



SYSTEMATIC REVIEW

A blind spot? Confronting the stigma of hepatitis B virus (HBV) infection - A systematic review [version 1; referees: 2 approved with reservations]

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Abstract

Background: The Global Hepatitis Health Sector Strategy is aiming for the elimination of viral hepatitis as a public health threat by 2030. Successful diagnostic, treatment and preventive strategies can reduce incidence and morbidity; it is important to ensure that these interventions and services are not only available, but also accessible. Stigma, poverty, and lack of knowledge may present a substantial barrier, especially in resource limited settings. We therefore set out to assimilate evidence for the nature and impact of stigma on the lives of people with HBV infection and on the community, and to suggest ways to tackle stigma and discrimination.

Methods: We carried out a literature search in PubMed using the search terms 'hepatitis B', 'stigma' to identify relevant papers published between 2007 and 2017 (inclusive), with a particular focus on Africa.

Results: We identified a total of 34 articles, of which only one study was conducted in Africa. Lack of knowledge on HBV was consistently identified: there were misconceptions about HBV transmission among the public, healthcare workers (HCWs) provided inaccurate information to individuals diagnosed with HBV, and poor understanding resulted in lack of preventive precautions. Stigma negatively impacted on health behaviour such as help-seeking, screening, disclosure, prevention of transmission, and adherence to treatment.

Conclusion: Stigma is a potentially major barrier to the successful implementation of preventive, diagnostic and treatment strategies for HBV infection, and yet there is very limited recognition of the magnitude of this challenge, especially in Africa. There is a need for more research in this area, to

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- 2 **Herbert Muyinda**, Makerere University, Uganda

Discuss this article

identify and evaluate interventions that can be used effectively to tackle stigma in HBV, and to inform collaborative efforts between policy makers, HCWs, traditional healers, religious leaders, charity organisations and support groups, to improve awareness and tackle stigma in HBV in Africa.

Comments (0)

Keywords

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Abbreviations

- PMTCT – Prevention of mother to child transmission
- TB – Tuberculosis
- HBV – Hepatitis B virus
- HCC – Hepatocellular carcinoma
- WHO – World Health Organisation
- HIV/AIDS – Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome
- HCWs – Healthcare workers
- THs – Traditional healers
- CHB – Chronic Hepatitis B

Introduction

Hepatitis B virus (HBV) infection has been reported worldwide, with an estimated burden of 250 million cases, and has been associated with high mortality rates resulting from complications including cirrhosis and hepatocellular carcinoma (HCC)¹. There are effective prevention and treatment strategies available, including vaccination and suppressive antiviral therapy, both of which also contribute to prevention of vertical transmission². The Global Hepatitis Health Sector Strategy is aiming for the elimination of viral hepatitis as a public health threat by 2030³. However, there are important challenges still to be addressed including gaps in vaccine coverage^{4,5}, limited access to diagnostic tests and treatment¹ and lack of a curative therapy^{2,4}. Stigma, poverty, and lack of knowledge add further to the challenge, especially in resource-limited settings². There is a growing body of personal testimonies providing evidence of stigma associated with HBV^{5,6}. However, there is a very limited literature to describe this, and more work is required to understand the nature and impact of stigma for individuals with HBV infection.

Individuals who are stigmatised as a result of illness or infection not only have to bear potential challenges to health, but may also be denied the opportunities that define quality of life such as education, employment, access to appropriate health care and interaction with a diverse cross-section of society⁷. Although many diseases are stigmatised, awareness of – and investigation into – stigma is better represented in some areas than others. In HIV, stigma has been shown to limit engagement with services including screening and prevention of mother to child transmission (PMTCT), and uptake of antiretroviral therapy^{8–11}; in tuberculosis (TB) it has been shown to cause diagnostic delays and treatment non-compliance^{12,13}, and in mental illness, stigma has been associated with delays in help-seeking, discontinuation of treatment, suboptimal therapeutic relationships, patient safety concerns, and poorer quality mental and physical care^{14–16}.

Stereotypes and prejudice may stem from physical differences attributable to the condition, misconceptions associated with fear of contagion, and judgements about routes of transmission, all of which may be underpinned by lack of knowledge^{17–19}. Beyond the physical manifestations and potential complications

of an illness, stigma usually arises from lack of awareness, lack of education and lack of perception²⁰. People living with HIV/AIDS, especially those displaying wasting syndrome and certain identifiable opportunistic infections are more prone to stigma compared to those who are asymptomatic⁸. HIV and TB may be stigmatised as a result of anxieties about spread of infection, and may also be regarded as a punishment for ‘irresponsible’ or ‘immoral’ behaviour^{13,21–23}. People with mental illnesses may be considered ‘dangerous’ or provoke fear, may lose their autonomy, or be treated as ‘childlike’⁷. Understanding why society reacts in a particular way is one way to address stigma¹⁸, and could therefore help to guide approaches to tackling stigma in HBV.

HBV is highly endemic in Africa, a continent that faces huge challenges in prevention, diagnosis and treatment¹. The situation is further complicated by the substantial public health challenge of co-endemic HIV and HBV²⁴. An understanding of the breadth and scope of stigma in HBV, especially in Africa, is an essential part of any strategy that seeks to tackle and eventually eliminate HBV infection as a public health problem. As the improvement of universal availability and accessibility of diagnostic, treatment and vaccination options are underway, it is important to ensure that products and services are not only available, but also accessible; people with HBV infection must be able to access education, clinical care, and support from their partners and families, healthcare workers, and members of their communities. Also, the WHO recommends HBV treatment in an environment that minimizes stigma and discrimination²⁵.

We therefore set out to assimilate evidence for the nature and impact of stigma on the lives of people with HBV infection and on the community, to describe coping strategies employed by people with HBV, and to suggest ways to tackle stigma and discrimination.

Methods

Search strategy

In November–December 2017, we undertook a literature search in PubMed; our search strategy is detailed in [Supplementary file 1](#). We carried out two searches: the first search focused on stigma in HBV in Africa; and a second search which was not limited to Africa. These searches yielded 50 and 879 articles, respectively. 49 articles were duplicates. On reviewing the titles and abstracts, 827 were excluded from search results as they were not on stigma or HBV. Full texts of 53 articles were reviewed and 19 were excluded (3 were reviews, 3 were reports, 1 was not available, and 12 did not report on stigma). A total of 34 articles were therefore downloaded in full ([Supplementary file 3](#)). From each publication, we extracted: citation, study design, sample size, study population, country, factors associated with stigma, impact of stigma on the lives of people with HBV, and proposed interventions to tackle stigma in the society. Data were curated using MS Excel software (Microsoft, Redmond, WA). Ethics approval was not required for this study.

Results

The full metadata generated from our literature search are available in [Supplementary file 2](#).

Factors associated with creating or perpetuating stigma for individuals with HBV infection

Some of the common themes identified from literature that are associated with stigma and HBV are summarised in [Table 1](#).

Lack of knowledge is a central theme in perpetuation of stigma. This applies to education among individuals with the infection, but also their families, society and health care workers (HCW). Failure of HCWs to provide adequate and accurate information may be a barrier to treatment, reduce the likelihood of disclosure to family, and contribute to fear, anxiety and depression which in turn negatively impact on coping strategies²⁶. Lack of knowledge may also be a reason why some HCWs are not themselves vaccinated against HBV and therefore are at an increased risk of acquiring HBV. A study carried out in Cameroon reported a HBV vaccination rate of only 12% among HCW²⁷, and a study in Nigeria reported a 25% prevalence of HBV infection among surgeons²⁸. Lack of awareness among policy makers negatively impacts on appropriate prioritisation, and this can be an important contributor to poor advocacy, inadequate allocation of resources²⁹ and poor levels of education.

Given that HBV is not well understood in some communities, it may be considered a punishment or linked to 'evil spirits'^{26,30,31}. Some individuals may therefore opt to seek assistance

from traditional healers (THs) or faith leaders, seeking 'purification'. Although THs and religious healers can have an important role in providing psychosocial support, there is also the potential for harm and/or delaying presentation to clinical care^{32,33}. A recent report showed that in Africa, HCC presents at a late stage, where effective treatment would be challenging for any healthcare system³⁴. Specialised training on HBV for THs and ministers of faith, and healthcare programs that work collaboratively with these groups, could be a valuable approach in some settings³⁵.

Although stigma has also been associated with old age and following of traditional values³⁶, this may primarily reflect lack of knowledge or exposure, while younger people tend to have more access to information, and are less defined by traditional values^{36,37}. However, this relationship is not consistent, as one study found an association between old age and decreased prejudice in HBV infection³⁸. It is important to pay special consideration to specific groups of people who might be most vulnerable to the effects of stigma when designing interventions.

Stigma affects various aspects of everyday lives of people with HBV infection ([Table 2](#)). Similar to mental disorders and HIV/AIDS, stigma in HBV can negatively impact on health behaviour such as help-seeking, screening, disclosure, prevention of transmission, access and adherence to treatment, and poorer quality mental and physical care^{8,14,20}.

Table 1. Factors underpinning stigma in HBV infection, identified from a literature review.

Lack of knowledge or awareness
<p>Lack of knowledge among the public was represented by:</p> <ul style="list-style-type: none"> • Misconceptions that HBV can be transmitted through sharing of utensils, via food or eating together³⁹⁻⁴⁶; • Beliefs that HBV is a genetic trait⁴⁷; • Lack of awareness that HBV could be transmitted sexually⁴¹; • Representation of HBV as a consequence of bad behaviour, or perception of individuals with HBV as 'bad' people³¹. <p>Lack of knowledge among healthcare workers (HCWs) was represented by:</p> <ul style="list-style-type: none"> • Lacking or inaccurate information provided by HCWs regarding HBV diagnosis or treatment^{40,48}; • Provision of inappropriate reassurance, or overemphasis of potential complications⁴⁸; • Poor understanding among HCWs regarding appropriate laboratory testing to diagnose HBV infection⁴⁴; <p>Lack of knowledge among individuals with HBV was represented by:</p> <ul style="list-style-type: none"> • Lack of necessary precautions for prevention of transmission³⁰; • Difficulty processing information about the infection, leading to anxiety or depression⁴⁸; • Pursuit of traditional or religious interventions reflecting the belief that infection may be caused by evil spirits^{26,30}.
Other factors associated with stigma
<p>Stigma in HBV has been associated with:</p> <ul style="list-style-type: none"> • Extremes of age (In some cases this is evident in older age^{36,37,41,49} and in other reports, in younger age groups³⁸); • People strongly defined by traditional values^{37,41}; • Lower education levels^{36,37}; • People who have not themselves been screened or vaccinated against HBV⁴⁹. <p>Among HCWs, hesitation to provide care to individuals with HBV infection was noted among:</p> <ul style="list-style-type: none"> • Those who had not come across or offered healthcare to an individual with HBV infection^{50,51}; • Those who perceived an infection risk to themselves⁵² or had low individual confidence in protecting themselves⁵³.

Table 2. Evidence for the impact of HBV infection, identified from a literature review.

Reduced access to appropriate health care
<ul style="list-style-type: none"> Stigma is associated with reduced uptake of opportunities for diagnostic screening and clinical care^{30,39,44,47,54,55}.
Impact on family and relationships
<p>People living with HBV infection:</p> <ul style="list-style-type: none"> May be anxious about spreading the infection to family members, and therefore distance themselves from close relationships^{36,39,40,43,56}; Report feeling of bringing shame upon the family^{54,57,58}; Can experience difficulties in establishing and/or maintaining intimate relationships^{40,54}.
Impact on work and career
<ul style="list-style-type: none"> HBV may lead to inappropriate exclusion from certain career choices (e.g. healthcare, childcare, food handling)^{54,59,60}; Individuals with HBV infection are discriminated against at work, lose employment, or are unable to find work^{47,56}.
Impact on mental health
<p>People living with HBV infection:</p> <ul style="list-style-type: none"> May fear the physical consequences of disease progression and/or treatment side effects^{39,56}; this fear can perpetuate discrimination⁴⁹; May have negative self-image and experience feelings of guilt and shame⁴¹; these are associated with shame about disclosing diagnosis³⁶; May experience anxiety about economic cost of treatment⁵⁶; Fear being stigmatised⁶¹; May suffer significant psychosocial morbidity, which can be more substantial than physical symptoms⁵⁹; May face deportation if not resident in their country of origin⁶²; May seek privacy and suffer fear of disclosure; this can be distinct in African communities³⁷. Report feeling humiliated, embarrassed, or inferior, together with a sense of guilt and shame⁵⁷.
Impact on social behavior
<p>People living with HBV infection may suffer the following social discrimination:</p> <ul style="list-style-type: none"> Are not allowed to share utensils / food / towels / soap, for fear of transmitting the infection^{36,40,54,63}; Suffer feelings of rejection or isolation, including perceptions that other people are avoiding them^{40,57,59,63}; Suffer feelings of 'passivity' because of lack of treatment, or cost of treatment, which results in missing opportunities to start treatment and defaulting clinical follow-up⁴⁸; Develop a habit of secrecy, in order to avoid disclosure^{62,64}.
Relationship with education / knowledge
<ul style="list-style-type: none"> Stigma may contribute to lack of awareness⁶⁵; Lack of education about HBV is associated with discrimination⁴²; There is less stigma if people are more educated or if they have a family member with HBV^{43,58}; conversely, familiarity with the disease and higher levels of knowledge have been associated with lower stigma^{43,54}; There is a lack of concordance as to whether education/knowledge makes stigma towards HBV better or worse – e.g. in some studies, those with more education were more worried³⁶.

Coping strategies and interventions for HBV stigma

Coping strategies that have been described for HBV are listed (Table 3). Depending on the coping strategies used, not everyone experiencing stigma will necessarily suffer emotional distress or have diminished well-being as a consequence⁶⁶. In HIV, avoidant coping strategies such as denial have been associated with higher levels of depression whereas acceptance of the diagnosis, associated with personal control and self-efficacy, is associated with reduced levels of depression⁶⁷. Among patients with schizophrenia, the ability to use positive coping strategies was associated with reduced self-stigma⁶⁸. Further studies are needed to explore coping strategies used to deal with HBV stigma, to exploring the choice of coping strategy, and to determine outcomes.

As well as individual coping strategies, a variety of other interventions have been proposed to tackle stigma (Table 3). In many cases, attitudes may improve after realising that infection can be prevented and managed therapeutically³¹. This is in line with a report from the WHO about mental illness, highlighting that stigma can be combated through educational messages representing conditions as illnesses that respond to specific treatment⁶⁹.

Counselling can provide several benefits, alleviating anxiety associated with a new diagnosis, as well as providing an opportunity to share factual information regarding treatment, prevention, self-care and overall well-being^{26,48}. Counselling should cover a broad range of information such as the natural history

Table 3. Coping strategies and other interventions that have been used to tackle stigma in HBV, identified from a literature review.**Coping strategies for individuals with HBV infection**

- Seeking words of encouragement and prayers from spiritual leaders or family members^{26,37};
- Lifestyle modification, such as reduced intake of alcohol and fatty foods²⁶;
- Reaching out for support from family members and friends⁷⁰;
- Use of support groups⁵;
- Note that certain coping strategies may also result in negative influences, such as avoiding disclosure³⁷, disengagement from seeking active treatment⁴⁸, and emotional responses including grief, denial, anger and aggression^{26,57}.

Coping strategies associated with negative influence

- Establishing culturally appropriate public education or awareness programmes that promote surveillance and treatment^{30,36,37,39,41,42,48,49,58,71,72}. One study presented a real-life narrative where influential people from that community talked about their experiences with HBV, emphasising the availability of treatment and prevention strategies³¹.
- Providing specialised training about HBV infection, which may be designed to target people living with HBV, HCWs, THs, the wider public^{26,30,35,39,46,48,50,72,73};
- Training of policy makers and healthcare professionals on the urgency of tackling HBV, and on prevention, diagnosis and treatment^{30,39,40,48,72};
- Training of healthcare workers to provide pre- and post-test counselling^{26,48,56};
- Developing national campaigns to promote HBV screening and vaccination. Screening and vaccination can reduce social stigma surrounding HBV³⁶.

of the disease, diagnosis, treatment, prevention and living with the infection²⁶. This should be delivered sensitively, at a time and in a manner that supports the individual in accepting and processing the information.

There are several strategies that have been used to raise awareness of HIV/AIDS which could be applied to HBV. Dissemination of factual information through use of radio, television, posters, pamphlets and drama has been widely used to diminish stigma towards HIV in resource limited settings⁸. Multiple educational sessions can also be an effective way of increasing awareness and therefore reducing stigma, as participants have the opportunity to reflect on the concepts learnt in the previous sessions⁷⁴. Another successful method for training HCWs is perspective-taking and empathy: participation is associated with 'increased willingness to treat people with certain illnesses, decreased stigma and increased awareness of confidentiality among healthcare workers'⁷⁴. These approaches could be used to tackle HBV stigma among HCWs and community members.

On-line support groups provide a platform for people living with HBV to share their experiences⁵, and charities can be influential in raising awareness, and promoting important health messages^{5,75}. The internet is widely used as a tool for sharing experiences, and as such can raise awareness of stigma⁶, as well as uniting individuals and communities as a support network. It is important for HCWs to introduce newly diagnosed individuals to these avenues to help people living with HBV. Importantly, more charities and support groups that are well suited for people with HBV infection in Africa are needed.

Discussion

Despite the limited evidence from Africa, the data we have gathered reflect consistent themes in stigma and discrimination

affecting individuals with chronic viral hepatitis infection. These may have a wide-reaching influence on physical health (for example inhibiting interaction with clinical services and reducing treatment adherence), psychological well-being (through increasing isolation, anxiety and depression), and interactions with family and the wider society (by limiting relationships, social interactions and employment opportunities). Recognising, understanding and tackling the issue of this stigma in African populations could be a valuable tool to improve population health and to underpin advances towards elimination strategies proposed for the year 2030.

Limitations and caveats

There are very few data to inform this discussion: we identified only two studies on stigma from Africa^{26,76} and three other studies included African participants in North America³⁷, Australia⁶⁵ and in UK⁷⁷. Although we did a robust search of the peer-reviewed scientific literature, there may be other sources that are not captured by this scientific style of approach. Most studies had very small sample sizes and some were opportunistic in recruiting participants, thus limiting generalisability of the findings. We have therefore also drawn on the literature for HIV, TB and mental illness.

Future aspiration and challenges

Studies looking at stigma may benefit from a mixed method study design, providing stronger evidence and increasing generalisability of the findings. It is important to carry out research on stigma with the aim of demonstrating its burden and its effects, while also considering how to establish and evaluate interventions that tackle stigma within communities. We identified only one study that evaluated the effectiveness of stigma reduction programmes among Asians in USA³¹. More studies like this are needed in Africa as they will also help to deploy resources in the most appropriate and effective ways.

In addition to raising awareness among individuals with HBV infection, the general public and HCWs, enhanced communication with policy makers is also crucial. Despite the high burden of HBV in low and middle-income countries, there is limited infrastructure to support diagnosis and treatment, and disproportionately little international research funding for HBV compared to other infectious diseases².

Conclusion

Stigma is a potentially major barrier to the successful implementation of preventive, diagnostic and treatment strategies for HBV infection, and yet there is very limited recognition of the magnitude of this challenge, especially in Africa. Lack of knowledge among policymakers, HCWs, the general public and patients is a potent driver of stigma. Stigma in turn, negatively impacts health behaviour such as help-seeking, screening, disclosure, prevention of transmission and adherence to treatment. Establishing education programmes and awareness campaigns is crucial. There is also a pressing need for more research in this area, to identify and evaluate interventions that can be used effectively to tackle stigma in HBV,

and for collaborative efforts between policy makers, HCWs, traditional healers, religious leaders, charity organisations and support groups, to improve awareness and tackle stigma in HBV in Africa.

Data availability

All data underlying the results are available as part of the article and [supplementary files](#), and no additional source data are required.

Competing interests

No competing interests were disclosed.

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Supplementary material

Supplementary file 1: Details of search strategy used to identify studies on stigma in Hepatitis B virus (HBV) infection, from PubMed database. The terms in each row were combined by Boolean operator 'OR', the columns were combined by Boolean term 'AND'. We carried out two searches: the first search focused on stigma in HBV in Africa - we combined all the columns in search strategy (#1 AND #2 AND #3); a second search was not limited to Africa - for this we only combined columns (#1 AND #3).

[Click here to access the data.](#)

Supplementary file 2: Full details of 34 studies identified by a systematic literature search of stigma in Hepatitis B virus (HBV) infection published between 2005 and 2017.

[Click here to access the data.](#)

Supplementary file 3. Flow diagram illustrating identification and inclusion of studies for a systematic review of stigma in Hepatitis B virus (HBV) infection, based on PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria.

[Click here to access the data.](#)

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1. Are the rationale for, and objectives of, the Systematic Review clearly stated?

Yes: The article addresses the important health aspect of HBV stigma. It states that there is minimal recognition of the challenge stigma poses especially in Africa, yet it is a potentially major barrier to the successful delivery and access to care. The authors set out to fully understand [assimilate] the evidence for the nature and impact of stigma on the lives of people with HBV infection, and on the community, and to suggest ways to tackle stigma and discrimination.

1. Are sufficient details of the methods and analysis provided to allow replication by others?

Partly: This was a systematic literature review using a search in PubMed focusing on information published between 2007 and 2017, with a particular focus on Africa. However, although the target area of analysis was 'Africa', in the limitations section they state that there were only two studies conducted in Africa, in fact in the abstract they state that it was only one. This paucity of published information on the subject matter would call for triangulation – additional sources of information would be sought to supplement the one or two published articles reviewed.

1. Are the conclusions drawn adequately supported by the results presented in the review?

Partly: While this topic is important and merits careful analysis, this article presents over generalized already known assertions regarding stigma, with hardly new contribution to the topic. The authors approach the topic by posing a question in their title: "A blind spot? ..." The implication here is that the article should explicitly articulate the nature of 'blindspotness' of HBV stigma. Non-availability or presence of few articles of published work on this particular topic may not be enough to make it a blind spot. To satisfy such a claim, it would be useful to address some of these questions: Do people (particularly in Africa) know what Hepatitis B disease is? What are some of the local names/labels/terminologies used in describing it? What are the individual and collective experiences of the disease, and what are the common social responses? In other words, a more detailed description and analysis of how stigma manifests itself and experienced by the affected individuals (in Africa) would be the way to illustrate the social (in)visibility and/or extent/magnitude of the 'blindspotness' of HBV stigma, as referred to in the article.

First of all, focusing on Africa as a whole (as a target population) is one of the main challenges of the paper. Africa is too diverse to have such generalized 'lack of knowledge', 'misconceptions and prejudices' regarding HBV. The Moslem North and part of west Africa, the Sub-Saharan Africa, and the relatively wealthy South Africa are different cultures and the knowledge, manifestations, and experience of stigma is bound to be different. The paper can benefit from referring to examples, references in particular places

or countries.

While the article states the intention to assimilate the available evidence for the nature and impact of stigma on the lives of people with HBV infection and on the community, this does not seem to have been effectively achieved. The paper states very generalized and quite obvious views, which makes it difficult to find new contribution the paper makes to the topic of HBV stigma.

There is a general tendency to be unspecific regarding manifestation and experience of stigma, by referring to experiences in other conditions – HIV and AIDS, and mental illness, and areas outside Africa. For instance, the authors emphasized lack of knowledge of HBV among different players (health workers, people with HBV infection themselves, community) as potent driver of stigma, and then link the negative effects thereof to prevention, treatment seeking and provision of care. On pg. 3 the authors state that “stereotypes and prejudice may stem from physical differences attributable to the condition, misconceptions associated with fear of contagion, and judgements about routes of transmission, all of which may be underpinned by lack of knowledge ... arises from lack of awareness, lack of education and lack of perception ... and that healthcare workers provided inaccurate information to those diagnosed by HBV.” While these assertions may be true, the kind of ‘knowledge’ being referred to as lacking in this case, is not clear. First, if there was ‘lack of knowledge’, then what would shape the HBV stigma stated in the paper? The fact that there was stigma, means that there was some form of knowledge; probably ‘inappropriate’ but some knowledge. Quite often, there is a tendency to disregard local/indigenous (African) knowledge and understanding of disease and/or health conditions including HBV, and emphasis placed on the biomedical knowledge and quoting sources from the Western World.

Further, generally stigma is known to be characterized by labelling, and social constructs and actions that discount one’s identity (see Goffman: Notes on spoilt Identity). For example, it is not clear what knowledge of HBV bodily signs and symptoms people have, their local names/labels/terminologies, and how this knowledge shapes different forms of stigma. All these seem to have been missing in the literature, which makes it difficult to conclude from the review that people with HBV (in Africa) were actually being stigmatized, leave alone HBV stigma being a blind spot. In other words, the paper does not explicitly show whether or how HBV related stigma (in Africa), is blind spot.

Other comments:

- Coping strategies and interventions for HBV stigma” (Table 3)

The coping strategies listed in the table and discussed in the paper assume existence of particular forms of stigma, that have not been shown to be evident or experienced in Africa. The paper can be improved by linking particular ‘coping’ strategies to particular forms of stigma (in Africa). In fact, in some cases the stigmatized hardly cope, but just endure, and the boundary between coping, and endurance is so blurred.

Discussion:

The claim in the paper, that the data gathered reflect consistent themes of stigma and discrimination ... is not adequately illustrated in the results section. Most of the examples given were from Asia and other areas other than Africa, and of other conditions – mental illness and HIV and AIDS, and not HBV, which hardly reflects any consistency at stated.

Limitations:

The limitations as stated, considerably weakens the paper. Given the paucity of data, a ‘blind spot on HBV stigma in Africa would be verified by triangulation of information clearly showing what is (in)visible/blindspot, rather than simply interpreting it as lack of literature on the subject matter.

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Yes

Are sufficient details of the methods and analysis provided to allow replication by others?

Yes

Is the statistical analysis and its interpretation appropriate?

Not applicable

Are the conclusions drawn adequately supported by the results presented in the review?

Partly

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 14 Aug 2018

Philippa Matthews, Nuffield Department of Medicine, Peter Medawar Building for Pathogen Research, University of Oxford, UK

REVIEWER: Are sufficient details of the methods and analysis provided to allow replication by others? **Partly:** This was a systematic literature review using a search in PubMed focusing on information published between 2007 and 2017, with a particular focus on Africa. However, although the target area of analysis was 'Africa', in the limitations section they state that there were only two studies conducted in Africa, in fact in the abstract they state that it was only one.

RESPONSE: We have corrected this statement in the abstract, this now reads "We identified a total of 32 articles, of which only two studies were conducted in Africa". As per responses to reviewer 1, this information has also been presented more clearly in the form of a new table 1.

REVIEWER: This paucity of published information on the subject matter would call for triangulation – additional sources of information would be sought to supplement the one or two published articles reviewed.

RESPONSE: We agree that additional sources of information are required, and this provides the justification for drawing on the literature for HIV, TB and mental health to provide more insights than can be gained from the HBV literature alone. In response to comments from reviewer 1, we have adopted a clearer stance on which sections of the manuscript draw on just the HBV literature, and which sections have included reference to wider sources. Please see our comments to reviewer 1 for more details.

REVIEWER: While this topic is important and merits careful analysis, this article presents over generalized already known assertions regarding stigma, with hardly new contribution to the topic. The authors approach the topic by posing a question in their title: "A blind spot? ..." The implication here is that the article should explicitly articulate the nature of 'blindspotness' of HBV stigma. Non-availability or presence of few articles of published work on this particular topic may not be enough to make it a blind spot. To satisfy such a claim, it would be useful to address some of these questions: Do people (particularly in Africa) know what Hepatitis B disease is? What are some of the local names/labels/terminologies used in describing it? What are the individual and collective

experiences of the disease, and what are the common social responses? In other words, a more detailed description and analysis of how stigma manifests itself and experienced by the affected individuals (in Africa) would be the way to illustrate the social (in)visibility and/or extent/magnitude of the 'blindspotness' of HBV stigma, as referred to in the article.

RESPONSE: We believe our work is a new contribution to the topic, as no prior attempt has been made to review the existing literature in a systematic way. To explain the use of the 'blind spot' metaphor in the title, we have added some text to the introduction to explain the use of this metaphor as a way of describing the lack of recognition (including lack of local words to describe the infection), the paucity of existing data, and a neglect of the problem to date. We also return to this point in the discussion, to emphasise the consequences of the blind spot through missed or late diagnosis. The questions posed by the reviewer cannot be completely addressed, due to missing data, but our results do incorporate the lack of missing words to describe the infection in certain languages and the individual and collective responses to infection. These points are more clearly presented as a result of the more robust structure to the results section that we have undertaken in response to feedback from reviewer 1.

REVIEWER: First of all, focusing on Africa as a whole (as a target population) is one of the main challenges of the paper. Africa is too diverse to have such generalized 'lack of knowledge', 'misconceptions and prejudices' regarding HBV. The Moslem North and part of west Africa, the Sub-Saharan Africa, and the relatively wealthy South Africa are different cultures and the knowledge, manifestations, and experience of stigma is bound to be different. The paper can benefit from referring to examples, references in particular places or countries.

RESPONSE: We agree with this important point, and have added to the discussion accordingly: 'Sub-Saharan Africa encompasses huge diversity, and as such it would be misleading to assume that we can generalise about culture, beliefs and stigma, or that findings that arise in one setting can be extrapolated to others; the knowledge, manifestations, and experience of stigma is bound to be different between settings. Further work will be needed to develop insights that are relevant to particular populations in order to develop the most effective interventions. Referring to specific examples for particular places or countries is currently difficult in the absence of more published data. However, to understand some of the specific challenges of HBV, we have previously collated individual experiences of HBV from patients, researchers and healthcare workers representing different settings across sub-Saharan Africa (O'Hara et al, doi: 10.1371/journal.pntd.0005842).

REVIEWER: While the article states the intention to assimilate the available evidence for the nature and impact of stigma on the lives of people with HBV infection and on the community, this does not seem to have been effectively achieved. The paper states very generalized and quite obvious views, which makes it difficult to find new contribution the paper makes to the topic of HBV stigma.

RESPONSE: We agree with the frustrations expressed here; it is indeed difficult to make advances in the absence of a better literature. However, we see the publication of this article as providing important advocacy for the future development of this field. Although the data may seem 'generalised and obvious', they have not currently been translated into any consistent recognition or action. We have added this specifically to the discussion (section headed 'future aspirations and challenges') as follows: 'We see this article as a starting point for this field, as it is currently very difficult to make substantial advances in the absence of better data. By collating the existing literature, we hope to raise the profile of this topic overall, and to highlight specific areas of neglect. This provides a foundation for clinicians and researchers to build on over time.'

REVIEWER: There is a general tendency to be unspecific regarding manifestation and experience of stigma, by referring to experiences in other conditions – HIV and AIDS, and mental illness, and areas outside Africa. For instance, the authors emphasized lack of knowledge of HBV among different players (health workers, people with HBV infection themselves, community) as potent driver of stigma, and then link the negative effects thereof to prevention, treatment seeking and provision of care.

RESPONSE: In keeping with comments also raised by reviewer 1, we have improved the clarity around evidence that is HBV-specific, vs. insights that have been gained from sources pertaining to other diseases/infections. The results now contain only HBV-specific findings based on a systematic approach.

REVIEWER: The authors state that “stereotypes and prejudice may stem from physical differences attributable to the condition, misconceptions associated with fear of contagion, and judgements about routes of transmission, all of which may be underpinned by lack of knowledge ... arises from lack of awareness, lack of education and lack of perception ... and that healthcare workers provided inaccurate information to those diagnosed by HBV.” While these assertions may be true, the kind of ‘knowledge’ being referred to as lacking in this case, is not clear. First, if there was ‘lack of knowledge’, then what would shape the HBV stigma stated in the paper? The fact that there was stigma, means that there was some form of knowledge; probably ‘inappropriate’ but some knowledge.

RESPONSE: We have expanded table 2 content regarding ‘lack of knowledge’ to be specific about the gaps in knowledge/understanding, e.g. lack of knowledge ‘about transmission routes’, ‘about treatment availability’, ‘about chronic and asymptomatic nature of HBV infection’, and specific misconceptions e.g. that tobacco causes HBV infection. In this way, we recognise that the lack of knowledge is not absolute but that specific gaps in knowledge can be detrimental.

REVIEWER: Quite often, there is a tendency to disregard local/indigenous (African) knowledge and understanding of disease and/or health conditions including HBV, and emphasis placed on the biomedical knowledge and quoting sources from the Western World.

RESPONSE: Thank you for highlighting this omission. As above, we have added specific reference to our previous publication (O'Hara et al, doi: 10.1371/journal.pntd.0005842) in which local experiences are better individually represented. Although most of us currently have affiliations in the UK, it is noteworthy that our authorship list represents personal and individual experience from Uganda, South Africa, Kenya and Zimbabwe. It is difficult to add more robust representation of local beliefs as this is just not apparent in the literature, but we agree that this is a crucial aspiration, and we have therefore added to the discussion to highlight this point, as follows: ‘It is frequently the case that local, indigenous knowledge and understanding of disease and/or health conditions is not well reflected in the published literature’, and subsequently ‘More studies like this are needed in Africa, in order to provide insights into local understanding and beliefs, as they will also help to deploy resources in the most appropriate and effective ways with particular relevance to individual settings’.

REVIEWER: Further, generally stigma is known to be characterized by labelling, and social constructs and actions that discount one’s identity (see Goffman: Notes on spoilt Identity). For example, it is not clear what knowledge of HBV bodily signs and symptoms people have, their local

names/labels/terminologies, and how this knowledge shapes different forms of stigma. All these seem to have been missing in the literature, which makes it difficult to conclude from the review that people with HBV (in Africa) were actually being stigmatized, leave alone HBV stigma being a blind spot. In other words, the paper does not explicitly show whether or how HBV related stigma (in Africa), is blind spot.

RESPONSE: We agree that these are important aspirations for ongoing research. We have expanded on the ways in which the 'blind spot' metaphor is pertinent (see point above). We have added the reference to Goffman in order to support the point raised about identity, and have expanded the discussion as follows: 'Findings in Africa demonstrate a general lack of knowledge on HBV, an inability to define the disease, confusion of HBV with other diseases such as malaria and yellow fever, and the association of HBV symptoms with witchcraft or poisoning. Such negative associations have been described to have the potential to 'spoil the identity' of the individual: the individual ceases to be perceived as a normal person but rather one who is tainted and discounted from society. Lack of knowledge or awareness leads to misinformation that feeds stigma and discrimination.'

REVIEWER: The coping strategies listed in table 3 and discussed in the paper assume existence of particular forms of stigma, that have not been shown to be evident or experienced in Africa. The paper can be improved by linking particular 'coping' strategies to particular forms of stigma (in Africa). In fact, in some cases the stigmatized hardly cope, but just endure, and the boundary between coping, and endurance is so blurred.

RESPONSE: In the results section, we have improved the layout of this table to reduce duplication (see feedback to reviewer 1). Within the discussion section entitled 'limitations and caveats', we have added as follows: 'Our description of 'coping strategies' is an over-simplification of the complex responses that arise as a result of stigma. We recognise that many individuals who suffer stigma may not be able to deploy specific active coping mechanisms, and indeed may simply 'endure' their situation'.

REVIEWER: Discussion: The claim in the paper, that the data gathered reflect consistent themes of stigma and discrimination ... is not adequately illustrated in the results section. Most of the examples given were from Asia and other areas other than Africa, and of other conditions – mental illness and HIV and AIDS, and not HBV, which hardly reflects any consistency at stated.

RESPONSE: We have removed the use of the description of our results as identifying 'consistent themes', and simply state that 'the data we have gathered reflect stigma and discrimination affecting individuals with chronic viral hepatitis infection'. The new table 1 provides the reader with clearer oversight regarding the geographical origin of the dataset we have used.

REVIEWER: Limitations: The limitations as stated, considerably weakens the paper. Given the paucity of data, a 'blind spot on HBV stigma in Africa would be verified by triangulation of information clearly showing what is (in)visible/blindspot, rather than simply interpreting it as lack of literature on the subject matter.

RESPONSE: We have addressed this point through our specific responses to individual points raised earlier in both reviews. Specifically, this includes a clear comment in the introduction and methods about triangulation of data sources, drawing on HIV, TB and mental illness, and

expanded introduction and discussion to include a better description of the 'blind spot'. It is an interesting point that the blind spot is not as simple as merely a lack of data.

Competing Interests: No competing interests were disclosed.

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Summary: The article presents findings from a systematic review on HBV stigma. The authors recognize the large burden of HBV globally and the potential for stigma to hamper prevention, diagnosis and treatment. They unpack the lack of knowledge underpinning the stigmatization of HBV as well as some factors associated with stigmatization of HBV. They also present findings on how HBV stigma impacts health care, familial and social relationships, employment, mental health, and behavior. The authors also describe strategies individuals use to cope with or manage HBV stigma and interventions to address HPV stigma. Finally, the authors conclude by identifying gaps in the literature, particularly a paucity of research conducted in Africa, and provide guidance for future research.

Specific Comments to explain ratings:

With respect to rating for Question 1 (partly): The rationale for the paper is clear, however the objectives of this paper are less clear. We are uncertain what the word assimilate means with respect to the literature. Did the authors mean to use this term? If so, it may be helpful to explain it further. As well, it's unclear if the authors are going to abstract suggestions to address stigma and discrimination from the included articles or if they are going to use their findings to provide suggestions, drawing on literature from other stigmatized conditions. It is also unclear from the results section, and in particular the literature included in the tables, if this literature review is restricted to HBV stigma, or also includes HIV and mental health stigma (in which case the review is not extensive enough). The supplementary material showing the search strategy indicates it is restricted to HBV stigma, yet the results section suggests otherwise. The paper would be strengthened by a clearer statement of the objectives and then ensuring that those objectives are adhered to throughout.

With respect to rating for Question 2 (partly): The authors do not include their specific inclusion/exclusion criteria, which relates to the point above with respect to the mixing of what looks like included literature from the search, with other literature from HIV and Mental Health in the results section. It is also unclear how "factors associated with stigma," "impact of stigma on the lives of people with HBV," and "proposed interventions to tackle stigma in the society" were systematically captured. There is one article included in the data abstraction supplementary file (Cochrane et al 2016¹) for which "not/applicable" is listed for all of the data abstraction categories related to stigma. It is unclear why this article is included.

More detail is needed on the process of reviewing and selecting which abstracts went to full review and then which articles were included. Was this done by one person? Two people who then compared results with a third as tie breaker in cases of disagreement? This information will help the reader assess the strength of the review.

A standard figure showing the two searches graphically would be helpful for the reader (how many initial abstracts, how many of those went to full review and then how many of those were included).

With respect to rating for Question 4 (partly): The manuscript would benefit from the authors including a discussion on risk of bias in their process and review. They do not mention bias or describe any methods used for assessing risk of bias of individual included studies. Other limitations that need to be mentioned include that many of the findings presented in the results section come from a single article (e.g. in most of the tables, each point often only has one reference attached to it, and in some cases not even a reference from the search itself).

Other comments:

Abstract: The authors state that only one study was conducted in Africa, while in the limitations it states that two studies were conducted in Africa.

Overall language comment: Please do not use HIV/AIDS, it is considered stigmatizing. UNAIDS language guidelines recommend using HIV, HIV and AIDS, or HIV or AIDS, depending on the context. Using HIV/AIDS implies HIV=AIDS and that one cannot live a long, healthy and productive life with HIV.

Methods: See comment above on explanation for rating for Question 2.

Results: The results section would be strengthened by presenting only the results of the search in the results section and keeping discussion (and inclusion of non-HBV stigma literature) to the discussion section. The results section often seems more like a discussion section and it is sometimes difficult to tell what findings are coming from the HBV stigma literature review, versus what are coming from other articles not included in the review (e.g. some of the findings presented in tables are from HIV, mental health or general stigma literature), or are views/conclusion the authors have drawn. For example, in the 4th paragraph of the “Factors associated with creating or perpetuating stigma for individuals with HBV Infection” section, the authors hypothesize about why a certain trend is observed. As well, the “coping strategies and interventions for HBV stigma” section is almost entirely a discussion of coping strategies that have been used to tackle stigma in other fields or interventions that have been used to address stigma related to diseases other than HBV. While pertinent, this information probably belongs in the discussion section.

The results section would benefit from a clearer organizational structure and ensuring only results from the HBV literature are included. For example,

- “Factors associated with creating or perpetuating stigma for individuals with HBV Infection”
 - It seems the first section” is trying to unpack factors driving or causing stigma and factors associated with higher levels of stigma. However, this section also includes some behavioral impacts, such as pursuing traditional or religious intervention at the individual level, which could be considered “impact on access to care”
 - At the health care level, providing inaccurate information and the provision of inappropriate reassurance or over emphasis of potential complications seem to be the result of lack of knowledge, rather than evidence of lack of knowledge, that could be considered “impact on access to care” or “impact on quality of care.”
 - The text notes stigma among policy makers can be problematic, but this isn’t supported by evidence in the table.

- Table 1: Unclear if these factors are actually coming from the HBV literature or not, given the inclusion of HIV articles in the table that from the supplementary material describing the literature search, were not included. For example references 40, 41.
- Table 2:
 1. The “Impact on mental health” section of the table seems to have some redundant items, particularly around guilt and shame
 2. The “Impact on social behavior” section of the table seems to largely encompass manifestations of stigma, but not necessarily social behaviors. It is unclear what is meant by “suffer feelings of “passivity” because of lack of treatment, or cost of treatment, which results in missing...”
 3. The “relationship with education/knowledge” section seems to almost entirely overlap with the previous table, highlighting factors associated with stigma. However, it is interesting to highlight that stigma may drive lack of knowledge just as lack of knowledge may drive stigma. However, this might be better said in the text.
 4. All references to articles that were not part of the actual HBV stigma review should be removed. This includes references 40, 41, 57,58, 59. The articles should instead be referred to in the discussion section if the authors feel they are important to discuss around a key result.
- Coping strategies and interventions for HBV stigma”
 - Table 3
 1. The title “Coping strategies associated with negative influence” is unclear. It seems like this bullet is for interventions.
 2. All references that are not coming directly from the review need to be removed. Specifically, #'s 40,48, 57, 58, 70
- The table included in the supplementary material showing the articles should be included within the body of the article in a reduced format, given it is central to the review process.

Discussion: The discussion section paragraph reads more like a conclusion paragraph, while there is much discussion embedded in the results section. Moving the discussion from the results into the discussion section will strengthen both the results and discussions section and also make clearer to the reader what is emanating directly from the review of the HBV literature versus what the authors are supplementing from other fields, because of the sparse HBV stigma literature. The discussion section could be expanded by discussing what the gaps are that were found—and then using the literature from other fields to suggest how those gaps might be filled etc.

Limitations: In addition to comments above to Q.4, it would be appropriate to discuss the strength of findings/quality of included articles. Was any rating of the quality of articles conducted? We also find the statement at the end of the limitations section that literature from HIV, TB and mental illness was drawn on, because of the limitations of the literature found to be confusing. The fact that this was done, muddies

the methods and results sections. If the literature review is only focused on HBV stigma, no matter how scarce the literature is, only this literature should be drawn on/presented in the results section. Other literature can/should be discussed in the discussion section. This is conflating of the results coming from the search itself, with 'supplementary' literature from other fields in the result section is problematic. Please move all discussion of other literature not coming from the literature search on HBV to the discussion section.

Conclusions: The conclusions state stigma may disrupt adherence, however, adherence to treatment is not discussed in the results. However, hampered adherence is listed as an impact of stigma in the abstraction table for the Huang *et al* 2016² article.

References

1. Cochrane A, Collins P, Horwood JP: Barriers and opportunities for hepatitis B testing and contact tracing in a UK Somali population: a qualitative study. *Eur J Public Health*. **26** (3): 389-95 [PubMed Abstract](#) | [Publisher Full Text](#)
2. Huang J, Guan ML, Balch J, Wu E, Rao H, Lin A, Wei L, Lok AS: Survey of hepatitis B knowledge and stigma among chronically infected patients and uninfected persons in Beijing, China. *Liver Int*. **36** (11): 1595-1603 [PubMed Abstract](#) | [Publisher Full Text](#)

Are the rationale for, and objectives of, the Systematic Review clearly stated?

Partly

Are sufficient details of the methods and analysis provided to allow replication by others?

Partly

Is the statistical analysis and its interpretation appropriate?

Not applicable

Are the conclusions drawn adequately supported by the results presented in the review?

Partly

Competing Interests: No competing interests were disclosed.

We have read this submission. We believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.

Author Response 14 Aug 2018

Philippa Matthews, Nuffield Department of Medicine, Peter Medawar Building for Pathogen Research, University of Oxford, UK

REVIEWER: The rationale for the paper is clear, however the objectives of this paper are less clear. We are uncertain what the word assimilate means with respect to the literature. Did the authors mean to use this term? If so, it may be helpful to explain it further.

AUTHOR RESPONSE: As defined by the Oxford English dictionary, the term 'assimilate' means to 'take in and understand fully (information or ideas)'. We have added to the final paragraph of the introduction to clarify this: 'Our approach was to gather relevant information from the published

literature, to curate it in order to be able to unify key messages, and to highlight gaps where future work is still needed'. By strengthening our consistent adherence to the principles of a systematic literature review throughout the paper (addressed in more detail in the points below), our objectives are now set out in a more transparent way.

REVIEWER: As well, it's unclear if the authors are going to abstract suggestions to address stigma and discrimination from the included articles or if they are going to use their findings to provide suggestions, drawing on literature from other stigmatized conditions.

RESPONSE: We have used the reviewer's suggested text at the end of the introduction, to describe both of these approaches, adding: 'We have been able to develop suggestions to address HBV stigma and discrimination from the existing literature, but in light of the paucity of HBV-specific studies, we have also drawn on literature from other stigmatized conditions'.

REVIEWER: It is also unclear from the results section, and in particular the literature included in the tables, if this literature review is restricted to HBV stigma, or also includes HIV and mental health stigma (in which case the review is not extensive enough). The supplementary material showing the search strategy indicates it is restricted to HBV stigma, yet the results section suggests otherwise. The paper would be strengthened by a clearer statement of the objectives and then ensuring that those objectives are adhered to throughout.

RESPONSE: The primary focus of our review is HBV stigma, however in the absence of clear literature on this topic we have also drawn on wider literature about stigma in other conditions. We agree that this was not sufficiently clear or consistent as an approach in our initial version, and have amended the article accordingly as follows:

1. Introduction: we have amended the final paragraph to set out the approach more clearly, describing a systematic approach, curation to unify key themes, and highlighting gaps where future work is still needed. We also explain the need to triangulate our approach by drawing on resources from other stigmatized conditions including HIV, TB and mental illness to inform the discussion.
2. Methods: we have made a clear distinction between the systematic literature review undertaken for HBV stigma, versus a more general use of literature on other conditions to provide additional breadth and context.
3. Results: these are now clearly presented as pertaining only to the systematic literature review, reflecting HBV-specific data (see opening sentence of results section).
4. Discussion: we have used this section to reference the wider literature on stigma, using HIV, mental health and TB as examples.

REVIEWER: The authors do not include their specific inclusion/exclusion criteria, which relates to the point above with respect to the mixing of what looks like included literature from the search, with other literature from HIV and Mental Health in the results section.

RESPONSE: We have tackled this in a number of ways:

1. We have improved a description of our search strategy to make clear the specific focus on HBV stigma. This expanded section now reads as follows: 'we undertook a systematic literature search in PubMed; our search strategy focused entirely on the evidence surrounding stigma in HBV'.
2. We have moved the PRISMA flow diagram into the paper as Fig 1, thus providing the reader with a clear summary of our approach.

3. We have divided our methods surrounding the literature search into two sections, first ‘**Search strategy: systematic literature review**’, and second ‘**Search strategy: other relevant resources**’. This makes a distinction between the HBV component of the research, that has been conducted as a robust systematic literature review, versus other supporting references that ‘were not identified through a formal systematic review, but were identified as relevant sources from robust, peer reviewed literature.’

REVIEWER: It is also unclear how “factors associated with stigma,” “impact of stigma on the lives of people with HBV,” and “proposed interventions to tackle stigma in the society” were systematically captured. There is one article included in the data abstraction supplementary file (Cochrane et al 2016) for which “not/applicable” is listed for all of the data abstraction categories related to stigma. It is unclear why this article is included.

RESPONSE: We have included a description of representing our results as a number of themes. This now reads ‘We used our research question to group data into four major themes: factors underpinning stigma in HBV infection; evidence for the impact of stigma; coping strategies for individuals with HBV infection’. We have revised the metadata for all included studies: Cochrane et al 2016 does meet our inclusion criteria and we have included information on stigma extracted from this study in the results.

REVIEWER: More detail is needed on the process of reviewing and selecting which abstracts went to full review and then which articles were included. Was this done by one person? Two people who then compared results with a third as tie breaker in cases of disagreement? This information will help the reader assess the strength of the review.

RESPONSE: The initial review of abstracts was performed by one individual according to prospectively agreed, objective criteria, as set out in the PRISMA document. Two individuals contributed to the next stage of the review; this is now included in methods.

REVIEWER: A standard figure showing the two searches graphically would be helpful for the reader (how many initial abstracts, how many of those went to full review and then how many of those were included).

RESPONSE: This was originally in supplementary data, but we have now included a PRISMA flow diagram as fig 1 in the manuscript, as well as adding the relevant numbers to the text.

REVIEWER: The manuscript would benefit from the authors including a discussion on risk of bias in their process and review. They do not mention bias or describe any methods used for assessing risk of bias of individual included studies.

RESPONSE: We have now added a ‘risk of bias assessment’ approach; for qualitative studies we used the qualitative appraisal checklist by NICE public health guidance and for quantitative studies we used the Centre of Evidence based Management checklist. This has been added to the methods, and has informed a new paragraph in the results entitled ‘quality of’. We have added new suppl tables 3 and 4 containing the detailed results of this assessment for each paper. Under the section of limitations/ caveats, we also describe some of the shortfalls of the included studies, recognising the paucity of the literature overall and in particular for Africa.

REVIEWER: Other limitations that need to be mentioned include that many of the findings

presented in the results section come from a single article (e.g. in most of the tables, each point often only has one reference attached to it, and in some cases not even a reference from the search itself).

RESPONSE: We have rectified this. The all results presented in the tables include only studies on HBV stigma identified from our systematic literature search. Where possible, we have added more than one reference for each point that is included; this now represents a comprehensive summary of all 34 included studies. However, we recognise that the literature is limited and therefore some points can only be supported by only one citation.

REVIEWER: Abstract: The authors state that only one study was conducted in Africa, while in the limitations it states that two studies were conducted in Africa.

RESPONSE: We have corrected accordingly (two studies were conducted in Africa). We have also improved the clarity of this in the new table 1, by dividing the literature by geographical region so it is easy to pick out the studies that are set in any given location.

REVIEWER: Please do not use HIV/AIDS, it is considered stigmatizing. UNAIDS language guidelines recommend using HIV, HIV and AIDS, or HIV or AIDS, depending on the context. Using HIV/AIDS implies HIV=AIDS and that one cannot live a long, healthy and productive life with HIV.

RESPONSE: Thank you for this feedback, we have corrected accordingly (although please note that several of our references use this abbreviation in their titles).

REVIEWER: The results section would be strengthened by presenting only the results of the search in the results section and keeping discussion (and inclusion of non-HBV stigma literature) to the discussion section. The results section often seems more like a discussion section and it is sometimes difficult to tell what findings are coming from the HBV stigma literature review, versus what are coming from other articles not included in the review (e.g. some of the findings presented in tables are from HIV, mental health or general stigma literature), or are views/conclusion the authors have drawn. For example, in the 4th paragraph of the “Factors associated with creating or perpetuating stigma for individuals with HBV Infection” section, the authors hypothesize about why a certain trend is observed.

RESPONSE: We have taken a careful approach to improving this; our results tables now cite only references that are derived from the systematic literature review. We have now moved all hypotheses and references to other diseases into the discussion section.

REVIEWER: As well, the “coping strategies and interventions for HBV stigma” section is almost entirely a discussion of coping strategies that have been used to tackle stigma in other fields or interventions that have been used to address stigma related to diseases other than HBV. While pertinent, this information probably belongs in the discussion section.

RESPONSE: We agree; we have trimmed the inclusion of coping strategies out of the results section and now feature more of this text in the discussion.

REVIEWER: The results section would benefit from a clearer organizational structure and ensuring only results from the HBV literature are included. For example,

- “Factors associated with creating or perpetuating stigma for individuals with HBV Infection”
 - It seems the first section” is trying to unpack factors driving or causing stigma and factors associated with higher levels of stigma. However, this section also includes some behavioral impacts, such as pursuing traditional or religious intervention at the individual level, which could be considered “impact on access to care”
 - At the health care level, providing inaccurate information and the provision of inappropriate reassurance or over emphasis of potential complications seem to be the result of lack of knowledge, rather than evidence of lack of knowledge, that could be considered “impact on access to care” or “impact on quality of care.”
 - The text notes stigma among policy makers can be problematic, but this isn’t supported by evidence in the table.

RESPONSE: As per our responses to points above, we have improved the results section to make it more consistent and relating only to the HBV literature in the papers we identified through a systematic approach. Most of the additional text has been relocated to the discussion section. We have revisited the classification of each individual point into four different themes (represented by tables 2-5), although there is naturally some cross-referencing between these closely related areas. We have removed the inclusion of stigma among policy makers as we agree it is not sufficiently supported by the literature that we have identified.

REVIEWER: Table 1: Unclear if these factors are actually coming from the HBV literature or not, given the inclusion of HIV articles in the table that from the supplementary material describing the literature search, were not included. For example references 40, 41.

RESPONSE: We have corrected the tables, all the information included are from studies on HBV stigma identified from systematic literature review, and provided table 1 to summarise the literature on which we have based all other results tables.

REVIEWER: Table 2: The “Impact on mental health” section of the table seems to have some redundant items, particularly around guilt and shame.

RESPONSE: We agree, and have collated the relevant points and references into a single statement supported by several references.

REVIEWER: The “Impact on social behavior” section of the table seems to largely encompass manifestations of stigma, but not necessarily social behaviors. It is unclear what is meant by “suffer feelings of “passivity” because of lack of treatment, or cost of treatment, which results in missing...”

RESPONSE: We have changed this sub-heading from ‘impact on social behaviour’ to ‘impact on social interactions’ which better encompasses the points that follow. We have also rephrased the statement to describe instead a ‘passive’ attitude towards treatment.

REVIEWER: Table 2: The “relationship with education/knowledge” section seems to almost entirely overlap with the previous table, highlighting factors associated with stigma. However, it is interesting to highlight that stigma may drive lack of knowledge just as lack of knowledge may drive stigma. However, this might be better said in the text.

RESPONSE: We agree that the sections referring to knowledge and education in Tables 1 and 2

can be assimilated, and have moved all of this into a single section in Table 1. We agree with this interesting reflection raised by the reviewer, which we have added to the discussion as follows: 'Education clearly provides a very important role in reducing discrimination and stigma; it is interesting to note that stigma may drive lack of knowledge, just as lack of knowledge may drive stigma.'

REVIEWER: All references to articles that were not part of the actual HBV stigma review should be removed. This includes references 40, 41, 57,58, 59. The articles should instead be referred to in the discussion section if the authors feel they are important to discuss around a key result.

RESPONSE: As above, we have removed any references that are not HBV-specific from the tables.

REVIEWER: Coping strategies and interventions for HBV stigma - Table 3:1. The title "Coping strategies associated with negative influence" is unclear. It seems like this bullet is for interventions.

RESPONSE: We agree this was not clearly presented; we have changed this table to remove the first rows and to remove the idea of 'coping strategies associated with negative influence'. The point we made here is now included in the previous table, listed simply as 'emotional responses including grief, denial, anger and aggression'.

REVIEWER: All references that are not coming directly from the review need to be removed. Specifically, #'s 40,48, 57, 58, 70

RESPONSE: This has been done, as per responses to points above.

REVIEWER: The table included in the supplementary material showing the articles should be included within the body of the article in a reduced format, given it is central to the review process.

RESPONSE: Thank you – this is a good suggestion. We have added a reduced version of this table as Table 1 in the results section, grouping the results by geographical area. We have also retained the link to a Suppl data file in order to provide interested readers with further details.

REVIEWER: Discussion: The discussion section paragraph reads more like a conclusion paragraph, while there is much discussion embedded in the results section. Moving the discussion from the results into the discussion section will strengthen both the results and discussions section and also make clearer to the reader what is emanating directly from the review of the HBV literature versus what the authors are supplementing from other fields, because of the sparse HBV stigma literature. The discussion section could be expanded by discussing what the gaps are that were found—and then using the literature from other fields to suggest how those gaps might be filled etc.

RESPONSE: We have taken a careful approach to dividing the results and discussion. The results are now condensed largely into a series of tables, presenting only objective findings from the systematic literature review. Other points, building on literature for other diseases, have now all been moved into the discussion.

REVIEWER: Limitations: In addition to comments above, it would be appropriate to discuss the

strength of findings/quality of included articles. Was any rating of the quality of articles conducted? We also find the statement at the end of the limitations section that literature from HIV, TB and mental illness was drawn on, because of the limitations of the literature found to be confusing. The fact that this was done, muddies the methods and results sections. If the literature review is only focused on HBV stigma, no matter how scarce the literature is, only this literature should be drawn on/presented in the results section. Other literature can/should be discussed in the discussion section. This is conflating of the results coming from the search itself, with 'supplementary' literature from other fields in the result section is problematic. Please move all discussion of other literature not coming from the literature search on HBV to the discussion section.

RESPONSE: As above, this has been done.

REVIEWER: Conclusions: The conclusions state stigma may disrupt adherence, however, adherence to treatment is not discussed in the results. However, hampered adherence is listed as an impact of stigma in the abstraction table for the Huang *et al* 2016 article.

RESPONSE: Specific reference to treatment adherence is now included in the results section (table 3), supported by relevant references. These do not now include the paper by Huang *et al*, as this study did not provide primary data on adherence (it is mentioned briefly as a discussion point only, supported by other references).

Competing Interests: No competing interests were disclosed.
