Prevalence of HIV, hepatitis B, and hepatitis C in people with severe mental illness: a systematic review and meta-analysis

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Summary
Background Although people with serious mental illnesses have a high risk of contracting blood-borne viral infections, sexual health has largely been neglected by researchers and policy makers involved in mental health. Failure to address this shortcoming could increase morbidity and mortality as a result of undetected and untreated infection. We did a systematic review and meta-analysis to estimate the prevalence of blood-borne viral infection in people with serious mental illness.

Method We searched the Cochrane Library, Medline, Embase, PsycInfo, CINAHL, and DARE for studies of the prevalence of HIV, hepatitis B virus, and hepatitis C virus in people with serious mental illness, published between Jan 1, 1980, and Jan 1, 2015. We group prevalence data by region and by virus and estimated pooled prevalence. We did a sensitivity analysis of the effect of study quality on prevalence.

Findings After removal of duplicates, we found 373 abstracts, 91 of which met our eligibility criteria. The prevalences of blood-borne viral infections in people with serious mental illness were higher than in the general population in places with low prevalence of blood-borne viruses, such as the USA and Europe, and on par with the general population in regions with high prevalence of blood-borne viruses (Africa for HIV and southeast Asia for hepatitis B virus and hepatitis C virus). Pooled prevalence of HIV in people with serious mental illness in the USA was 6·0% (95% CI 4·3–8·3). Sensitivity analysis showed that quality scores did not significantly affect prevalence.

Interpretation People with serious mental illness are at risk of blood-borne viral infections. However, because of methodological limitations of the studies the prevalence might be overestimated. Serious mental illness is unlikely to be a sole risk factor and risk of blood-borne viral infection is probably multifactorial and associated with low socioeconomic status, drug and alcohol misuse, ethnic origin, and sex. Health providers should routinely discuss sexual health and risks for blood-borne viruses (including risks related to drug misuse) with people who have serious mental illness, as well as offering testing and treatment for those at risk.

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co-occurring substance misuse problems that can lead to sexual risks while intoxicated. Finally, people with serious mental illness who live in shared accommodation might share personal equipment (eg, razors, toothbrushes), which might increase the risk of hepatitis B and hepatitis C transmission.

In the UK, 93 000 men and 40 000 women are infected with HIV, and in 2013, there were 6000 new cases of HIV. In 2012, the incidence of hepatitis B in England was 1.4 cases per 100 000 people per year and prevalence was 0.1–0.5%. In 2009, the overall incidence of reported acute hepatitis B in the USA was 1.5 per 100 000 people per year and 800 000–1.4 million people in the USA have chronic hepatitis B virus infection. 786 000 people worldwide die from hepatitis B virus-related liver disease each year. About 3% of the world’s population are infected with hepatitis C virus, with about 4 million carriers in Europe alone and 214 000 in the UK. There were 17 000 new cases of hepatitis C in the USA in 2007, with 3.2 million people infected in total.

Although previous reviews of blood-borne infection in people with serious mental illness have been published, no systematic reviews have been done and the reviews rarely reported the rate of HIV, hepatitis B, and hepatitis C. We did a systematic review and meta-analysis of prevalence studies to understand the global prevalence of HIV, hepatitis B virus, and hepatitis C virus in people with serious mental illness.

Methods

Search strategy

Data collection
We systematically searched the scientific literature for observational cross-sectional studies that reported the seroprevalence of HIV, hepatitis B virus, or hepatitis C virus according to opt-in, opt-out, or anonymous unlinked blood or other bodily fluids research methods, in people aged older than 15 years, diagnosed with serious mental illness, and treated in a psychiatric setting. We excluded studies in which prevalence data were only obtained from case notes or only from self-report (not independently verified by testing). We did not include grey literature.

After removing duplicates, SB screened the titles and abstracts using the eligibility criteria, with independent verification by EH and FM. For studies deemed suitable, we obtained the full text and they were again scrutinised against the eligibility criteria by SB and FM. Reports about which there was uncertainty were discussed by FM and EH with SB until a consensus about eligibility was achieved. We extracted data from eligible full-text articles including...
study characteristics, study date, publication date, location, diagnostic criteria, demographics (age, sex, ethnicity), consent, consent rate, ethics approval, posttest treatment, sample size, testing procedure, and prevalence.

We used the Quality Assessment Tool for Systematic Reviews of Observational Studies to assess the quality of the data. This instrument is reliable compared with other quality assessment tools. We modified the tool and each report was scored as follows: whether participants were clearly defined as representing the serious mental illness population (yes=1, no=0); participation rate (response rate >60%=1, response rate ≤60% or not reported=0); whether investigators controlled for confounding (eg, stratification, matching, restriction, adjustment) when analysing associations controlled for confounding (eg, stratification, matching, restriction, adjustment) when analysing associations; and sample size restriction, adjustment) when analysing associations controlled for confounding (eg, stratification, matching, restriction, adjustment) when analysing associations. We did logistic regression to allow for the difficulties caused by

Data analysis
We did a meta-analysis to calculate combined estimates and 95% CIs for each continent separately. We did logistic regression to allow for the difficulties caused by proportions being unable to have values less than 0. We assumed random effects because there was clear clinical heterogeneity between the populations sampled. We did the calculations using Comprehensive Meta-Analysis 2. We transformed logits of estimated prevalence and their 95% CIs back to percentages. We prepared forest plots using Stata (version 12). We calculated relative weights for each continent, so that the weights for each continent sum to 100.

We did a sensitivity analysis relating to quality scores using Stata 13. The outcome variable was the logit-transformation of prevalence. We did two such analyses: one for all studies with quality score as a quantitative predictor, and one for all studies using quality score as a quantitative predictor and region as a qualitative predictor. The results are presented as odds ratio (OR) per unit increase in quality score with 95% CIs.

Results
Our literature search identified 373 reports, 169 of which were duplicates (figure 1). 41 publications were excluded because the full text was not available in English, followed by another 74 that were ineligible. With the addition of two papers from an updated search, we had 93 articles for quality assessment and meta-analysis.

44 studies assessed HIV infection (table 1), including a total of 21071 patients. The pooled prevalence of HIV was highest in Africa (19%, 95% CI 14–25) and it was 2% in Europe and 6% in the USA (tables 1, 2, figure 2). Few data were available from Europe, Central and South America, and Asia, and the prevalence of HIV was very poorly recorded in these regions. Only three studies were done in India, and only one study, done more than 20 years ago, was from Spain.

19 studies reported prevalence of hepatitis B virus, including a total of 8163 patients with serious mental illness tested for hepatitis B virus (table 3). The pooled prevalence of hepatitis B virus was 2.2% (95% CI 0.5–9.9) in North America, and 9.7% (95% CI 0.6–15.3) in Asia (table 2, figure 3). A study from Turkey reported 51% hepatitis B virus prevalence with 10% HBsAg positivity indicating active infection; the virus is highly prevalent in the general population of Turkey. A study from Taiwan reported an 18% prevalence of HBsAg, which is consistent with the general population: hepatitis B virus infection is endemic in Taiwan, with 80–90% of adults infected.
28 studies tested 14888 patients with serious mental illness for hepatitis C virus (tables 2, 4, figure 4). This set of participants was the largest of the three viral infections we investigated. The prevalence of hepatitis C in people with serious mental illness was greatest in Turkey, perhaps a result of the high prevalence in the general population, of whom roughly 1% are infected (2·7 million). In Asia, pooled hepatitis C virus prevalence was 4·4% (95% CI 2·8–6·9). However, these data are from large and diverse geographical areas including southeast Asia and Turkey. Most studies consisted of convenience samples of people recruited from a particular treatment setting, typically inpatient psychiatric care. Although all the studies included patients with serious mental illness, the proportions of specific diagnoses in each sample varied.

We assessed the effect of study quality on virus prevalence by meta-regression on quality score, for all studies combined and adjusting for geographical region. No analysis showed a significant effect of study quality on prevalence (table 5).

Most of the studies had additional data on risk factors for blood-borne viruses, such as intravenous drug use and sexual behaviour, to test associations with infection. The reporting and the nature of these risk factors varied widely. Information on risk factors was mainly extracted from routine clinical case notes as opposed to using a standardized risk tool. Because of the variability of data quality and reporting consistency, we could not calculate adjusted prevalence after controlling for these risk factors. However, three common factors seem to increase the likelihood of infection with a blood-borne virus: first, being black or from the USA gave a prevalence of 17·4% (95% CI 13·2–22·6), which is higher than in the general population, of whom roughly 1% are infected (2·7 million). In Asia, pooled hepatitis C virus prevalence was 4·4% (95% CI 2·8–6·9). However, these data are from large and diverse geographical areas including southeast Asia and Turkey. Most studies consisted of convenience samples of people recruited from a particular treatment setting, typically inpatient psychiatric care. Although all the studies included patients with serious mental illness, the proportions of specific diagnoses in each sample varied. We assessed the effect of study quality on virus prevalence by meta-regression on quality score, for all studies combined and adjusting for geographical region. No analysis showed a significant effect of study quality on prevalence (table 5).
and female; second, injecting drug use; and third, engaging in risky sexual behaviour, including not using a condom, having multiple partners, sex trading, and unprotected sex with a partner who is infected with a blood-borne virus.

**Discussion**

Our aim was to estimate the prevalence of blood-borne infection in people with serious mental illness. Most of the studies were of moderate to low quality, and based on convenience samples drawn from treatment settings rather than representative samples. This sampling method means that the prevalence reported was possibly overestimated. However, a study in Brazil, which used a representative sample drawn from the community as well as treatment settings, still showed that blood-borne infections are common in people with serious mental illness. The quality of defining the sample in terms of diagnoses of mental illness varied. Many studies used case note diagnoses rather than independently verified diagnoses made with gold standard diagnostic tools. Inpatient settings are likely to treat the most acutely ill people often with complex needs and a history of substance misuse.

The prevalences of blood-borne viruses in people with serious mental illness were consistently higher than in the general population in regions with a low prevalence of blood-borne viruses, such as North America and Europe, and on par with the general population in regions with high general prevalence such as Africa for HIV and southeast Asia for hepatitis B virus and hepatitis C virus. The estimated prevalence of HIV in people with serious mental illness in the USA was 6% (95% CI 4.3–8.3), which is considerably higher than the 0.6% of the general population of the USA who have HIV.

However, serious mental illness might not be an isolated risk factor for blood-borne virus infection, but might be better thought of as a potentially confounded association with poor socioeconomic background, drug and alcohol misuse, sex, and ethnic origin.

Three USA studies included odds ratios adjusted for risk factors and showed that they significantly increased the risk of HIV and other blood-borne viral infections. However, these studies were done in settings where dual diagnosis of substance misuse and mental illness is very common. The samples were drawn from psychiatric inpatient and outpatient services in deprived urban areas with substantial social deprivation and health inequality, especially in those of non-white ethnic backgrounds.

Several studies, from both high prevalence and low prevalence locations, individually found a positive association between sex and infection. Women had a significantly higher risk of HIV infection than did men drawn from the same populations. One explanation might be that women with serious mental illness are

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**Figure 3: Prevalence of hepatitis B virus in people with serious mental illness**

<table>
<thead>
<tr>
<th>Year</th>
<th>Location</th>
<th>Number of patients</th>
<th>Hepatitis B virus (%)</th>
<th>Quality score</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>USA</td>
<td>238</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>2003</td>
<td>USA</td>
<td>204</td>
<td>30</td>
<td>2</td>
</tr>
<tr>
<td>2003</td>
<td>USA</td>
<td>668</td>
<td>18</td>
<td>3</td>
</tr>
<tr>
<td>2003</td>
<td>USA</td>
<td>1556</td>
<td>95</td>
<td>3</td>
</tr>
<tr>
<td>2003</td>
<td>USA</td>
<td>376</td>
<td>189</td>
<td>2</td>
</tr>
<tr>
<td>2003</td>
<td>USA</td>
<td>755</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>2007</td>
<td>USA</td>
<td>98</td>
<td>82</td>
<td>2</td>
</tr>
<tr>
<td>2008</td>
<td>USA</td>
<td>129</td>
<td>38</td>
<td>1</td>
</tr>
<tr>
<td>2008</td>
<td>USA</td>
<td>100</td>
<td>31</td>
<td>1</td>
</tr>
<tr>
<td>2008</td>
<td>USA</td>
<td>112</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>2009</td>
<td>USA</td>
<td>588</td>
<td>21</td>
<td>2</td>
</tr>
<tr>
<td>2010</td>
<td>Canada</td>
<td>110</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>2011</td>
<td>USA</td>
<td>153</td>
<td>24</td>
<td>8</td>
</tr>
</tbody>
</table>

North America

- Al Jurdi et al 2003 USA 238 16 3
- Klinkenberg et al 2003 USA 204 30 2
- Osher et al 2003 USA 668 18 3
- Dinwiddie et al 2003 USA 1556 95 3
- Butterfield et al 2003 USA 376 189 2
- Rosenberg et al 2005 USA 755 14 3
- Freudenreich et al 2007 USA 98 82 2
- Tabibian et al 2008 USA 129 38 1
- Goldberg et al 2008 USA 100 31 1
- Matthews et al 2008 USA 112 12 0
- Rothbard et al 2009 USA 588 21 2
- Sncaling et al 2010 Canada 110 7 1
- Himelhoch et al 2011 USA 153 24 8 1

Europe

- Di Nardo et al 1995 Italy 206 107 1
- Cividini et al 1997 Italy 1180 67 2
- Stroffolini et al 2003 Italy 526 51 1
- Raja et al 2006 Italy 1492 28 3
- De Hert et al 2009 Belgium 595 07 2
- Kakisi et al 2009 Greece 805 9 1
- Central and South America
- Alvarado-Esquivel et al 2008 Mexico 99 48 0
- Guimarães et al 2009 Brazil 2238 263 3

(Table 4 continues on next page)
Articles

Prevalence of hepatitis C virus in people with serious mental illness

<table>
<thead>
<tr>
<th>Year</th>
<th>Location</th>
<th>Number of patients</th>
<th>Hepatitis C virus (%)</th>
<th>Quality score</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>Australia</td>
<td>95</td>
<td>3·1 (1·8–5·0)</td>
<td>1</td>
</tr>
<tr>
<td>1993</td>
<td>Taiwan</td>
<td>780</td>
<td>6·8 (2·0–3·4)</td>
<td>3</td>
</tr>
<tr>
<td>1997</td>
<td>Isreal</td>
<td>121</td>
<td>4·8 (1·3–5·6)</td>
<td>3</td>
</tr>
<tr>
<td>2000</td>
<td>Japan</td>
<td>196</td>
<td>4·4 (2·8–6·9)</td>
<td>2</td>
</tr>
<tr>
<td>2004</td>
<td>Japan</td>
<td>455</td>
<td>1·9 (1·1–3·4)</td>
<td>0</td>
</tr>
<tr>
<td>2006</td>
<td>Turkey</td>
<td>255</td>
<td>1·8 (0·6–5·4)</td>
<td>1</td>
</tr>
<tr>
<td>2009</td>
<td>Iran</td>
<td>170</td>
<td>2·7 (1·3–5·6)</td>
<td>3</td>
</tr>
<tr>
<td>2012</td>
<td>Taiwan</td>
<td>588</td>
<td>1·8 (0·6–5·4)</td>
<td>1</td>
</tr>
</tbody>
</table>

(Continued from previous page)

Oceania
Gunewardene et al60 2010 Australia 95 3·1 1

Asia
Chang et al61 1993 Taiwan 780 6·8 3
Kimhi et al61 1997 Isreal 121 4·8 3
Sawayama et al61 2000 Japan 196 10·2 2
Nakamura et al60 2004 Japan 455 6·15 3
Kuloglu et al60 2006 Turkey 255 2·7 3
Mamani et al72 2009 Iran 170 1·8 1
Hung et al72 2012 Taiwan 588 1·9 3

Table 4: Included studies of hepatitis C virus in people with serious mental illness

Table 5: Sensitivity analysis

Hepatitis C Region 0·86 (0·63–1·19) 0·36
Hepatitis B Region 0·69 (0·44–1·10) 0·49
HIV Region 0·90 (0·67–1·21) 0·49
Hepatitis C None 0·92 (0·61–1·40) 0·69
Hepatitis B None 0·84 (0·46–1·55) 0·55
HIV None 1·00 (0·68–1·48) 0·99

Figure 4: Prevalence of hepatitis C virus in people with serious mental illness

contrast, men with serious mental illness were more likely to carry hepatitis B virus or hepatitis C virus, which could be because injecting drug use is more common in men. However, the causes of these sex differences were probably multifactorial, which we could not assess because of the heterogeneity of geography, demographics, and risk factors in the studies we included.

Many of the studies have been done in the USA, with fewer located in other countries. Of particular note is the paucity of research in Europe, and there have been no prevalence studies done in the UK. However, two articles suggest a potential problem in the UK. A hepatitis C virus screening and referral project done by an assertive outreach mental health team92 showed more than expected infections amongst users of the service. Of 76 users, ten (13%) were hepatitis C virus positive, and almost half had a history of intravenous drug use. Another article93 reported on the acceptability and feasibility of offering testing for blood-borne viruses in psychiatric inpatient settings. The results suggest more HIV, hepatitis B virus, and hepatitis C virus in patients who participated in the study. Overall, 18% of participants had current or past exposure to a blood-borne virus, one of whom was newly diagnosed with HIV and three were newly diagnosed with hepatitis B virus. Therefore, there is an urgent need to undertake high quality epidemiological studies of blood-borne virus infections and their associated risk behaviours in the people with serious mental illness in the UK and northern Europe.

Few studies systematically collected data for risk factors directly from the participants. The risk data were mainly collected from case notes and routine clinical record systems. Sexual and drug use behaviours are probably under-reported in case notes, because there is evidence that mental health services do not consistently assess these behaviours in routine care.94,95 Without accurate and consistent measurement of risks, we could not calculate the effect of the risk factors as mediators of infection in this population, and have merely mentioned the factors identified by individual studies that warrant more rigorous investigation. There is a need for a prospective longitudinal study of a cohort of people with serious mental illness, which can track risk behaviour and infections powered sufficiently to identify the mediating factors between serious mental illness and blood-borne virus infection.
We included cross-sectional studies. None of the studies included a matched comparison group of people without serious mental illness. Prospective cohort studies are needed that use representative samples alongside matched controls of people without serious mental illness. Such studies are the only way to accurately test whether the prevalence of blood-borne viruses is significantly elevated in people with serious mental illness compared with the general population. Comparing the estimated prevalence with available data for the country or region is limited but it does offer some indication that prevalence is higher in people with serious mental illness. The prevalence of HIV infection in the general population is much lower in the UK than in the USA, and therefore the assumption is that HIV infection is less of a risk for people with serious mental illness who live in the UK. However, hepatitis C virus is prevalent in drug users in the UK, and there could be a risk of hepatitis C virus infection and co-infections in people with serious mental illness as a result of substance misuse.

This meta-analysis estimated pooled prevalence of HIV, hepatitis B virus, and hepatitis C virus in people with serious mental illness. Our review included only published work, and therefore might have missed studies yet to be reported. In addition, the search strategy included only reports published in English, which might have biased our findings towards English-speaking countries.

It is unclear why sexual health has been neglected as part of the physical health agenda for people with serious mental illness. One reason might be the perception that people with serious mental illness do not engage in activities that place them at risk, such as intravenous drug use or unprotected sex. However, 30–50% of people with serious mental illness have substance misuse disorders, and, although intravenous drug use is rare, patients might have sexual partners who inject drugs, facilitating viral transmission. Additionally, as with the population as a whole, a substantial proportion of people with serious mental illness are sexually active and see intimate relationships as an important part of their lives. The lack of attention of policy makers and educators has led to a lack of awareness and a failure to provide people with serious mental illness with access to assessment, screening, and education for sexually transmitted infections, including blood-borne viruses.

A qualitative study in London documented that most people with psychosis were engaged in seeking and forming intimate relationships. Additionally, some had negative and harmful relationship experiences, including sexual exploitation and violence, yet these issues were rarely part of their routine consultation with their health-care providers. This lack of attention to sexual health and safety has also been reported in a review, which found that although women with serious mental illness were twice as likely to be exposed to severe domestic violence compared with women in the general population, these incidents were rarely detected by the health-care services they attended. A survey of psychiatrists in a Sydney, Australia, mental health service found poor knowledge of hepatitis C virus, and clinicians perceived their patients to be at lower risk than prevalence studies suggest. A survey of mental health staff at a London NHS service also showed that workers underestimated the risk of HIV in people with schizophrenia. Although they reported feeling comfortable discussing sexual health, this rarely happened in practice. In addition, a qualitative study of Australian mental health nurses showed that discussions of sex and sexuality were generally avoided.

In summary, we show the high prevalence of blood-borne infections in people with serious mental illness, but more importantly we document the paucity of data on this topic. Although the physical health inequalities of people with serious mental illness have been identified and health policy is developing to ensure that these inequalities are addressed, little attention has been given to the sexual health and specifically risk factors facilitating transmission of blood-borne viruses in people with serious mental illness in the UK and worldwide. There is an urgent need for further robust epidemiological research using representative samples of people with serious mental illness to assess the relationship between lifestyle behaviour and risk of infections to more fully understand the relationship between serious mental illness and viral infection, and to inform preventive strategies in this population.

**Contributors**

EH, FM, and SG designed the study. SB did the literature search with support from EH and FM. MB analysed the data. FM, EH, and SG interpreted the data. EH, SB, and FM wrote the report, with input from SG and MB.

**Declaration of interests**

We declare no competing interests.

**Acknowledgments**

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