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Compliance and immunogenicity of two hepatitis B vaccination schedules in sex workers in Belgium

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Abstract

Objectives: To compare the coverage for the third dose and the compliance to two hepatitis B vaccination schedules: 0,1,4 versus 0,1,6 months, in commercial sex workers (CSW) in Belgium; to compare the immunogenicity of the actually administered schedules.
Methods: In seven health centres in Belgium, hepatitis B vaccination was offered free of charge to CSW. In a randomised, prospective study a commercialised hepatitis B vaccine (Engerix-B™ 20 mcgr) was offered according to one of both schedules. After complete vaccination, bleeding was performed to assess immunogenicity.
Results: Between June 2003 and September 2004, 615 non-immune CSW were enrolled, of whom 52% in the 0,1,4 month schedule ($n = 322$). Coverage of the third dose was 57% overall, 59% (0,1,4) and 54% (0,1,6), respectively. Age, the health centre and drug use significantly influenced the compliance and the coverage of dose 3, whereas the planned vaccination did not.

When comparing the immunogenicity results as a function of the actually administered vaccination schedule, immune responses did not significantly differ between CSW receiving the third dose 4–6 months and those receiving it at least 6 months after the first dose. In total, 19 persons (8%) were not protected after a full vaccination course (anti-HBs <10 IU/L). Two health centres measured markedly lower anti-HBs levels.
Conclusions: In this highly mobile at-risk population, a 0,1,4 month schedule is more easy to offer and confers equal protection within a shorter period of time. We therefore propose this 0,1,4 month schedule to vaccinate CSW in the future.

Keywords: Hepatitis B vaccination; Schedule; Sex worker; Outreach programme; Effectiveness

1. Introduction

Sex workers are at risk of sexually transmitted infections (STI) [1]. For some years, outreach programmes in several Belgian cities have shown to improve access to healthcare and to reduce STI in commercial sex workers (CSW) [2–4]. The aim of these outreach programmes is to provide job-specific health and social services, tailor-cut to the needs of the CSW: they check and treat STI among CSW, set up STI prevention programmes and evaluate the feasibility of these programmes, amongst which the hepatitis B vaccination programme [5]. Between September 1999 and March 2003, 64% of all non-immune sex workers seen at Gh@pro (Health House for Antwerp Prostitutes, Antwerp,

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Belgium) completed a three-dose vaccination course (0,1,6 month schedule) and 44% were tested for post-vaccination response [6]. Existing guidelines for hepatitis B vaccination, set in 1999 by the Medical Society for the Study of Venereal Disease (MSSVD) and last updated in 2005 by the British Association for Sexual Health and HIV (BASHH), recommend that non-immune persons at continuing risk for hepatitis B are offered hepatitis B vaccination, and that >50% of them complete the vaccination course and be tested for post-vaccination response [7,8].

Completing a hepatitis B vaccination course in high-risk groups such as CSW is often very difficult [9–11]. The reason is mostly the high mobility, illegal status, cost of the vaccine, lack of awareness of the importance of hepatitis B transmission in their profession, and the limited possibility to consult the regular healthcare services. The most frequently used vaccination schedules in adolescents and adults are the standard 0,1,6 months, the accelerated 0,1,2 months and the super-accelerated 0,7,21 days, with the latter two requiring the administration of a fourth dose at month 12 to complete the vaccination course [12,13]. The Centers for Disease Control and Prevention (CDC) recommends a minimum interval between the first two doses of 4 weeks and between the first and last injection no less than 16 weeks [14]. According to these criteria, a schedule offering the vaccine at months 0, 1 and 4 could be presented as a feasible alternative and the shortest three-dose schedule possible, without endangering the expected long-term immunogenicity. Experiences in CSW, in prisons, in healthy adult volunteers in the US, in patients of a genitourinary medicine clinic in London, and in high-risk youth in Australia have shown that a rapid schedule over a 3-week period (0, 7 and 21 days) generates better compliance compared to longer schedules [15–18]. However, independently of an eventual risk of hepatitis B infection before completion of the vaccination schedule, no long-term protection can be expected as long as a fourth dose at day 360 is not administered [8,19].

This study was set up to compare the coverage for the third dose and the compliance to two hepatitis B vaccination schedules: 0,1,4 versus 0,1,6 months, under field conditions in commercial sex workers (CSW) in Belgium. Additionally, this study aimed to compare the immunogenicity of the actually administered schedules.

2. Methods

2.1. Setting

The study was performed in seven different health centres for CSW: Gh@pro (Antwerp), Pasop (Ghent), Espace P (Brussels, Charleroi, Liège and Namur) and Icar (Liège). CSW, men and women, were approached in or nearby their working places. Outreachers informed and tried to motivate CSW to participate in the programme. At first consult, information on STI and risk behaviour was provided and the CSW were screened amongst others for HBV markers (HBsAg, anti-HBs and anti-HBc). Furthermore, they were interviewed about their practices regarding the risks for STI in their profession, and if desired or indicated further clinical examinations (e.g. gynaecological) were performed. Those negative for HBV were offered hepatitis B vaccines. In these health settings vaccinations, screening, clinical examinations and consultations are offered free of charge. Administrative and clinical records of CSW are kept strictly confidential.

2.2. Study

The study started 1 July 2003 and inclusions ended 30 September 2004. To maintain the anonymity of the CSW, for reasons of language and illiteracy problems, and in view of the use of a commercially available vaccine, oral informed consent was obtained from all participants. The study, including this oral consent procedure, was approved on 16 June 2003 by the Ethics Committee of the Antwerp University Hospital (UZA).

The main objective of the study was to assess and compare immunogenicity and feasibility (coverage of dose three and compliance to the planned schedule) of hepatitis B vaccination in CSW for two different vaccination schedules: 0,1,4 months against 0,1,6 months. For this purpose, third dose coverage was defined as the proportion of subjects who received three doses of vaccine, irrespective of the schedule followed, and compliance to the planned vaccination schedule was defined as the proportion of subjects receiving three vaccine doses within all predefined time intervals according to their planned schedule (either 0,1,4 or 0,1,6). All CSW were randomised based on their administrative number in the health centre, with odd numbers foreseen to receive the 0,1,4 month schedule, and even numbers to receive the 0,1,6 month schedule. In two health centres, for sake of workload and organizational aspects, CSW in far-off outreach activities were randomised per setting, i.e. per bar or private house. Those who did not consent to participate in this study received the hepatitis B vaccines according to the standard schedule at the health houses, i.e. a 0,1,6 month course.

Pre- and post-vaccination testing was performed at the respective peripheral laboratories with commercially available laboratory tests, as described in Table 1. CSW were first screened and those without serological evidence of past HBV infection or immunization were offered vaccination through the regular service of the health centres. Intervals between first and second vaccination had to be between 28 and 42 days; between second and third vaccination 80–110 days (0,1,4) or 140–170 days (0,1,6). Vaccinations were administered by intramuscular injection (M. Deltoideus). The vaccine used was Engerix-B® vaccine, containing 20 mcg recombinant HBsAg per dose (GlaxoSmithKline Biologicals, Rixensart, Belgium). A blood sample was taken to assess the anti-HBs response, 14–90 days after the third injection.

All CSW were routinely, and outside the objectives of this vaccination study, also tested for HIV and syphilis.

Table 1
Tests used for screening for different hepatitis B markers

Centre	Anti-HBs	Anti-HBc	HBsAg
1	AUSAB AxSYM Abbott Laboratories (IL, USA)	Elecsys Roche Diagnostics (Basle, Switzerland)	AxSYM Abbott Laboratories (IL, USA)
2, 3, 5, 7	AUSAB AxSYM Abbott Laboratories (IL, USA)	CORE AxSYM Abbott Laboratories (IL, USA)	HBSAG PRISM Abbott Laboratories (IL, USA)
4	AHB Immulite 2000 DPC (LA, USA)	ABC Immulite 2000 DPC (LA, USA)	HBS Immulite 2000 DPC (LA, USA)
6	AUSAB AxSYM Abbott Laboratories (IL, USA)	CORE AxSYM Abbott Laboratories (IL, USA)	Elecsys Roche Diagnostics (Basle, Switzerland)

Nationality, working sector and birthday were noted as independent variables. In all but two centres, CSW were invited to participate in a structured interview on their current smoking behaviour, alcohol consumption, IV and non-IV drug use and on their medical history. However, lack of willingness, lack of time, and language barriers interfered with the participation rate to these interviews.

2.3. Analysis plan

Statistical analysis was performed with SPSS 11.5 (SPSS Inc., Chicago, IL, USA). Pearson χ^2 and Fisher's Exact test were used to compare the independent variables between both groups (as such evaluating the randomisation). Associations between independent variables and different outcome variables (third dose coverage, compliance to the planned schedule, and immunogenicity) were studied using univariate and multivariate logistic regression (results shown as odds ratios (OR) and their 95% confidence intervals).

Seroprotection was defined as an anti-HBs titre $\geq$10 IU/L, measured 14–90 days after the third vaccination. The different laboratories determined anti-HBs concentrations until the category $\geq$1000 IU/L (in one centre $\geq$2000 IU/L) without further detailed titrations, which rends calculation of geometric mean concentrations (GMC) impossible. Therefore, we also looked at the distribution of individual antibody levels over categories <10 IU/L, 10–100 IU/L, 100–1000 IU/L and $\geq$1000 IU/L. All data available on 28 October 2005 were included.

3. Results

3.1. Study population

A total of 615 HBV-seronegative CSW were enrolled in this multicentre study, of whom 322 (52%) in the 0,1,4 month schedule and 293 (48%) in the 0,1,6 month schedule. Both groups were comparable for all characteristics, except for smoking (0,1,6 > 0,1,4; $p = 0.045$). The characteristics of the population are described in Table 2. Gender, region of origin, age, working sector and health centre are routinely noted for every CSW. HIV-status and syphilis are routinely tested together with HBV-serology, missing are the ones who did not accept those tests. Information on drug use, smoking, alcohol use and medical problems was gathered by a structured interview, taken from only 258 CSW (42%).

3.2. Coverage and compliance

By 28 October 2005, 348 CSW had received all three vaccines (third dose coverage: 57%). No significant difference was found between both groups, with third dose coverage being 59% (0,1,4) and 54% (0,1,6), respectively ($p = 0.22$).

Of these CSW receiving three doses, 140 (40%) were compliant to the schedule as planned and 208 (60%) did not adhere to the planned schedule. The compliance of 42% (0,1,4) and 38% (0,1,6) was not significantly different between both groups ($p = 0.21$), as shown in Fig. 1.

Third dose coverage and compliance to the planned vaccination schedule in those receiving three doses by health centre are shown in Table 3.

3.3. Coverage of the third dose

In univariate logistic regression, four factors were found to significantly influence coverage: previous or active syphilis infection (FTA/TPHA $\geq$ 50), age group, intravenous drug use and the health centre. Persons, who ever had a syphilis infection, had a better coverage (OR = 2.87; 95% CI 1.05–7.83). The youngest age group (<21 years) was performing significantly worse than all older groups (OR between 1.86 and 3.57). Using IV drugs was a negative factor for the coverage (OR = 0.21 compared to non-drug users; 95% CI 0.09–0.52). Four health centres are performing significantly worse than the centre used as comparator (OR between 0.17 and 0.49).

In a backward stepwise multiple logistic regression analysis including health centre, schedule, age category and syphilis screening result, the final model had age category and health centre as significantly influencing factors on the coverage of the third vaccine dose; schedule was also included in the final model, being the main topic under study (Table 4). All age categories have significantly higher coverage than CSW <21 years of age (OR between 1.77 and 4.12). Four health centres perform significantly worse than the centre used as comparator (OR from 0.19 to 0.44).

A second multiple logistic regression procedure also included drug use; however, the low number of interview

Table 2
Characteristics of the population

Independent variables	Category	% (*n*)
Total		615
Schedule	0,1,4	52% (322)
	0,1,6	48% (293)
Gender	**Female**	93% (574)
	Male	7% (41)
Region of origin	**Western Europe**[a]	56% (343)
	Latin-America[b]	4% (23)
	Asia[c]	2% (15)
	Eastern Europe[d]	15% (95)
	Sub-Saharan Africa[e]	15% (91)
	Northern Africa[f]	2% (11)
	Missing	6% (37)
Age category	**<21**	14% (84)
	21–25	35% (216)
	26–30	23% (141)
	31–40	21% (127)
	>40	7% (43)
	Missing	1% (4)
Working sector	**Street**	21% (127)
	Bar	18% (112)
	Window	31% (190)
	Private	26% (157)
	Missing	5% (29)
Health centre	**1**	45% (277)
	2	12% (73)
	3	6% (34)
	4	21% (129)
	5	10% (60)
	6	6% (37)
	7	1% (5)
HIV-status	**Negative**	97% (596)
	Positive	1% (7)
	Missing	2% (12)
Syphilis	**FTA <50**	95% (582)
	FTA 50–200	3% (18)
	FTA >200	1% (5)
	Missing	2% (10)
Drug use (current)	**None**	31% (192)
	Not IV	7% (40)
	IVDU	4% (25)
	Missing	58% (357)
Smoking (current)	**No**	15% (94)
	Yes	27% (164)
	Missing	58% (357)
Alcohol use (current)	**No**	21% (128)
	≤20 units/week	15% (95)
	>20 units/week	5% (33)

Bolds are the reference categories for the logistic regression analyses.
[a] Western Europe: Belgium, France, The Netherlands, Germany, Italy, Spain, Greece, Portugal, UK.
[b] Latin-America: Antilles, Brazil, Chile, Columbia, Cuba, Dominican Republic, Ecuador, Jamaica, Suriname.
[c] Asia: China, Iran, Jordan, Philippines, Thailand, Turkey.
[d] Eastern Europe: Albania, Belarus, Bulgaria, Hungary, Kosovo, Lithuania, Poland, Roumania, Russia, Serbia, Slovakia, Slovenia, Ukraina, Yugoslavia.
[e] Sub-Saharan Africa: Congo, Ghana, Liberia, Mauritius, Nigeria, Senegal, Sierra Leone, Sudan, Togo.
[f] Northern Africa: Algeria, Morocco.

responses resulted in the exclusion of half of the CSW due to missingness. In that analysis, drug use was not found to be significantly influencing the coverage.

3.4. Compliance to the planned vaccination schedule

In univariate logistic regression, drug use and health centre were significantly associated to the compliance: drug use (intravenous and not IV compared to no drug use) (OR between 0.16 and 0.38), and health centre 2 compared to centre 1 (OR = 0.33; 95% CI 0.15–0.71) had a significantly lower compliance. Moreover, persons older than 40 had a higher compliance than those under 21 (OR = 2.93; 95% CI 1.24–6.93). The schedule showed no significant influence.

The multivariate logistic regression analysis on the compliance included the same variables as for the coverage (Table 5). The same variables as in the univariate regression were significant.

When again the analysis was repeated including the variable drug use, for the subgroup of CSW who completed the structured interview, drug use markedly decreased the compliance (OR 0.29; 95% CI 0.11–0.71 for non-IV, and 0.21; 95% CI 0.04–1.10 for IV drug users). Unlike in the previous analysis, no significant effect of the age group could be demonstrated. Health centre 3 was shown to have a lower compliance compared to centre 1 (OR 0.21; 95% CI 0.06–0.77).

3.5. Schedule effect by health centre

We looked also with logistic regression whether the planned vaccination schedule (0,1,4 compared to 0,1,6) had a different effect on the third dose coverage or on the compliance in the centres performing worse than in the ones performing better. Both centres 1 and 6, reaching about 70% coverage with a 0,1,6 month schedule had no improvement with a 0,1,4 schedule (Fisher's exact test, $p > 0.999$). Health centres 2–5, with a lower coverage to the standard 0,1,6 schedule might have obtained a higher coverage with the shorter schedule: 47% for 0,1,4, compared to 38% for 0,1,6, even if we could not demonstrate a statistically significant difference (Fisher's exact test, $p = 0.10$).

As for the compliance, only centre 6 showed a significant improvement with a 0,1,4 schedule (85% for 0,1,4 and 17% for 0,1,6; $p = 0.001$), while the results in all other centres showed no differences (see Table 3).

3.6. Immunogenicity

Unlike for the coverage and compliance analyses, for the immunogenicity analyses the actually followed vaccination schedule was studied instead of the originally planned schedule. Two hundred and forty-six CSW were bled for anti-HBs testing after three vaccinations (42% of total included, but 71% of those who received three vaccine

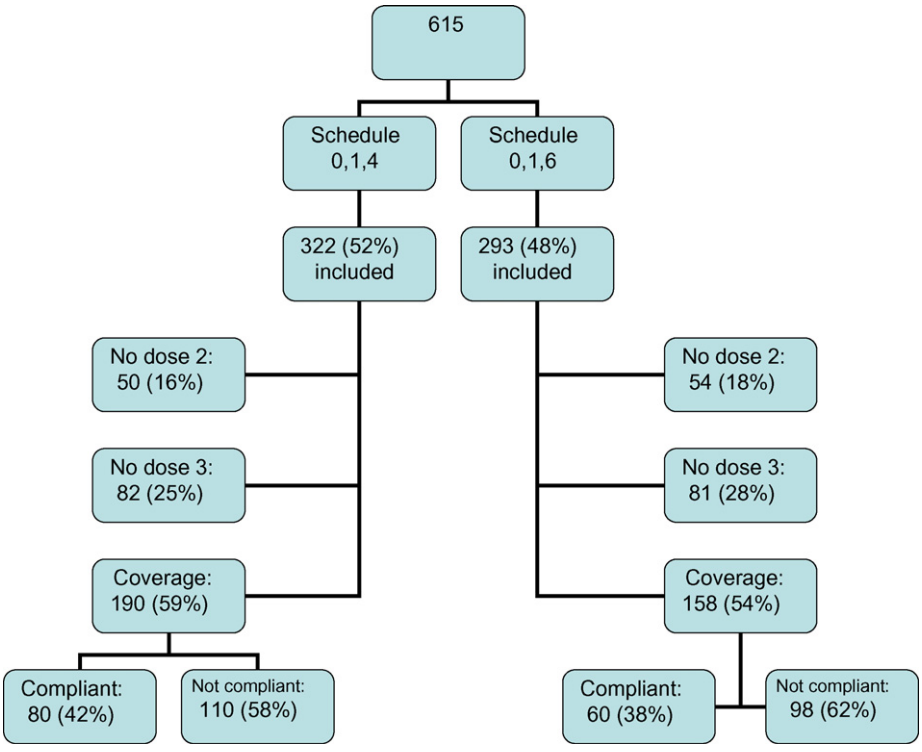

Fig. 1. Coverage of the third vaccine dose and compliance to planned vaccination schedules.

doses). Those vaccinated without the necessary interval of at least 4 months between first and third vaccination ($n = 5$) were excluded; another three did not have an anti-HBs result, leaving 238 valid results (Table 6).

Eight percent of persons vaccinated with an interval between first and third vaccine of at least 4 months did not develop an anti-HBs titre ≥10 IU/L. CSW receiving the third vaccination before month 6 were compared to those who received their third vaccination at month 6 or later (no upper limit). Either when including all available blood samples or when looking at subgroups having their blood sample taken 14–90 days after the last vaccine dose or more than 90 days (no upper limit) separately, no significant differences in anti-HBs distribution could be demonstrated between those completing their vaccination schedule within 4–6 months and those receiving their third dose at least 6 months after the first (Table 6).

The timing of the immune response measurement after vaccination is important. Blood tests performed more than 90 days after vaccination were shown to be significantly associated with lower anti-HBs measurements. When controlling for this effect, logistic regression analyses suggested that lower immunogenicity results were associated with centre 3 and centre 6 (as compared to centre 1). Smoking significantly reduced the probability to measure an anti-HBs level ≥1000 IU/L (OR 0.47; 95% CI 0.23–0.98). While the estimated OR for males (compared to females) and for increasing age (compared to those <21-year old) were suggestive for a negative effect on the immunogenicity, no significant associations could be demonstrated.

Table 3
Third dose coverage and compliance to the vaccination schedule in CSW receiving three doses, by health centre

Health centre	Coverage, *n* (%)			Compliance in three-dose recipients, *n* (%)		
	0,1,4	0,1,6	Total	0,1,4	0,1,6	Total
1	103/147 (70%)	91/130 (70%)	194/277 (70%)	44/103 (43%)	32/91 (35%)	76/194 (39%)
2	14/35 (40%)	7/38 (18%)	21/73 (29%)	4/14 (29%)	4/7 (57%)	8/21 (38%)
3	6/15 (40%)	6/19 (32%)	12/34 (35%)	2/6 (33%)	2/6 (33%)	4/12 (33%)
4	37/70 (53%)	32/59 (54%)	69/129 (54%)	14/37 (38%)	14/32 (44%)	28/69 (41%)
5	15/31 (48%)	10/29 (35%)	25/60 (42%)	4/15 (27%)	6/10 (60%)	10/25 (40%)
6	13/19 (68%)	12/18 (67%)	25/37 (68%)	**11/13 (85%)**	**2/12 (17%)**	**13/25 (52%)**
7	2/5 (40%)	NA	2/5 (40%)	1/2 (50%)	NA	1/2 (50%)
Total	190/322 (59%)	158/293 (54%)	348/615 (57%)	80/190 (42%)	60/158 (38%)	140/348 (40%)

Marked in bold: centre with significant difference between both schedules (Fisher exact test, $p = 0.001$). NA, not applicable (no subjects enrolled in this schedule).

Table 4
Multivariate logistic regression analysis on the coverage of the third dose

Variable	All CSW ($n=601$)[a]		CSW with interview ($n=253$)[b]	
	OR (95% CI)	p^*	OR (95% CI)	p^*
Schedule 0,1,4 (*0,1,6*)	1.26 (0.89–1.79)	0.190	1.23 (0.64–2.36)	0.526
Age <21 years				
Age 21–25 years	1.77 (1.02–3.07)	**0.044**	1.13 (0.38–3.33)	0.831
Age 26–30 years	2.53 (1.39–4.62)	**0.003**	3.10 (0.90–10.7)	0.074
Age 31–40 years	1.93 (1.05–3.55)	**0.035**	1.80 (0.59–5.44)	0.300
Age >40 years	4.12 (1.73–9.78)	**0.001**	3.01 (0.71–12.8)	0.135
Centre 1				
Centre 2	0.19 (0.10–0.35)	**<0.001**	NA	
Centre 3	0.22 (0.10–0.49)	**<0.001**	0.06 (0.02–0.17)	**<0.001**
Centre 4	0.44 (0.28–0.69)	**<0.001**	NA	
Centre 5	0.28 (0.15–0.50)	**<0.001**	0.10 (0.04–0.24)	**<0.001**
Centre 6	1.03 (0.48–2.24)	0.934	0.24 (0.09–0.63)	**0.004**
Centre 7	0.49 (0.06–3.74)	0.490	NA	>0.999
No drug use[c]				
Non-IV drug use			0.96 (0.33–2.88)	0.963
IV drug use			0.45 (0.15–1.34)	0.152

Italics are the reference categories. NA, not applicable (interview results not available for these centres).
[a] After excluding 14 records due to missing values for at least one of the variables.
[b] After excluding five records due to missing values for at least one of the variables.
[c] Only included in the second analysis.
[*] *p*-Values in bold mark significant associations.

Table 5
Multivariate logistic regression analysis on the compliance to the planned vaccination schedule

Variable	All CSW ($n=601$)[a]		CSW with interview ($n=253$)[b]	
	OR (95% CI)	p^*	OR (95% CI)	p^*
Schedule 0,1,4 (*0,1,6*)	1.24 (0.84–1.83)	0.289	1.46 (0.81–2.63)	0.208
Age <21 years				
Age 21–25 years	1.75 (0.88–3.49)	0.112	1.27 (0.47–3.45)	0.636
Age 26–30 years	1.79 (0.87–3.69)	0.114	1.27 (0.44–3.70)	0.657
Age 31–40 years	1.15 (0.53–2.48)	0.728	0.65 (0.22–1.91)	0.437
Age >40 years	3.02 (1.23–7.40)	**0.016**	0.84 (0.21–3.37)	0.800
Centre 1				
Centre 2	0.36 (0.16–0.79)	**0.012**	NA	
Centre 3	0.36 (0.12–1.09)	0.071	0.21 (0.06–0.77)	**0.018**
Centre 4	0.75 (0.45–1.24)	0.261	NA	
Centre 5	0.54 (0.26–1.13)	0.099	0.46 (0.19–1.11)	0.084
Centre 6	1.75 (0.82–3.70)	0.146	0.95 (0.42–2.13)	0.891
Centre 7	0.83 (0.09–7.86)	0.871	2.53 (0.10–64.5)	0.575
No drug use[c]				
Non-IV drug use			0.29 (0.11–0.71)	**0.007**
IV drug use			0.21 (0.04–1.10)	0.064

Italics are the reference categories. NA, not applicable (interview results not available for these centres).
[a] After excluding 14 records due to missing values for at least one of the variables.
[b] After excluding five records due to missing values for at least one of the variables.
[c] Only included in the second analysis.
[*] *p*-Values in bold mark significant associations.

4. Discussion

This study shows that the schedule of hepatitis B vaccination can be used in a flexible way: even if the 0,1,4 month schedule did not result in a significantly higher coverage or compliance in this study, it neither substantially reduced the immunogenicity. An earlier timing of the final dose completing the vaccination schedule offers earlier protection and might be beneficial for the coverage, as has been shown many times before, e.g. in an enhanced-outreach programme of hepatitis B vaccination in The Netherlands among high-risk groups (1998–2000) [20].

Table 6
Anti-HBs levels after HB vaccination in relation to the interval between first and third vaccination

V3–bs[a]	v1–v3[b]	Anti-HBs level				
		<10 IU/L, *n* (%)	10–100 IU/L, *n* (%)	100–1000 IU/L, *n* (%)	≥1000 IU/L, *n* (%)	Total, *n* (%)
14–90 days	4–6 months	10 (10%)	10 (10%)	23 (23%)	55 (56%)	98
	≥6 months	4 (4%)	7 (8%)	27 (29%)	54 (59%)	92
	Total	14 (7%)	17 (9%)	50 (26%)	109 (57%)	190
>90 days	4–6 months	2 (9%)	6 (26%)	9 (39%)	6 (26%)	23
	≥6 months	3 (12%)	3 (12%)	10 (40%)	9 (36%)	25
	Total	5 (10%)	9 (19%)	19 (40%)	15 (31%)	48
Overall	4–6 months	12 (10%)	16 (13%)	32 (26%)	61 (50%)	121
	≥6 months	7 (6%)	10 (9%)	37 (32%)	63 (54%)	117
	Total	19 (8%)	26 (11%)	69 (29%)	124 (52%)	238

[a] v3–bs, interval between third vaccine dose and blood sampling for anti-HBs measurement.
[b] v1–v3, interval between first and third vaccine dose.

Two factors influencing the third dose coverage were recognised: age group and the health centre. Persons younger than 21-year old had less good coverage than older ones. This might be explained by the fact that older CSW were often longer and more stable in the business than younger ones who could be more temporary working in sex work.

For the compliance, age, health centre and drug use showed significant associations. Both IV and non-IV drugs were negatively influencing. There could be a bias on this response, because in many places it is forbidden to use drugs, what makes that people are lying on this issue. People who inject drugs could mostly be identified correctly by the medical staff.

The health centre in which they were reached was a very important factor in the coverage and compliance. This illustrates the importance of the management and involvement of the health centre, the financial means obtained by these centres and the way how preventive medical activities fit in the daily practice of such health centres [21]. Very important is active outreach, with peer-educators who go to find CSW actively and have contact with them on their working places. The health centres need to be very easily accessible to have a good coverage of CSW. A mobile team of doctor and nurse that can perform the vaccination on the spot, without expecting the CSW to come to the health centre, is the best approach [22]. Another important argument might be the fact that the vaccination is given for free and also the consultation is free of charge [2].

In view of the differences between health centres, it was also studied whether third dose coverage and compliance to the planned schedule were different in the centres performing worse than in the ones performing better. Centres with a high coverage with a 0,1,6 schedule showed no improvement with a 0,1,4 schedule (70% for both schedules), whereas centres with a lower coverage to the standard schedule might have some benefit from using a shorter schedule. On the contrary we see no improvement in compliance with the 0,1,4 schedule in centres with low compliance, but there might be some positive effect for centres with higher compliance to the normal vaccination schedule.

It has to be kept in mind that this study was performed in a real-life setting, as such inducing a number of limitations. Each health centre kept using its standard laboratory procedures, which might influence the comparability of the immunogenicity results. Each centre also works slightly differently, which explains the relatively high degree of missingness in the data obtained by structured interview. Moreover, the benefits of the CSW always had highest priority, at times resulting in taking advantage of a chance to vaccinate, even if the timing would deviate from what the study protocol prescribed.

We found 8% non-responders after complete vaccination course. Of non-immune CSW 59% could be fully vaccinated in the 0,1,4 month group, of whom 90% had a protective immunological response, compared to 54% fully vaccinated with the 0,1,6 month schedule with a 94% protection rate. By multiplication of compliance and seroprotection results, in this population of CSW in Belgium, 53% in the 0,1,4 group has been successfully vaccinated compared to 51% in the 0,1,6 group. According to the BASHH guidelines, these both are acceptable results [8]. The difference is not significant, but each single case to whom a shorter schedule could be offered, is easier to administer the vaccine and to follow up.

Considering the immunogenicity, there are no factors significantly influencing the seroprotection rates. While this study showed some indications of the negative effect of smoking, male gender and older age on the immune response to hepatitis B vaccination, the health centre was the most important factor. Whether this was due to the centre's population and/or its working (including laboratory) methods, this clearly illustrates the diversity that has to be taken into account when working with a multicentric study design.

In conclusion, vaccination against hepatitis B with a 0,1,4 month schedule in CSW can more rapidly offer equivalent protective immunity to this very mobile high-risk population.

Vaccination courses for CSW can be offered very flexibly, as long as the minimum intervals of 4 weeks between first and second vaccine and of 16 weeks between first and third vaccine dose are respected.

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