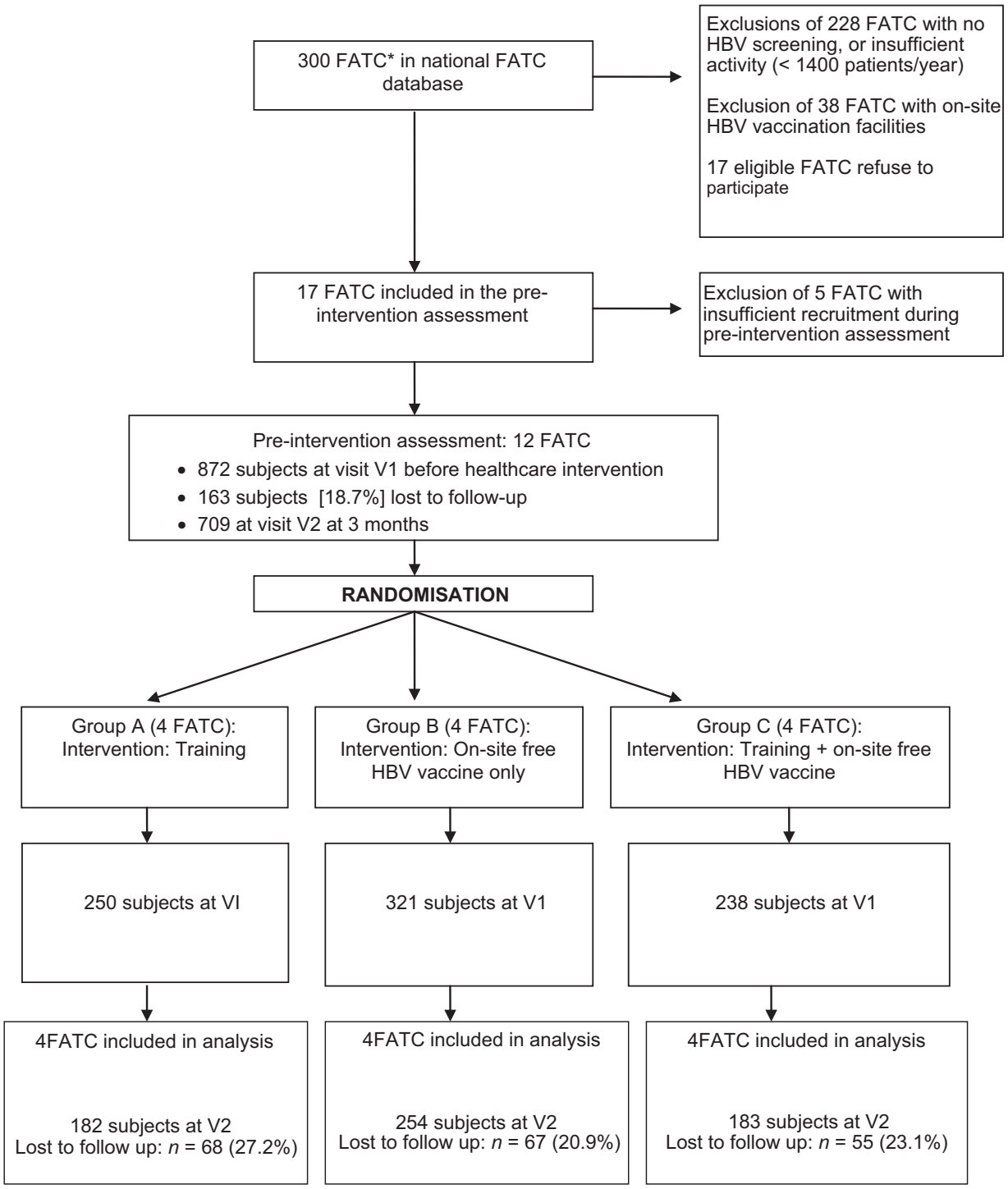

FIG. 1. Flow chart for participation of FATC and patients as well as randomization process. *FATC, Free and Anonymous HIV and hepatitis B and C Testing Centres.

participate in the study, including an agreement to provide personal phone contact. If the subject declined to participate in the study, the reasons were reported.

Three months after their inclusion (visit V2), the subjects included in the study were called by phone by the study staff to complete a questionnaire including the number of doses of

HBV vaccines administered, the main reason for vaccination or no vaccination and the date and place of vaccination.

Sample size

The sample size was estimated to allow the observation of a 15% difference in acceptability of HBV vaccination before and after intervention in each group of FATC and between the three groups after intervention. For a design effect estimated at 1.2 and a loss of follow up estimated at 35%, 350 individuals per group were needed after intervention (with α risk at 5%, and β risk at 10%) in the worst hypothesis for HBV vaccination acceptability (42%) [13]. An interim analysis conducted during the pre-intervention phase yielded an HBV vaccination acceptability rate around 10% and a loss of follow-up rate of <25%. A new calculation of the sample size with the same α and β risks based on those figures yielded a minimum sample size of 168 per group. Based on four FATC in each of the three groups after intervention, the minimum number of inclusions per FATC was set at 50. Subjects already included above that figure in FATC with high recruitment capacity were kept in the analysis. To account for a possible drop-out of FATC between the first and the second phase, linked for instance to difficulties in recruiting enough participants, it was decided to include 18 FATC in the first phase so as to have at least 12 FATC participating in the second phase.

Sequence generation

As a result of the small number of clusters, a stratification on the annual level of HBV screening activity (low, moderate, high activity) was used in the initial selection of FATC, to avoid an unbalanced selection of FATC related to some of their characteristics, such as their size. Those levels were defined by the 33rd and 66th centiles of number of subjects tested for HBV immunity (corresponding to 2200 and 4000 subjects per year, respectively). Therefore, six FATC were to be randomly selected in each stratum.

The FATC that participated in the study in the pre-intervention phase were randomly allocated to one of the three intervention groups at the end of this phase. Randomization was performed by one of the researchers (DLB) on an Excel file where FATC were identified through a number not allowing the identification of the FATC.

Statistical analysis

In each of the three groups defined by the intervention implemented, HBV vaccination acceptability and coverage were compared, before and after intervention. HBV vaccination acceptability and coverage were also compared between groups within each phase.

The data were analysed using multivariate Poisson regression models with robust variance taking into account the study design [14,15]. The choice of this type of regression was based on our objective to assess HBV vaccination acceptability/coverage ratios rather than approximate them (e.g. odds ratio from logistic regressions). The multivariate Poisson regressions to explain HBV vaccination acceptability/coverage were adjusted on the following potentially associated variables: delivery of a prescription, sex, age, endemic rate of HBV in the country of origin, close contacts with an HBV-infected individual, multiple sexual partners, sexual partner with HBV infection, travelling/living in country with moderate/high HBV prevalence, occupational risk. Age was introduced as a continuous variable modeled with a fractional polynomial [16]. Two additional statistical models were performed, including all the variables listed above: one explored factors associated with HBV vaccination acceptability before intervention in the three groups considered together; the other one explored the factors associated with HBV vaccination acceptability and coverage after intervention in group C. This latter analysis was aimed at identifying potential residual risk factors associated with declining the proposal of HBV vaccination despite the vaccine being available and free and the staff having been recently re-trained.

Results

Selection of centres and subjects' characteristics

Within all eligible FATC, 17 agreed to participate (six in a stratum with low activity for HBV screening, six with moderate activity and five with high activity; Fig. 1). Five FATC were excluded at the end of the pre-intervention assessment due to insufficient recruitment (<30 subjects). In the 12 active FATC (four FATC in each intervention group), 872 subjects were included in the pre-intervention assessment (September 2009–March 2010); 809 subjects were included in the post-intervention assessment (September 2010–March 2011). One hundred and three subjects (10.6%) declined to participate in the pre-intervention assessment and 87 (9.7%) in the post-intervention assessment. The distribution of patients before and after intervention in the three groups, and patients lost to follow up are reported in Fig. 1. The baseline characteristics of the participants are described in Table 1. The characteristics of patients who participated and of those who declined to participate did not differ (see Supporting information; Table S1). The subjects enrolled before and after intervention were comparable except for homo/bisexual practices (p 0.009). According to the multivariate regression model, no factor was significantly associated with loss to follow up after 3 months, both before and after intervention.

TABLE 1. Characteristics of participants before and after intervention

	Before intervention *n* = 709	After intervention *n* = 619
Women	283 (40.3)	391 (64.1)
HBV prevalence in country of origin		
<2% (low)	580 (84.7)	511 (85.9)
2–7% (moderate)	45 (6.6)	37 (6.2)
>7% (high)	60 (8.8)	47 (7.9)
Missing	24	24
Risk factors[a]		
Multiple sexual partners	574 (81.3)	508 (83.1)
Homosexual or bisexual	92 (13.1)	111 (18.3)
Sexual partner with HBV infection	8 (1.2)	6 (1.0)
Drug user	49 (7.0)	38 (6.4)
Travelling/living in country with moderate/high prevalence	214 (30.5)	178 (29.7)
Professional risk	62 (8.9)	37 (6.3)
Close contacts infected by HBV	19 (2.7)	8 (1.3)
No social insurance	16 (2.3)	5 (0.8)

Results given as *n* (%). HBV, hepatitis B virus.
[a]More than one answer possible.

HBV vaccination acceptability and vaccine coverage

Before intervention, HBV vaccination acceptability (at least one dose of vaccine) did not differ between the three groups determined by the randomization of FATC (14.9%, 14.0% and 17.1% in groups A, B and C, respectively; p 0.8). Adjusted on age (p 0.09), the factors associated with HBV vaccination acceptability before intervention when combining the three groups were: delivery of an HBV vaccine prescription (p <0.001), the level of endemicity of HBV in the country of origin (p 0.04), having an HBV-infected sexual partner (p 0.002) and having multiple sexual partners (p 0.01).

Acceptability of HBV vaccination increased significantly after intervention in Groups B and C (Fig. 2a). No significant change was observed in Group A. The association of training and HBV vaccine availability (Group C) had a significantly higher impact on acceptability than vaccine availability alone (Group B; ratio, 1.14 (95% CI 1.02–1.26), p 0.017).

No factor was found to be significantly associated with HBV vaccination acceptability after intervention in Group C.

The HBV vaccine coverage (at least two doses of vaccine) increased significantly after intervention in Groups B and C (Fig. 2b). No significant change was observed in Group A. The impact of the association of training and vaccine availability (Group C) on vaccine coverage was not significantly different from that of vaccine availability alone (Group B).

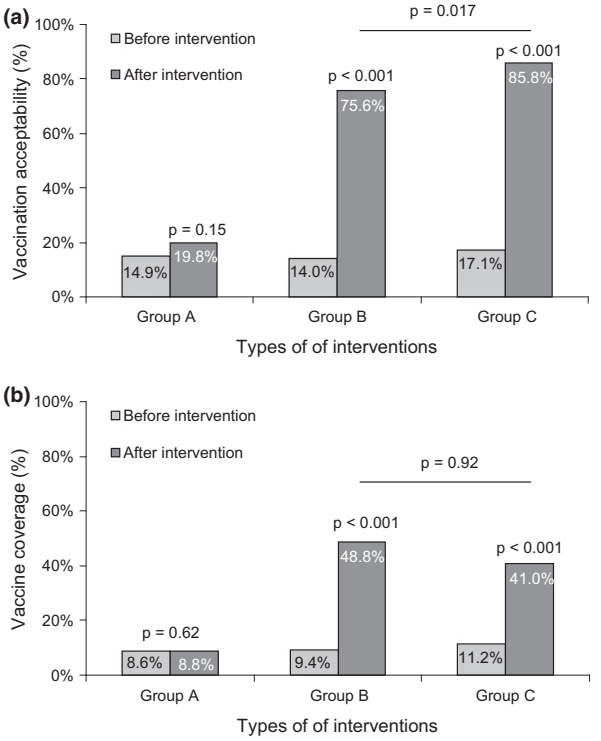

FIG. 2. Evolution of HBV vaccination acceptability (a) and vaccine coverage (b) according to the type of intervention (Group A: training on hepatitis B virus infection and its prevention; Group B: free hepatitis B virus vaccine administration in the centre; Group C: both interventions), using a multivariate Poisson regression model.

Discussion

In this study, HBV vaccine availability induced a dramatic increase in vaccination acceptability and, to a lesser extent, in vaccine coverage. Training of healthcare workers alone had no significant impact on HBV vaccination acceptability or coverage. One explanation for this disappointing result for training could be that the prevention of HBV infection is already included in FATC missions. Therefore, training relying on the capacity and willingness of the regular FATC staff to educate and motivate their patients does not appear as a promising intervention to increase HBV vaccine coverage.

Interestingly, healthcare worker training associated with availability of free HBV vaccines did better than free vaccines alone in terms of vaccination acceptability, but the difference disappeared when considering the vaccine coverage. This finding could reflect a transient synergy of training and free vaccine availability that does not last beyond the immediate incentive effect related to the interaction with trained staff during the consultation.

Our results are comparable with the overall HBV vaccine acceptance of 69% (55% for the second dose) reported in a study conducted in a Californian sexually transmitted disease clinic, where the HBV vaccine was administered without additional charge [17]. Similarly, in a Dutch HBV vaccination programme, where some Municipal Health Services offered the HBV vaccine free to high-risk groups, the coverage in

those who reported their status was 59% for the full vaccination series [18]. Of interest, the HBV vaccine coverage increased over time, suggesting the importance of sustained efforts over many years in these high-risk populations. On-site provision of free vaccine has been shown to increase healthcare workers' influenza vaccination coverage [19].

Our cluster randomized control trial design including a before and after intervention assessment has allowed us to minimize bias. The short duration of the study together with the absence of increase in the vaccination coverage in the group without free on-site HBV vaccine availability makes the conclusion of the impact of this latter strategy on vaccine coverage quite robust. The relatively low percentage of refusal to participate in both phases, (around 10%) and of loss to follow up at the 3-month visit (<25%) is another strength of the study. One of its main limitations is that the vaccination status was not validated through official records. However, there is no reason to think that the potential bias so induced would differ between groups or between phases and it therefore does not affect our conclusions. Another limitation is that only the first two injections were monitored. However, this was chosen to limit the delay between the initial and the final visit, and hence to reduce the risk of loss to follow up of participants. Moreover, recent data in adolescents suggested that two doses of vaccine are sufficient for protection [20].

In conclusion, the availability of free on-site HBV vaccine was highly effective in increasing HBV vaccination acceptability in high-risk adults. Further studies are necessary to identify the barriers that still prevent a substantial number of high-risk patients from achieving a complete HBV immunization schedule when an immediate opportunity for vaccination is offered by well-trained staff.

Authorship

OL had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. OL, SL, JH, EB, DL-B contributed to the study concept and design; WT contributed to acquisition of data; OL, YL-S, WT, LK, SQ, SL, EB, DL-B contributed to analysis and interpretation of data; OL, EB, DL-B drafted the manuscript; OL, YL-S, WT, LK, SQ, SL, EB, DL-B contributed to critical revision of the manuscript for important intellectual content; YL-S, DL-B contributed to statistical analysis; OL, EB obtained funding; OL, LK, JD, JR, SL contributed to administrative, technical, or material support; and OL, LK, JD, JR, DL-B supervised the study.

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The sponsor had no role in the design and conduct of the study; in the collection, management, analysis, and interpretation of the data; or in the preparation, review, or approval of the manuscript.

The statistical analysis of the data was conducted independently from the sponsor by co-authors Yan Le Strat and Daniel Lévy-Bruhl, from the Institut de Veille Sanitaire. Mr Le Strat and Mr Lévy-Bruhl had access to all the data used in the study and ran the analysis. They were not compensated for this work.

We also thank the study participants and the participating clinicians at each site, and Francis Beauvais for his help in preparing the manuscript (financial compensation).

Transparency Declaration

OL reported not having shares or paid employment with pharmaceutical companies; being an investigator on vaccine studies sponsored by Sanofi Pasteur-MSD and other companies and received travel support to attend scientific meetings from Sanofi Pasteur-MSD and other companies. SQ reported not having shares or paid employment with pharmaceutical companies; and received travel support to attend scientific meetings from Sanofi Pasteur-MSD and other companies. All other authors declare no conflicts of interest.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Table S1. Characteristics of the patients who declined to participate before and after interventions.

References

1. World Health Organization. Fact sheet N°204: hepatitis B. Available at: http://www.who.int/mediacentre/factsheets/fs204/en/index.html [Accessed January 18, 2014].

2. Meffre C, Le Strat Y, Delarocque-Astagneau E, *et al.* Prevalence of hepatitis B and hepatitis C virus infections in France in 2004: social factors are important predictors after adjusting for known risk factors. *J Med Virol* 2010; 82: 546–555.
3. Institut de veille sanitaire. Prévalence des hépatites B et C en France en 2004. Available at: http://www.invs.sante.fr/publications/2006/prevalence_b_c/vhb_france_2004.pdf [accessed January 18, 2014].
4. Hepatitis B. Vaccines: WHO position paper—recommendations. *Vaccine* 2010; 28: 589–590.
5. Calendrier vaccinal 2007 - Avis du Haut conseil de la santé publique. 24 juillet 2007. *Bull Epidemiol Hebd* no. 31–32.
6. Mele A, Stroffolini T, Zanetti AR. Hepatitis B in Italy: where we are ten years after the introduction of mass vaccination. *J Med Virol* 2002; 67: 440–443.
7. Antona D, Fonteneau L, Levy Bruhl D, *et al.* Couverture vaccinale des enfants et des adolescents en France: résultats des enquêtes menées en milieu scolaire, 2001–2004. *Bull Epidemiol Hebd* 2007; n°6: 45–49.
8. Denis F, Abitbol V, Aufrere A. Évolution des stratégies vaccinales et couverture vaccinale contre l'hépatite B en France, pays de faible endémie. *Med Mal Infect* 2004; 34: 149–158.
9. Ministère de la santé. Mission d'expertise sur la politique de vaccination contre l'hépatite B en France. Available at: http://www.ladocumentationfrancaise.fr/rapports-publics/024000604/index.shtml [assessed January 14, 2014].
10. Ascherio A, Zhang SM, Hernan MA, *et al.* Hepatitis B vaccination and the risk of multiple sclerosis. *N Engl J Med* 2001; 344: 327–332.
11. Hernan MA, Jick SS, Olek MJ, Jick H. Recombinant hepatitis B vaccine and the risk of multiple sclerosis: a prospective study. *Neurology* 2004; 63: 838–842.
12. Prévention de l'hépatite B auprès des personnes les plus exposées. Collection INPES "Repères pour votre pratique". Available at: http://www.inpes.sante.fr/CFESBases/catalogue/pdf/931.pdf [accessed January 18, 2014].
13. Julious SA. *Sample Sizes for Clinical Trials*. Boca Raton: CRC Press, 2009.
14. Yelland LN, Salter AB, Ryan P. Performance of the modified Poisson regression approach for estimating relative risks from clustered prospective data. *Am J Epidemiol* 2011; 174: 984–992.
15. Zou G. A modified Poisson regression approach to prospective studies with binary data. *Am J Epidemiol* 2004; 159: 702–706.
16. Royston P, Ambler G, Sauerbrei W. The use of fractional polynomials to model continuous risk variables in epidemiology. *Int J Epidemiol* 1999; 28: 964–974.
17. Gunn RA, Lee MA, Murray PJ, Gilchick RA, Margolis HS. Hepatitis B vaccination of men who have sex with men attending an urban STD clinic: impact of an ongoing vaccination program, 1998–2003. *Sex Transm Dis* 2007; 34: 663–668.
18. van Steenbergen JE. Results of an enhanced-outreach programme of hepatitis B vaccination in the Netherlands (1998–2000) among men who have sex with men, hard drug users, sex workers and heterosexual persons with multiple partners. *J Hepatol* 2002; 37: 507–513.
19. Hollmeyer H, Hayden F, Mounts A, Buchholz U. Review: interventions to increase influenza vaccination among healthcare workers in hospitals. *Influenza Other Respir Viruses* 2013; 7: 604–21.
20. Heron L, Selnikova O, Moiseieva A, *et al.* Immunogenicity, reactogenicity and safety of two-dose versus three-dose (standard care) hepatitis B immunisation of healthy adolescents aged 11–15 years: a randomised controlled trial. *Vaccine* 2007; 25: 2817–2822.

Appendix 1

ANRS French National Agency for Research on AIDS and Viral Hepatitis (ANRS) Formvac Study Group

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