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Development of immunity following financial incentives for hepatitis B vaccination among people who inject drugs: A randomized controlled trial

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ABSTRACT

Background: People who inject drugs (PWID) are at risk of hepatitis B virus (HBV) but have low rates of vaccination completion. The provision of modest financial incentives increases vaccination schedule completion, but their association with serological protection has yet to be determined.
Objective: To investigate factors associated with vaccine-induced immunity among a sample of PWID randomly allocated to receive AUD$30 cash following receipt of doses two and three ('incentive condition') or standard care ('control condition') using an accelerated 3-dose (0,7,21 days) HBV vaccination schedule.
Study design: A randomised controlled trial among PWID attending two inner-city health services and a field site in Sydney, Australia, assessing vaccine-induced immunity measured by hepatitis B surface antibodies (HBsAb $\geq$ 10 mIU/ml) at 12 weeks. The cost of the financial incentives and the provision of the vaccine program are also reported.
Results: Just over three-quarters of participants – 107/139 (77%) – completed the vaccination schedule and 79/139 (57%) were HBsAb $\geq$ 10 mIU/ml at 12 weeks. Vaccine series completion was the only variable significantly associated with vaccine-induced immunity in univariate analysis (62% vs 41%, $p < 0.035$) but was not significant in multivariate analysis. There was no statistically discernible association between group allocation and series completion (62% vs 53%). The mean costs were AUD$150.5, (95% confidence interval [CI]: 142.7–158.3) and AUD$76.9 (95% CI: 72.6–81.3) for the intervention and control groups respectively.
Conclusion: Despite increasing HBV vaccination completion, provision of financial incentives was not associated with enhanced serological protection. Further research into factors which affect response rates and the optimal vaccination regimen and incentive schemes for this population are needed.

Abbreviations: PWID, people who inject drugs; HBV, hepatitis B virus; HCV, hepatitis C virus; HbsAg, hepatitis B surface antigen; HBcAb, hepatitis B core antibody; HBsAb, hepatitis B surfaceantibody; IU/ml, international unit per milliliter; RNA, ribonucleic acid; HIV, human immunodeficiency virus; OST, opioid substitution treatment; HAVIT, the hepatitis acceptability and vaccine incentives trial; CI, confidence interval; IQR, inter quartile range; $AUD, Australian dollars; ICER, incremental cost effectiveness ratio; NHMRC, National Health and Medical Research Council.

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1. Background

Viral hepatitis causes liver-related disease. Globally, it is estimated that approximately 10 million people who inject drugs (PWID) are infected with the hepatitis C virus (HCV) [1]. PWID also experience higher rates of hepatitis B virus (HBV) infection [2], compounding the risk of liver disease [3]. Although a safe, effective HBV vaccine has been available for three decades, PWID typically have a low prevalence of vaccine-induced immunity [2].

In Australia, injecting drug use is among the leading known exposure for newly acquired HBV infection [4]. Universal infant vaccination was introduced in Australia in 2000, accompanied by an adolescent catch-up program that reached about half its target [5]. Several decades are therefore required before universally high levels of immunity among adults are achieved [6], thus PWID will remain at risk of infection for some time. Given the challenges associated with establishing and maintaining contact with PWID, various strategies for increasing vaccine uptake and completion have been recommended and endorsed by the World Health Organization [7]. Strategies include the provision of the first vaccine dose prior to serological confirmation of susceptibility [8,9] and the use of accelerated (0,7,21 days) schedules [10–13] to improve vaccination adherence [14]. Nonetheless, vaccination completion rates remain suboptimal even where these strategies have been employed [15].

The long term cost-effectiveness of offering HBV vaccination in the absence of incentive payments has been demonstrated [16]. Contingency management, also referred to as conditional cash transfers [17], uses behavioral principles through the provision of providing immediate monetary-based incentives in order to achieve a set of behaviors [18]. We have shown that the use of modest financial incentives increased vaccination schedule completion rates by 21% among PWID when compared to standard care (87% vs 66%) [19]; a result recently replicated by others, albeit with less striking completion rates (45–49%) [20]. To date there have been no studies assessing the impact of contingency management on serological evidence of immunity.

2. Objectives

We aimed to determine: (i) factors associated with serological evidence of HBV vaccine-induced immunity among PWID and (ii) the short-term cost-effectiveness of achieving vaccine-induced immunity associated with the use of financial incentives to bolster vaccination rates.

3. Study design

The methods have been reported elsewhere [19]. Briefly, participants were recruited through two inner-city low-threshold health services that target PWID [21,22] and a prospective observational study of HCV-negative PWID conducted in outreach settings from October 2008 to December 2010 [23]. Eligible participants were: aged $\geq$16 years; injected drugs in the preceding six months; reported no previous HBV infection and $\leq$1 previous HBV vaccination dose or unknown infection and vaccination status; able to provide informed consent; willing to be randomized and undertake vaccination; and to attend follow-up 12 weeks post-randomization. Exclusion criteria were: evidence of natural or vaccine-induced immunity; previous exposure or 2+ vaccination doses based on self-report and clinical records; mental or physical illness or disability likely to impact capacity to complete study procedures; insufficient English language skills, HIV infection and refusal to undertake vaccination. All participants provided written informed consent. The study was approved by the relevant Local Health Districts Human Research Ethics Committees.

4. Randomization

Randomization methodology development and access was restricted to the study biostatistician. The randomization scheme was developed using the SAS (version 9.1) pseudo-random number generator function. Following enrollment, research assistants randomized participants 1:1 to either the control or intervention arms according to allocations contained in pre-prepared sealed envelopes and concealed both from them, and participants, prior to opening (Fig. 1).

Of the 139 participants screened eligible, 74 were randomized to the control condition and 65 to the incentive condition [19]. Potential imbalances between control and incentive conditions respectively was noted for age (31.4 [SD 8.2, range 20–59] vs 34.6 [SD 8.3, range 20–56] years), current opioid substitution treatment (40% vs 26%) and current psychiatric medication (28% vs 43%) [19].

5. Study procedures

Engerix®-B 20 mcg (1 ml; GlaxoSmithKline) was injected into the deltoid muscle at 0, 7 and 21 days; all participants were advised to receive a booster at 12 months. Pre-test discussion and the first dose of vaccine were provided at enrollment. HBV core antibody (HBcAb) and HBsAb (and HBV surface antigen [HBsAg] where clinically indicated) were assessed at baseline; and HBsAb and HBsAg again at 12 weeks. Seroconversion was defined as HBsAb $\geq$ 10 mIU/ml. Baseline independent variables were: anti-HCV status, HCV RNA, gender, Aboriginal/Torres Strait Islander identity, daily+ injecting in preceding month, current opioid substitution treatment (OST), alcohol consumption (6+ standard drinks $\geq$ weekly in preceding 12 months), current prescribed psychiatric medication/s, age and duration of injecting (reported as years and divided into tertiles). Other variables included vaccination series completion and vaccination series completion within scheduled time ($\pm$7 days). The difference in time from visit one to visit four was measured in days.

Following administration of the first dose, potential participants were consented and randomized prior to completing the baseline survey. All participants were renumerated with a $20AUD shopping voucher and reminded to return seven days later for test results.

Participants serologically confirmed as susceptible to HBV infection received their second vaccine dose at visit 2. Participants allocated to the incentive arm who undertook visits 2 and 3 within $\pm$7 days of the scheduled visit received $30AUD cash.

Participants received $30AUD cash upon completion of the 12 weeks follow-up (visit 4). Eighty-seven percent (121/139) of eligible participants were followed up at 12 weeks.

6. Costs

All costs are reported in 2010 Australian dollars ($AUD). Costs included were those relevant to the healthcare provider: cost of the staff time, equipment, vaccine, incentive payments, time for pre- and post-test discussion, and record keeping. Two sites provided client reminders, thus associated staff costs were included. The time cost of administering the incentive payment was included, but neither direct research time nor research payments for both groups' baseline and follow-up interviews were included. The vaccine cost was $12AUD (2010) per dose. Staff time was costed using New South Wales State Awards for the mid-level range of staff employed [24].