Author's response to reviews

Title: The ongoing impacts of hepatitis C infection: a systematic narrative review of the literature

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Version: 5 Date: 13 August 2012

Author's response to reviews: see over
Dear Editors

Thank you for allowing me to review this document. As requested, the final version of the manuscript now includes a box 3 as described in my previous response to Reviewer 1.

Regards

Dr Emma Miller

Title: The ongoing impacts of hepatitis C infection: a systematic narrative review of the literature

Version: 4 Date: 11 August 2012

Editor:

Many thanks for returning the revised version of your manuscript (above) in response to the referees’ comments. I am delighted to say we consider the referees’ criticisms satisfactorily addressed, and anticipate acceptance of your revised manuscript. However, our Editor wants you to include Box 3 as mentioned in your cover letter.

Box 3 now inserted on page 18, between the ‘Discussion’ and ‘Conclusion’:
Box 3: Bullet list of findings from the biomedical and social literature on the ongoing clinical and psychosocial impacts of diagnoses with hepatitis C infection

**Transmission**
- Strongly associated with injection drug use – likely to occur early in injecting career.
- Maternal transmission associated with hepatitis C viraemia – more frequent in maternal HIV co-infection.
- Prisoner populations at enhanced risk for infection.

**Natural history**
- Chronic infection can progress to fibrotic changes and development of liver cirrhosis, development of hepatocellular carcinoma (HCC) and increased liver-specific mortality
  - Complications of chronic infection predicted by persistent viraemia, moderate to high alcohol consumption and increasing age.
  - Liver cirrhosis and HCC occur in persistently low serum alanine amino transaminase (ALT), but frequency and rate of disease progression low relative to consistently high serum ALT.
- Hepatitis B co-infection associated with greater incidence of HCC and lower survival than mono-infection with either virus.
- HIV-HCV co-infection found to accelerate progression to AIDS, end stage liver disease and liver-related death (mostly due to HCC).

**Health related quality of life (QoL)**
- Relatively consistent evidence of reduced QoL in untreated hepatitis C in most populations.
- Variation among studies about the relative impact of a range of co-factors on QoL, although disease activity found to be independent of QoL.
- Interferon-based treatments associated with further reductions in health related QoL, with depression playing a significant role.
  - QoL improves post treatment – particularly if sustained viral responses achieved.
  - QoL benefits of successful treatment can be sustained over time (possibly the deleterious effects).

**Health outcomes after antiviral treatment or liver transplant**
- In most populations, including IDUs, sustained viral responses attained from 20% to 80% depending on viral genotype (types other than 1 and 4 considered the most favourable).
- Sustained viral response associated with lower incidence of complications (e.g. HCC and death).
- Hepatitis C associated with lower survival and reduced overall health and function in organ transplant patients.

**Psychosocial experience of living with hepatitis C infection**
- Diagnosis with hepatitis C reported to have profound impacts on social function.
- Perceived stigma led to high levels of anxiety and over-inflated assessments of transmission risks.
- Fatigue the most common symptom reported, followed by depression and other mental health issues, myalgia.
- Symptoms independent of disease activity or disease severity, but reported to be associated with depression, anxiety and other psychosocial factors but some biological mechanisms proposed.

**Responses to diagnosis and management of hepatitis C**
- Diagnosis with hepatitis C often reported to be a stressful event, potentially mediated by personal and social context.
- Perceived discrimination reported in multiple settings, including in interactions with health care services.
  - Potentially a barrier to health service access and treatment
- Fear of side effects reported as a major influence on treatment decisions.