Reviewer’s report

Title: Personality disorders do not influence the outcomes of chronic HCV infection treatment in Spanish prisoners. Perseo Study.

Version: 4 Date: 10 April 2015

Reviewer: Kathryn Snow

Reviewer’s report:

Major Compulsory Revisions

Methods: Exposure Ascertainment.

Additional detail should be included regarding the definition of "personality disorder". What is the sensitivity and specificity of the screening questionnaire that was used to ascertain personality disorder against a gold standard? What is the clinical significance of a positive result on this instrument? Has the instrument been validated in an incarcerated population? Who administered the test, and what was their level of expertise? Given the high prevalence of PD in the study sample as defined by the instrument, might there be issues with positive predictive value? Are there more rigorous estimates of the prevalence of diagnosed PD in Spanish prisoners which this estimate could be compared against?

A brief search returned the following article, which demonstrates the poor positive predictive value of the PDQ-4 against another instrument, the SCID-II - it appears that the PDQ-4 returns prevalence estimates for several personality disorders orders of magnitude higher than the SCID-II. Given that prisoners will necessarily satisfy some diagnostic criteria for some personality disorders (criminal justice involvement) and are very likely to satisfy others (risk taking behaviour), the validity of the prevalence estimate presented here is questionable, and it seems possible that substantial misclassification may have occurred. Possibly this could be addressed by repeating the analysis using a higher cut-off value on the instrument to indicate PD?


Given the high prevalence of PD and the small sample, was the study adequately powered to detect a clinically significant difference in treatment completion? Only 49 participants without PD were included as the comparator. Are there previous estimates of the impact of PD on SVR which might be used as indicators of the expected difference in outcome? If not, what about other mental illness?

Results: Outcome measures.

If PD was only assessed in 178 participants, then in my opinion all analyses
should be restricted to this sample. In the results section, discontinuation is calculated using the initial sample of 255 as the denominator, but then reasons for discontinuation are referred to as not differing between those with and without PD - presumably the 77 participants among whom PD could not be assessed were not included in this analysis? For simplicity, I would recommend excluding them from all analyses and mentioning them only in the Methods section.

Discussion: Explaining an Unexpected Result

The result presented is not one of non-inferiority, as the authors imply in their discussion - in fact, it indicates that participants without personality disorder were significantly more likely to discontinue treatment than those with PD. This is counter-intuitive, and in my opinion requires explanation.

For example, it may be the case that participants with PD have a greater frequency or intensity of contact with health services, which improves the management of adverse events during HCV treatment. It may also be the case that some participants with PD were already on psychiatric medication prior to HCV treatment initiation, which may have a protective effect with regard to psychiatric adverse events. In the absence of such an explanation, though, the result seems unlikely to reflect a genuine causal relationship, and this should be explored.

In addition to my concerns about the validity of the PDQ-4 instrument in this population, I would suggest assessing the affect of discontinuation due to early release or transfer on the results. If participants with personality disorder were less likely to be released early or transferred, either for reasons related to the PD or due to common causes (e.g. age and sex, which were not included in the multivariate model as potential confounders), this would cause biased attrition which may explain the unexpected result. Given that early release / transfer accounted for 35% of discontinuations, the impact of this may be substantial. If participants who discontinued due to early release or transfer are excluded from the analysis entirely, what is the result? Does the apparent association between PD and treatment completion persist? If the analysis is further restricted to participants with a measured SVR, what then?

Minor Essential Revisions

Introduction: It would be good to clearly state whether PD is a contraindication for HCV treatment in Spain or the Spanish prison system, or whether the exclusion of patients with PD from treatment is the result of case-by-case clinical assessment.

Results: The variety of outcome measures used is confusing, and requires further justification and explanation. Why was treatment outcome described using three different indicators (RVR, Early VR, End VR), and then analysed in the final model using discontinuation rather than completion or SVR? Are there reasons to believe that these five indicators would differ substantially between the exposure groups?
Discretionary Revisions

I would suggest proof-reading by a native English speaker, the style is somewhat informal and there are several unusual or inaccurate turns of phrase:

The abstract contains in inappropriate use of a contraction, "there weren’t differences in relation to SVR, genotype and HIV infection".

The introduction refers to "mentally ill patients end[ing] up in prison". Not all people living with mental illness are "patients", in fact many justice-involved people are not engaged with care for their mental illness.

Under study population "foreseen stay in prison" should be "expected stay in prison" or similar.

In results: "Those that were coinfected with HIV had significantly: a) more cases of IDU;" should be "higher prevalence of previous IDU" or similar.

"there were no significant differences between those mono and coinfected with HIV in terms of the viral RNA of the HCV" - unclear. Should this be "there were no significant differences in HCV viraemia between those with and without HIV co-infection"?

"However, the inclusion direct-acting antivirals (DAAS) that reduce treatment duration will also most likely reduce the frequency and severity of these discontinuations." A discontinuation cannot be "severe".

"the large number of prisoners and cases with PD treated (n=236 and n=129, respectively)" - this is unclear. "The large number of participants (n=236) and participants with diagnosed PD (n=129) treated". However I would not consider sample size as a strength of the study - the effective sample size was only 178, and the control group numbered only 49.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:

I declare that I have no competing interests.