Impact of conditional cash transfers on hepatitis B vaccination completion in people who inject drugs: The Hepatitis B Acceptability and Vaccination Incentives Trial (HAVIT)

Professor Lisa Maher on behalf of the HAVIT Study Group*

Kirby Institute for Infection and Immunity
University of New South Wales

* Lisa Maher, Ingrid van Beek, Carolyn Day, Libby Topp, Handan Wand, Marian Shanahan, Gregory Dore, Andrew Lloyd, Paul Haber, Craig Rodgers, John Kaldor, and Nick Walsh
Introduction: HBV among PWID

• Injecting drug use leading exposure category for newly acquired HBV infection in Australia

• Despite safe and effective vaccine, immunisation coverage remains low among people who inject drugs:
  ▪ 28-59% HBV exposed (HBcAb positive)
  ▪ 26-37% evidence of vaccine-induced immunity (HBsAb ≥ 10IU/mL, HBcAb negative)
  ▪ 14-46% susceptible

• Poor concordance between self-report and serological HBV status.
Introduction: HBV among PWID

- HBV added to universal infant schedule in 2000
- School-based catch up reaches ~ 50%
- Possible severe complications of infection in adulthood
- Indigenous Australians at increased risk
- Excess mortality in HBV/HCV co-infection
  - ~60% prevalence of anti-HCV among PWID

→ Ongoing need to increase immunisation coverage

- Lessons learned may enhance uptake and completion of other vaccines e.g. HCV.
Introduction: CCT

• Conditional cash transfer (CCT) or Contingency management (CM) approaches offer incentives in return for behavioural/public health outcomes (Pettifor, McCoy and Padian 2012 *Lancet* and Baird et al. 2012 *Lancet*)

• Significant effects of moderate magnitude among PWID
  ▪ NICE Clinical Guidelines 51 and 52

• In Australia, financial incentives are part of a national program designed to increase early childhood immunisation
  ▪ Maternity Immunisation Allowance: $AUD 258 in 2 parts to care-givers of children who are fully immunised.
Introduction: CCT

- Financial incentives may facilitate adherence to multi-dose vaccine schedules among PWID
  - Seal et al. 2003 *Drug and Alcohol Dependence* – completion rates of 69% for cash incentives vs 23% for enhanced outreach
  - Des Jarlais et al. 2001 *AmJPH* – 83% for on-site vaccination vs 31% for off-site with cash incentives + referrals + transport.
Aims

→ Aim: To assess the efficacy of conditional cash transfers relative to a standard of care control condition in increasing vaccine completion in PWID using an accelerated 3-dose schedule (0,7,21 days) and a randomised controlled design

→ **Primary endpoint**: Proportion of participants who complete the vaccine series

→ **Secondary endpoints**: Cost effectiveness, immune response (HBsAb ≥10mIU/ml at 12 weeks) and HBV-related knowledge.
Methods

• Recruitment through two inner-city HR-oriented PHCs and a community-based research site

• Inclusion criteria:
  ▪ 16 years and above
  ▪ Injected in last 6 months
  ▪ No previous infection and maximum one previous dose vaccine or unknown infection and vaccination status
  ▪ English language skills and willing to provide informed consent

• Exclusion criteria:
  • Serological evidence of natural or vaccine-conferred immunity
  • Two+ vaccination doses.
Methods

• Pre-test counselling and dose 1 as per standard care
• Baseline serological testing to confirm eligibility
• Consent, randomisation and baseline questionnaires (ACASI)
• Visit 2 (+7 days): eligible participants received Dose 2 plus $30 cash (incentive condition)
• Visit 3 (+14 days): Dose 3 plus $30 cash (incentive condition)
• 12 week follow up serology and end-of-study interview.
Methods

**Figure 1**: Flow diagram of the Hepatitis Acceptability and Vaccine Incentives Trial

- **Enrollment**
  - Assessed for eligibility (n=442)
  - Excluded (n=239)
    - Previously vaccinated (n=142)
    - Previously infected (n=51)
    - Declined to participate (n=32)
    - Other reasons (n=3)

- **Randomized (n=201)**
  - **Allocation**
    - Standard of Care arm
      - Received dose 1 (n=97)
      - Ineligible (n=62)
        - Previous vaccination (n=29)
        - Past infection (n=32)
        - Current infection (n=1)
    - Eligible (n=65)
      - Received dose 2 (n=51)
        - In window period (n=38)
        - Did not attend (n=14)
      - Received dose 3 (n=43)
        - In window period (n=33)
        - Did not attend (n=22)
    - Attend (n=55)
      - Did not attend (n=9)

  - Incentive arm
    - Received dose 1 (n=104)
    - Eligible (n=74)
      - Received dose 2 (n=68)
        - In window period (n=65)
        - Did not attend (n=8)
      - Visit 3
        - Received dose 3 (n=64)
          - In window period (n=60)
          - Did not attend (n=10)

- **End of treatment visit**
  - Attended (n=66)
    - Did not attend (n=8)

- **Analysis**
  - Included in primary analysis (n=65)
  - Excluded from analysis (n=9)

  - Included in primary analysis (n=74)
  - Excluded from analysis (n=2)
Methods

• Comparison % participants in each condition who completed the three dose series

• Intention to treat (ITT) analyses:
  ▪ Included all participants enrolled and confirmed eligible (N=139)

• Per protocol (PP) analyses:
  ▪ Only participants who received all three doses (N=107)
  ▪ Comparison % participants who completed according to schedule (i.e. doses 2 and 3 ±7 days of scheduled visit)
  ▪ PP analysis considers effect of incentive on series schedule (whether doses are received on time).
## Results: Baseline sample characteristics

<table>
<thead>
<tr>
<th></th>
<th>Total (N=139)</th>
<th>Incentive (N=74)</th>
<th>Control (N=65)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>33.1</td>
<td>34.6</td>
<td>31.4</td>
</tr>
<tr>
<td>Male (%)</td>
<td>77</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ATSI (%)</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unstable accomm (%)</td>
<td>37</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Government benefit (%)</td>
<td>86</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Literacy problems (%)</td>
<td>12</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current psych meds (%)</td>
<td>59</td>
<td>66</td>
<td>51</td>
</tr>
<tr>
<td>Median years inject</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily+ inject (%)</td>
<td>45</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heroin preferred (%)</td>
<td>47</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dependent main drug (%)</td>
<td>71</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current OST (%)</td>
<td>32</td>
<td>26</td>
<td>40</td>
</tr>
</tbody>
</table>
## Results: ITT and PP

<table>
<thead>
<tr>
<th></th>
<th>Incentive (%)</th>
<th>Control (%)</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intention to treat (N=139)</td>
<td>87</td>
<td>66</td>
<td>&lt;.01</td>
</tr>
<tr>
<td>Per protocol (N=107)</td>
<td>92</td>
<td>67</td>
<td>&lt;.01</td>
</tr>
</tbody>
</table>

- Both ITT and PP found a significantly higher proportion of participants allocated to the incentive condition completed the three dose series.
# Results: Correlates of completion

<table>
<thead>
<tr>
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<th>AOR</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocated to incentive condition</td>
<td>3.30 (1.28-8.49)</td>
<td>0.013</td>
</tr>
<tr>
<td>Duration of injecting (years) (thirtiles)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤7 (reference)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>8-14</td>
<td>2.73 (0.99-7.55)</td>
<td>0.052</td>
</tr>
<tr>
<td>15+</td>
<td>5.11 (1.45-7.99)</td>
<td>0.011</td>
</tr>
<tr>
<td>Aboriginal/Torres Strait Islander identity</td>
<td>0.15 (0.04-0.53)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

**NS**: Age, gender, recruitment site, unstable accommodation, main source of income government benefit, lifetime imprisonment, low literacy, frequency of injecting, dependence on main drug, recent public injecting, current OST, risky alcohol consumption, BTOM social functioning score, lifetime mental health dx, currently prescribed psychiatric medications
Results: Immune response

- Seroconversion defined as HBsAb $\geq 10$mIU/ml
- Overall 77/121 (64%) had anti-HBs $\geq 10$IU/ml at 12 weeks
- Of these 66 (86%) received 3 doses and 11 (14%) received <3
- Of those who received all 3 doses and completed the 12 week end of study visit, 66/100 or 66% had anti-HBs $\geq 10$IU/ml at 12 weeks
- GMT higher among those who completed the course: 27.72 (95% CI, 17.49,43.94) compared to those who received <3 doses - 16.12 (95% CI, 4.05,64.13).
Results: Immune response

• Interesting and unanswered questions remain:
  • RCTs comparing the efficacy of high immunogenicity HBV vaccines versus standard vaccines on immune response and HBV incidence in PWID
  • RCT comparing the efficacy of new adjuvant vaccines vs. standard HBV vaccine on immune response and HBV incidence among PWID
  • RCT comparing standard vs. accelerated regimen using new adjuvant vaccine
  • RCT comparing intramuscular versus intradermal administration of HBV vaccine among PWID.
Conclusions

• First RCT to directly compare incentives versus no incentives in increasing hepatitis B vaccine completion in PWID

• Results consistent with growing literature on CCT and CM among PWID

• Strength of results lies in their establishment of the efficacy of this approach in real world clinical settings.
Strengths

• RCT
• Primary endpoint (completion) clearly defined and precisely measured
• High retention (87%)
• Use of ACASI to minimise social desirability bias.
Limitations

• Efficacy may degrade over time - our goal was time limited so lack of sustained intervention effect ‘doesn’t matter’
• Design did not allow us to compare completion rates for the 12 month booster
• Practical realities of health services handling cash incentives.
Conclusions

• Findings suggest that the provision of modest financial incentives to PWID may be a realistic public health strategy with the potential to reduce if not eradicate incident infections in this group.

• Contingency management approaches, including conditional cash transfers, should underlie more widespread efforts to prevent vaccine-preventable infections in this population.
Acknowledgements

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