Factors associated with sexually transmitted shigella in men who have sex with men: a systematic review

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ABSTRACT

Background Outbreaks of sexually transmitted shigella have been reported in men who have sex with men (MSM) since the 1970s and present a major public health issue. Understanding the factors associated with the sexual transmission of shigella may inform future control strategies.

Methods We systematically searched four bibliographical databases (January 2000–February 2022) for manuscripts in English. We used a two-stage process to assess eligibility: the primary author conducted an initial screen and then three authors conducted independent full-text reviews to determine the final eligible manuscripts. We only included manuscripts that included MSM diagnosed with sexually transmitted shigella where specific factors associated with transmission were identified.

Results Thirteen manuscripts met the inclusion criteria that included 547 individuals. Sexually transmitted shigella in MSM was associated with: residing in a capital city/urban region, living with HIV (including engaging in seroadaptive sexual behaviour, having a low CD4 count, having a HIV viral load >100 000 and not engaging with HIV care), using HIV pre-exposure prophylaxis, use of geospatial mobile phone applications to meet sexual partners, visiting sex on premises venues, and or using recreational drugs including chemsex, MSM living with HIV, and having a HIV viral load >100 000.

Conclusion We have highlighted some important risk behaviours and factors that are associated with sexually transmitted shigella in MSM that can be used to target future shigella control interventions.

INTRODUCTION

Shigellosis is caused by Shigella dysenteriae, Shigella flexneri, Shigella sonnei, and Shigella boydii and these organisms are transmitted via the faeco-oral route causing procto-colitis.1–3 (Shigella) are highly infectious (infection of fewer than 10 organisms can lead to shigellosis), have an incubation period of 1–2 days, and the diarrhoeal illness is usually self-limiting, not requiring antimicrobial treatment.4 Sporadic outbreaks of Shigella spp in middle-income and high-income settings are associated with returning foreign travel and more recently domestic sexual transmission within networks of men who have sex with men (MSM).5–7 Distinguishing between travel associated and domestic sexual transmission of Shigella spp in individuals relies on understanding and extrapolating local epidemiological patterns (eg, temporal outbreak clusters among MSM living with HIV) and where available, phylogenetic analysis (specific genomic strains, including antimicrobial-resistant strains which can be relatively unique for travel and sexual transmitted outbreaks). In addition, population-based studies have demonstrated significant changes and differences in the male:female ratio of incident shigella infections, where the assumption is that the increasing proportion of male shigella is driven by MSM.8–11 Despite these strategies, the classification and categorisation of potential transmission dynamics for some individuals may be challenging.

Sexually transmitted shigella is caused by both Shigella sonnei and Shigella flexneri and can lead to diarrhoea, abdominal pain, fever, rectal symptoms and, in severe cases, hospitalisation.12–17 Studies have shown that up to 1% of asymptomatic MSM have shigella; however, the impact of asymptomatic shigella on outbreaks and sexual transmission is unknown.18–21 Recently, there have been
outbreaks of extensively antimicrobial-resistant shigella in MSM described in the UK and Australia causing significant morbidity.\textsuperscript{12,13} To date, shigella prevention and control strategies have focused on case identification, partner notification and raising awareness particularly in MSM. Target populations of MSM for interventions to reduce shigella transmission have not been clearly defined. We aimed to systematically review the literature to identify any demographic and behavioural characteristics of MSM who were diagnosed with sexually transmitted shigella.

**METHODS**

**Search strategy and selection**

A systematic review of the literature was conducted in November 2021 to identify factors associated with sexually transmitted shigella in MSM using the National Institute for Health and Care Excellence healthcare databases advanced search tool using appropriate medical subject heading terms. We searched four bibliographical databases (Embase, MEDLINE, EMCARE and CINAHL) to identify relevant manuscripts using the following search terms ((Shigellosis OR Shigella OR “Bacillary dysentery” OR “Enteric infection” OR enterobacteria) AND (MSM OR Gay OR Bisexual OR homosexual)). Manuscripts meeting the following criteria were included in our review; the participants were identified as MSM, written in English language, published since the year 2000 and identified at least one sociodemographic or behavioural risk factor. We only included manuscripts where shigella was sexually transmitted; travel-associated shigella data were excluded. We excluded studies that involved non-MSM populations and participants under the age of 16 years. Where manuscripts contained mixed populations of MSM and other participants, we only extracted and analysed data from MSM. We included manuscripts that included asymptomatic shigella in MSM. All types of study where primary data were reported were included. Conference abstracts, editorials, review articles, opinion articles and grey literature were excluded.

**RESULTS**

Figure 1 presents the flow chart of the manuscript screening process. Thirteen manuscripts published between 2001 and 2022 met our inclusion criteria (table 1). The manuscripts were from Europe (n=8), North America (n=3), Taiwan (n=1) and Australia (n=1).\textsuperscript{3,7,10,14-23} The study designs included case–control studies (n=3), cross-sectional studies (n=4), case series (n=4) and a case report (n=1) and a qualitative study (n=1). In total, 547 individuals were included with sample sizes ranging from 1 to 194; 250 (46\%) of these participants were MSM living with HIV. Two studies included mixed populations of cis-gendered women and individuals who had acquired shigella following overseas travel; however, we only extracted data regarding MSM.\textsuperscript{3,15} We identified demographic, biological and behavioural factors associated with sexually transmitted shigella in MSM (table 2).

**Demographic factors**

We found that sexually transmitted shigella in MSM was associated with residing in a capital city or urbanised region, for example, London, Berlin or Copenhagen.\textsuperscript{14,17-19}
Biological factors
Living with HIV, having a higher plasma HIV viral load (over 100,000 copies per mL) and having significantly lower CD4 count and MSM who were not taking antiretroviral therapy (ART) were associated with sexually transmitted shigella.3 7 15–17 21 23 Sexual transmission of antimicrobial-resistant strains of shigella (including decreased susceptibility to azithromycin (DSA)) was more frequently seen in MSM living with HIV.25 Having a concomitant STI or having a history of an STI (chlamydia, gonorrhoea, syphilis or acute hepatitis C infection) was associated with sexually transmitted shigella in MSM.7 15 16 19 22

Behavioural factors
Sexually transmitted shigella was associated with HIV seroadaptive behaviour (where MSM living with HIV were seeking other MSM via condomless anal and oral sex). The presence of HIV (OR=5.0, 95% CI 2.4 to 10.1), recent syphilis (aOR=4.3, 95% CI 1.6 to 11.6), syphilis (aOR=3.3, 95% CI 1.5 to 7.0), condomless anal and oral sex (aOR=15.5, 95% CI 3.6 to 66.7) and HIV viral load >100,000 copies/mL (aOR=4.9, 95% CI 1.4 to 16.9) were all independent predictors of shigella in MSM.22

Table 1 Study design and risk factors for sexually transmitted shigella in men who have sex with men (MSM)

<table>
<thead>
<tr>
<th>Study</th>
<th>Publication year</th>
<th>Sample size, patient demographics</th>
<th>Study design</th>
<th>Population (MSM/mixed)</th>
<th>Risk factor(s) with sexually transmitted shigella</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kuhn et al (Denmark)</td>
<td>2021</td>
<td>n=64 Median age=40</td>
<td>Case–control study</td>
<td>MSM versus non-MSM case control</td>
<td>MSM with shigella more likely to reside in capital region=p&lt;0.0001</td>
</tr>
<tr>
<td>Eikmeier et al (USA)</td>
<td>2020</td>
<td>691 cases of shigella of which 194 were in non-travel-associated men</td>
<td>Cross-sectional study</td>
<td>Mixed population with 217 men</td>
<td>217 men with shigella, 65 (30%) were living with HIV and 36 (17%) had a recent bacterial STI, 42 (19%) had drug-resistant (decreased susceptibility to azithromycin (DSA)) shigella, men with DSA-shigella higher risk of: chlamydia (OR=8.3, 95% CI 3.2 to 21.1), gonorrhoea (OR=5.2, 95% CI 2.0 to 13.4), syphilis (OR=11.7 95% CI 2.2 to 62.6), HIV (OR=5.0, 95% CI 2.4 to 10.1), any bacterial STI (OR=9.0, 95% CI 4.1 to 20.0), multiple bacterial STIs (OR=9.3, 95% CI 2.9 to 29.4).</td>
</tr>
<tr>
<td>Serafina Wani et al (England)</td>
<td>2016</td>
<td>Living with HIV Previous history of syphilis</td>
<td>Case report</td>
<td>MSM</td>
<td>Living with HIV. Recent hepatitis C infection.</td>
</tr>
<tr>
<td>Gilbart et al (England and Wales)</td>
<td>2015</td>
<td>n=34/42 MSM with shigella interviewed Median age: 38 years Living with HIV: 20 (29%)</td>
<td>Qualitative</td>
<td>MSM</td>
<td>Themes generated: MSM living with HIV. MSM living in urban/capital regions. MSM using social media and geospatial sexual networking applications facilitating condomless sex. MSM engaging in chemsex (mephedrone, crystal methamphetamine, γ-butyrolactone and γ-hydroxybutyrate and phospho-diesterase-5 inhibitors) and injecting drug use. MSM attending sex parties and group sex sessions. Sexual behaviours: insertive fisting, receptive fisting and coprophilia. Seroadaptive preferences/behaviour.</td>
</tr>
<tr>
<td>Marcus et al (Germany)</td>
<td>2004</td>
<td>n=172/9 questionnaires analysed Mean age: 32.7 years</td>
<td>Case series</td>
<td>MSM</td>
<td>Oral-anal contact with sex partners.</td>
</tr>
<tr>
<td>Wu et al (Taiwan)</td>
<td>2015</td>
<td>n=79 All subjects living with HIV</td>
<td>Case–control study</td>
<td>MSM</td>
<td>Oral-anal sex (aOR=15.5, 95% CI 3.6 to 66.7). Chemsex (aOR=5.6, 95% CI 1.4 to 227). Poppers (aOR=10.9, 95% CI 1.9 to 64.2). HIV viral load &gt;100,000 copies/mL (aOR=4.9, 95% CI 1.4 to 16.9). Past gonorrhoea (aOR=29.4, 95% CI 2.3 to 340.2). Recent syphilis (aOR=4.3, 95% CI 1.6 to 11.6). Past syphilis (aOR=3.3, 95% CI 1.5 to 7.0).</td>
</tr>
<tr>
<td>Aragón et al (USA)</td>
<td>2007</td>
<td>n=76 Mean age (of cases): 37.4 years</td>
<td>Case–control study</td>
<td>Mixed population with 48 MSM</td>
<td>Living with HIV (OR=8.17, 95% CI 2.71 to 24.6) oral-anal contact (OR=7.5, 95% CI 1.74 to 32.3).</td>
</tr>
<tr>
<td>Centers for Disease Control and Prevention, (USA)</td>
<td>2001</td>
<td>n=62/67 MSM with shigella, Median age: 39 years Living with HIV: 35 living with HIV</td>
<td>Cross-sectional study</td>
<td>MSM</td>
<td>Oral-anal contact. Multiple sexual partners.</td>
</tr>
<tr>
<td>O’Sullivan et al (Australia)</td>
<td>2002</td>
<td>n=42 Median age: 38 years Living with HIV: 22 (52%)</td>
<td>Cross-sectional study</td>
<td>MSM</td>
<td>Living with HIV. Casual sex partners in the last 3 months. Visiting a sex venue in the last 2 weeks. Oral-anal contact in the last 2 weeks. Not always washing hands after sex in the last 2 weeks.</td>
</tr>
<tr>
<td>Morgan et al (England)</td>
<td>2006</td>
<td>n=17 Mean age: 37 years</td>
<td>Case series</td>
<td>MSM</td>
<td>Oral-anal contact. Casual sexual partners. Living with HIV.</td>
</tr>
<tr>
<td>Braam et al (The Netherlands)</td>
<td>2022</td>
<td>n=13/89 had shigella Median age=32 years</td>
<td>Cross-sectional study</td>
<td>MSM</td>
<td>HIV-negative MSM using or having used PrEP.</td>
</tr>
</tbody>
</table>

PrEP, pre-exposure prophylaxis.
men). HIV negative MSM using HIV pre-exposure prophylaxis (PrEP) was associated with sexually transmitted shigella and these MSM were significantly more likely to have shigella than MSM not using PrEP.10 22 The use of social media and websites, but in particular geospatial sexual networking mobile phone applications, particularly where these platforms provided information about sex parties and sources of chemsex drugs, was associated with sexually transmitted shigella in MSM.17 Visiting sex on premises venues (eg, gay saunas) was associated with sexually transmitted shigella.21 A public health investigation of the sex on premises venues revealed that there were inadequate hand washing amenities and inadequate dedicated anal douching facilities, poor lighting to assist personal hygiene and poor education of venue staff about infection control measures.21

Recreational drug use and chemsex, namely mephedrone, crystal methamphetamine, GBL, GHB, γ-hydroxybutyrate, and methamphetamine, was associated with sexually transmitted shigella in MSM. Recreational drug use including injecting (slamming) are all associated with sexually transmitted shigella in MSM as these behaviours and networks will readily facilitate outbreaks of sexually transmitted shigella.7 17 19 Chemsex provides an environment where some MSM show a willingness to push sexual boundaries such as fisting and other sexual practices (coprophilia). Chemsex has been shown to facilitate the transmission of STIs due to the number of sexual partners and the sexual behaviours engaged by MSM using chemsex drugs.17 Although oral-to-anal sex is not a new sexual practice, chemsex increases the number and duration of MSM engaging in oral-anal contact and facilitates outbreaks of shigella. Other sexual behaviours among MSM increasing the risk of faecal contact such as fisting, coprophilia as well as sex seeking behaviours involving groups may also be increased by chemsex. Shigella in MSM is associated with gonorrhoea, syphilis and hepatitis C most likely because they are circulating within the same sexual networks. Of concern, antimicrobial-resistant shigella (including DSA) is associated with having a concomitant bacterial STI.7 15 16 19 22 Population-based data have demonstrated the increasing ratio of cis-gendered males compared with cis-gendered females diagnosed with shigella, which has been attributed to sexual transmission of shigella among MSM.6 Shigella transmission in MSM has been described as a ‘perfect storm’.6 Sexual behaviours, drug using behaviours, the effect of living with HIV in an era of effective treatment and foreign travel have all facilitated shigella becoming an STI in MSM, which at the time of writing appears to also be happening with monkeypox.4 22 Epidemiological data from the UK suggests an almost sevenfold increase in sexually transmitted shigella in MSM between 2004 and 2015 with simultaneous large increases in diagnoses of gonorrhoea, lymphogranuloma venereum and other STIs, particularly in those living with

Table 2 Risk factors associated with sexually transmitted shigella in men who have sex with men (MSM)

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Behavioural</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residing in a capital city or urban area</td>
<td>Seroadaptive (HIV) sexual behaviour.</td>
</tr>
<tr>
<td>Living with HIV.</td>
<td>Using HIV pre-exposure prophylaxis.</td>
</tr>
<tr>
<td>Living with HIV and having a high plasma HIV viral load (not taking antiretroviral therapy).</td>
<td>Using social media to meet sexual partners, access sex parties and source chemsex drugs.</td>
</tr>
<tr>
<td>Living with HIV and having a low CD4 count (not taking antiretroviral therapy).</td>
<td>Visiting sex on premises venues.</td>
</tr>
<tr>
<td>Antimicrobial-resistant Shigella spp.</td>
<td>Using recreational drugs (mephedrone, crystal methamphetamine, GHB/GBL, PDE5 inhibitors, ecstasy, poppers, marijuana and injecting drug use.</td>
</tr>
<tr>
<td>Having an STI (chlamydia, gonorrhoea, syphilis, acute hepatitis C).</td>
<td>Oro-anal sexual behaviour (rimming).</td>
</tr>
</tbody>
</table>

GBL, γ-butyrolactone; GHB, γ-hydroxybutyrate.

DISCUSSION

Our review has identified some specific factors including demographic, biological, sex-seeking behaviours, recreational drug use and sexual behaviours associated with sexually transmitted shigella in MSM. We believe that this is the first systematic review to characterise specific risk factors associated with shigella in MSM. There are few public health interventions available for shigella prevention and control, and this review provides important insights into the target populations of MSM at risk of sexually transmitted shigella.

Dense sexual networks within large urban populations of MSM (with ready access to HIV PrEP or HIV care) appear to readily facilitate the transmission of shigella and present a significant public health issue.14 17 22 As shigella is a highly infectious STI in the context of these dense sexual networks, it is not surprising that sexually transmitted shigella appears to be associated with these specific geographical locations. MSM living with HIV, in particular those not using ART, are at significant risk of sexually transmitted shigella.3 7 13–17 19 21 25 The risk of shigella in MSM living with HIV may be biological (associated with immunosuppression); however, there is no evidence to support this, and we suggest that the association with HIV is behavioural. MSM living with HIV, not using ART and not engaged with HIV care with poor surrogates of HIV (high viral load and low CD4 count) have other poor determinants of health including not accessing interventions to reduce STI transmission, using recreational drugs and engaging in behaviours that increase STI and shigella transmission.2 10 22 MSM using PrEP are self-selecting and therefore may be more likely to be at risk of STIs due to the number of sexual partners and frequency of other behaviours associated with shigella.25 26 Meeting sex partners using geospatial mobile phone applications, seeking group sex and recreational drug use including injecting (slamming) are all associated with sexually transmitted shigella in MSM as these behaviours and networks readily facilitate outbreaks of sexually transmitted shigella.7 17 19 Chemsex provides an environment where some MSM show a willingness to push sexual boundaries such as fisting and other sexual practices (coprophilia). Chemsex has been shown to facilitate the transmission of STIs due to the number of sexual partners and the sexual behaviours engaged by MSM using chemsex drugs.17 Although oral-to-anal sex is not a new sexual practice, chemsex increases the number and duration of MSM engaging in oral-anal contact and facilitates outbreaks of shigella. Other sexual behaviours among MSM increasing the risk of faecal contact such as fisting, coprophilia as well as sex seeking behaviours involving groups may also be increased by chemsex. Shigella in MSM is associated with gonorrhoea, syphilis and hepatitis C most likely because they are circulating within the same sexual networks. Of concern, antimicrobial-resistant shigella (including DSA) is associated with having a concomitant bacterial STI.7 15 16 19 22
Recent data from the USA suggest that MSM have poor knowledge of shigella and that any intervention involving behavioural change may have poor uptake; they conclude that any health promotion strategies need to shift perceptions of shigella among MSM.

There are several limitations to this systematic review including significant reporting bias, particularly because most studies are from larger cities with denser populations of MSM. Furthermore, the manuscripts in this review only contained data from MSM who presented to healthcare settings and provided a specimen of their faeces. Asymptomatic MSM or those with mild symptoms of shigella may not seek help, or even symptomatic MSM who have poor access to healthcare would not be included in this review. There is a risk due to the nature of the studies that the reported sexual orientation of participants may not accurately describe their sexual behaviours. It is also feasible that studies may also under-report some risk behaviours such as recreational drug use or sexual behaviours because of participants fear of embarrassment or stigma. Furthermore, many studies rely on self-reporting of sexual behaviours and other risk behaviours. We were only able to include manuscripts in English, and some studies contained mixed populations of MSM and non-MSM. Identifying the source of shigella in population-based data may not accurately discriminate between travel-associated and sexually transmitted shigella, and it is also feasible that MSM living in high-income settings may travel and acquire shigella from sexual behaviours overseas. Some epidemiological studies make assumptions about the source of shigella transmission based on the crude male:female ratio, which may have introduced bias into our analysis. The studies in this review are highly heterogeneous with small numbers of participants that may impact on the generalisability of the overall findings. Our study has several strengths including using a robust systematic approach to a relevant research question to provide insights into the populations of MSM affected by shigella for the design and delivery of health interventions.

There are correlations between the risk factors associated with sexually transmitted shigella in MSM. For example, MSM (including MSM living with HIV) use geospatial mobile phone applications to seek both sexual partners and recreational drugs including chemsex. It is important that MSM who are diagnosed with shigella are tested and treated for other STIs. MSM with shigella seek care from either sexual health clinicians or in primary care settings, and therefore, cross-training is needed to educate providers for the prevention of shigella. Geospatial mobile phone applications (and social media) could play a part in control interventions with appropriate use of health information and health promotion. Providing online spaces via mobile phone applications to deliver health interventions for shigella has been found to be acceptable to MSM. Thoes to be targeted could include hosts and attendees of chemsex parties to encourage barriers to shigella transmission, for example, condom use and improved hygiene practices such as washing hands after sex and not sharing douching equipment. Working with sex venues such as s ‘gay saunas’ to increase awareness of shigella and to provide recommendations for reducing spread and transmission including sufficient light for cleaning equipment and surfaces, access to condoms and staff education on infection control. Sexual health clinics and care providers for specific regions with high populations of MSM should focus campaigns on raising awareness (in both communities and healthcare providers) of the symptoms of shigella, and prevention strategies, for example, hygiene during sexual activities, and an awareness of testing all asymptomatic MSM (with diarrhoea) including MSM living with HIV and MSM using PrEP. Outbreaks of antimicrobial-resistant shigella in MSM are a major public health concern, and all MSM with diarrhoea should be appropriately tested for shigella and other enteric pathogens. We need clearer guidance on the use of antimicrobials in MSM with presumptive or confirmed shigella to prevent inappropriate antimicrobial use and to establish more robust surveillance of antimicrobial-resistant outbreaks of shigella.

In conclusion, our review has identified specific risk factors associated with sexually transmitted shigella in MSM, and we suggest that public health interventions targeting the risk groups we have identified may improve shigella control strategies.