Preparedness for candidate HCV vaccine trials in people who inject drugs: Challenges and opportunities

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Candidate HCV Vaccine Trials: Challenges & Opportunities

Background

- 202,400 Australians living with chronic HCV infection; 45,400 with moderate-severe liver disease
- 10,000 new HCV infections pa, mainly PWID
- Low uptake of antiviral Rx among PWID due to:
  - Poor access
  - Distrust of medical community
  - Competing priorities
  - Stigma and discrimination
- At least 11 prophylactic and 7 immunotherapeutic candidates identified and first prophylactic vaccines entering Phase II trials
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Background

- Collaborative, multidisciplinary initiative
- Affected communities, social scientists, epidemiologists, infectious disease clinicians, immunologists, virologists and hepatologists
- Molecules to populations
- Initial funding: 2007 UNSW Strategic Research Fund $2.9 million, 2009 NHMRC HIV/HCV Program Grant $17 million (Basic Science)
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Aims

- Establish a comprehensive community, epidemiological, clinical and laboratory framework to conduct Australian field trials of candidate HCV vaccines
- Develop a program for candidate vaccine evaluation
- Foster collaborative relationships with public and private sector biotech partners with candidate vaccines
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Elements in preparation for HCV vaccine field trials

- Community interest, acceptability and engagement
- Accurate estimates of HCV incidence and related risk factors
- Capacity to recruit and retain HCV uninfected PWID
- Complementary prevention strategies
- Understanding of protective immunity
- Understanding of virology
- Expertise in conduct of clinical trials
- Trial literacy in affected community
- Vaccine candidates
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Structure

Prospective cohorts:

- **Hepatitis C Incidence and Transmission Studies (HITS)**
  - Prison (HITS-p)
  - Community (HITS-c)
  - Incident cases (HITS-i)

Three integrated programsstreams:

- Social Epidemiology and Prevention
- Natural History and Clinical Trials
- Immunovirology
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1. Social Epidemiology and Prevention Studies (Maher)

- Consultations with community and other stakeholders
- Identify acceptability and willingness of PWID to participate in future vaccine trials
- Determine HCV incidence within the HITS-c cohort and socio-behavioural and demographic factors associated with incident HCV infection
- Identify factors associated with retention and adherence to study protocol
- Identify prevention strategies associated with reduced incidence of infection
Undertake epidemiological analyses within the combined HITS cohorts to further explore factors associated with incident HCV infection and retention.

Characterise the natural history of incident HCV infection, including viral clearance time course and predictive factors.

Conduct population-level modelling of the impact of HCV vaccines on HCV transmission.

Attract collaborative partners with candidate vaccines and prepare for early phase clinical trials.
3. Immunovirology (Lloyd)

- Define the prevalence and protective efficacy of anti-HCV immunity in seronegative subjects in the HITS cohorts
- Identify virological predictors of clearance in the HITS-i (Incident Case Cohort)
- Develop efficient assay systems to study viral escape from host immunity – both from naturally-occurring immunity and vaccine-induced immune responses
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Research plan – Relationship of cohorts

**Field sites**
- Screening + Baseline interview and blood sample analysis + 3 months follow-up interview and 6 months blood sample
- Rolling Sample

**Clinics**
- HITS-c Community based N=300 seronegative

**Prisons**
- HITS-p Prison based N=300 seronegative
- Rolling Sample

**Screening** + Baseline interview and blood sample analysis + 6 months interview and blood sample

**Scientific streams of study:**
1. Social epidemiology & prevention
2. Immunovirology
3. Natural history, incident infection & clinical trials
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**Study Streams**
- Baseline interview and blood sample analysis + Blood sample @ 2, 4, 8, 12, 24 wks
- Seroconversion
  - Anti-HCV+/Acute Infection
- Anti-HCV+/Acute Infection
- >12 wks option of anti-viral treatment
- Anti-viral treatment/ Clinical Trials e.g. ATAHC
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Challenges: Vaccine-preventable Infections

- Lack knowledge of social/cultural dimensions of vaccine access and demand in PWID
- Lessons learned HBV – poor uptake and completion due to:
  - lack of awareness
  - limited access to medical care/cost
  - poor rapport with and lack of trust in health care providers
  - competing health and social priorities
  - multi-dose series (Maher in press)

“...consistent and disturbing finding in reviewing the published work on vaccination in IDUs is that they are at high risk for vaccine-preventable infections, but generally have among the lowest immunization coverage rates” (Baral et al. 2007:672)

- Efficacy-effectiveness gap
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Challenges: Community Cohort Study

- Ethnographic mapping to identify sites and potential seeds
- Pilot test recruitment and retention strategies and procedures
- RDS – first study with biological criteria and longitudinal application
- Realistic timeline and resource needs for enrolment period and follow-up
- Logistical issues in relation to recruitment and retention
- Accurate estimates of incidence necessary to determine size and duration of clinical trials – cohort studies provide most accurate estimates
Challenges: Clinical Trials

- **Doab et al. PWID understanding of key CT concepts:**
  - Knowledge of concepts prior to the provision of verbal explanations poor among TN participants and reasonable among TE participants
  - Equipoise (66%), placebo (49%), comparison (46%), and randomisation (21%) - 3% understood double blinding
  - Better understanding in TE participants, those who injected more frequently, and those who primarily injected OST
  - Results highlight need to invest in building CT literacy

- **Formative research to assess community and individual interest in CTs (including motivations and barriers to participation)**

- **Ethical issues associated with trial literacy and informed consent**

- **Social research and community development under-resourced**
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Opportunities

- Capacity for effective and sustained community engagement
- Considerable time and resources needed to build relationships with local investigators and local communities, conduct formative research and establish trial infrastructure (human, physical and regulatory)

“... such efforts are critical to ensuring high-quality research and the ultimate value to the community of trial results. Investigators and donors establishing new research sites should work with the community create a sustainability plan that will allow a site to continue to perform research after a trial closes, to enable the community to reap long-term benefit” (IOM 2008).
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Conclusions

- In contrast to HIV, high HCV incidence in PWID in resource-rich settings provides opportunities to develop models of best practice for conducting prevention trials
  - Community engagement, dialogue, partnership
  - Improved ethical standards
  - Importance of understanding social, cultural and community drivers of risk and protective behaviours among PWID
  - Getting the right balance between the social and the biomedical
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