

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, chemsex and recreational drug use, sexual behaviour (including multiple non-regular sexual partners and oral-anal sexual contact) and concomitant STIs.

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} (*Shigellae* are highly infectious (ingestion 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.¹ 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).^{2,3} Distinguishing between travel associated and domestic sexual transmission of *Shigella* spp in individuals relies on understanding and extrapolating local epidemiological patterns (eg, temporal outbreak

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Outbreaks of sexually transmitted shigella in men who have sex with men (MSM) are increasing, and more public health interventions are needed to reduce morbidity and mortality.
- ⇒ Populations of MSM at risk of sexually transmitted shigella are poorly defined.

WHAT THIS STUDY ADDS

- ⇒ We have clearly identified risk factors for sexually transmitted shigella in MSM: MSM living in urban/capital regions, MSM seeking sex and chemsex using geosocial mobile phone applications, MSM who visit sex on premises venues, MSM living with HIV, MSM using HIV pre-exposure prophylaxis, MSM using recreational drugs including chemsex, MSM engaging in oral-anal sexual behaviours with multiple non-regular partners and MSM with other STIs.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ We have highlighted target populations for interventions to reach and optimise shigella control in MSM.
- ⇒ Increasing awareness of shigella (and shigella control strategies) among MSM, healthcare workers and sex on premises venues workers.
- ⇒ Highlighted the importance of STI testing in MSM with shigella.

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.^{4–6} 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.^{3,7} 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.^{8–11} Recently, there have been



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outbreaks of extensively antimicrobial-resistant shigella in MSM described in the UK and Australia causing significant morbidity.^{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.

Study selection and data extraction

From our database search, we generated a list of relevant citations. We used a two-stage process, the primary author scanned the abstracts and then the full-text manuscripts to exclude citations that did not meet our criteria. Three authors then independently reviewed the remaining full-text articles to assess the quality and risk of bias of each manuscript and determine the final set of manuscripts according to the inclusion criteria. Additional relevant manuscripts found from the reference list of the eligible manuscripts were added where relevant. Inconsistencies were resolved by discussion between all authors. The review protocol was registered on the International Prospective Register of Systematic Reviews (PROSPERO reference: CRD42021289084).

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).^{3 7 10 14-23} The study designs included case-control studies (n=3), cross-sectional studies (n=4), case series (n=4) 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.^{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.^{14 17-19}

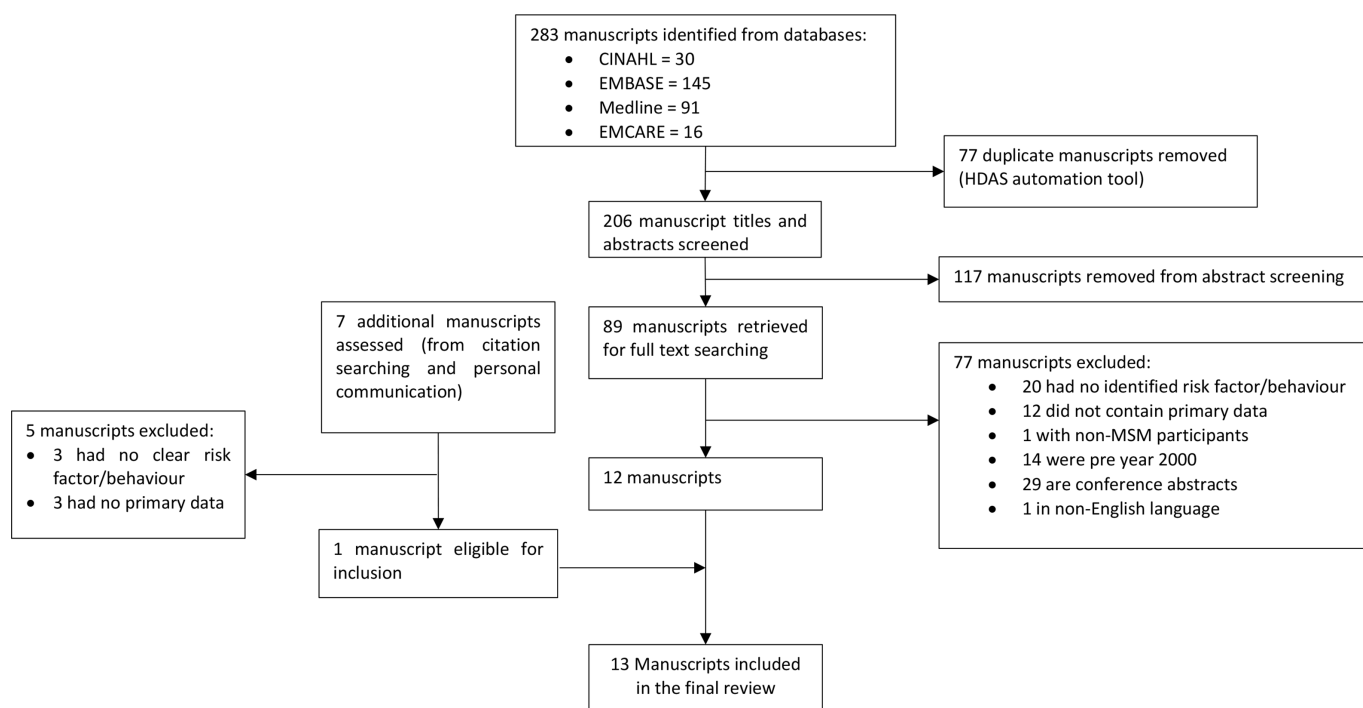


Figure 1 Flow chart of study selection for inclusion in the systematic review.

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

Study	Publication year	Sample size, patient demographics	Study design	Population (MSM/mixed)	Risk factor(s) with sexually transmitted shigella
Kuhn <i>et al</i> (Denmark) ¹⁴	2021	n=64 Median age=40	Case-control study	MSM versus non-MSM case control	MSM with shigella more likely to reside in capital region= $p<0.0001$
Eikmeier <i>et al</i> (USA) ¹⁵	2020	691 cases of shigella of which 194 were in non-travel-associated men	Cross-sectional study	Mixed population with 217 men	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).
Serafino Wani <i>et al</i> (England) ¹³	2016	Living with HIV Previous history of syphilis	Case report	MSM	Living with HIV. Recent hepatitis C infection.
Gilbart <i>et al</i> (England and Wales) ¹⁷	2015	n=34/42 MSM with shigella interviewed Median age: 38 years Living with HIV: 20 (29%)	Qualitative	MSM	Themes generated: MSM living with HIV. MSM living in urban/capital regions. MSM using social media and geospatial sexual networking applications facilitating condom less 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.
Marcus <i>et al</i> (Germany) ¹⁸	2004	n=17/29 questionnaires analysed Mean age: 32.7 years	Case series	MSM	Oral-anal contact with sex partners.
Wu <i>et al</i> (Taiwan) ¹⁹	2015	n=79 All subjects living with HIV	Case-control study	MSM	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 >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).
Aragón <i>et al</i> (USA) ³	2007	n=76 Mean age (of cases): 37.4 years	Case-control study	Mixed population with 48 MSM	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).
Centers for Disease Control and Prevention, (USA) ²⁰	2001	n=62/67 MSM with shigella, Median age: 39 years 35 living with HIV	Cross-sectional study	MSM	Oral-anal contact. Multiple sexual partners.
O'Sullivan <i>et al</i> (Australia) ²¹	2002	n=42 Median age: 38 years Living with HIV: 22 (52%)	Cross-sectional study	MSM	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.
Zayet <i>et al</i> (France) ²²	2021	n=3 Mean age: 32 years PrEP users: 2	Case series	MSM	Multiple sexual contacts. History of STIs. Condomless anal and oral sex. PrEP use.
Morgan <i>et al</i> (England) ²³	2006	n=17 Mean age: 37 years	Case series	MSM	Oral-anal contact. Casual sexual partners. Living with HIV.
Cresswell <i>et al</i> (England) ⁷	2015	n=24 Median age: 43 years Living with HIV: 13	Case series	MSM	Chem-sex. Concomitant STIs. Living with HIV. Condomless anal sex.
Braam <i>et al</i> (The Netherlands) ¹⁰	2022	n=13/389 had shigella Median age=32 years	Cross-sectional study	MSM	HIV-negative MSM using or having used PrEP.

PrEP, pre-exposure prophylaxis.

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.²² 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 living with HIV for condomless anal sex and some HIV seronegative men seeking condomless anal sex with other HIV-seronegative

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

Demographic	▶ Residing in a capital city or urban area
Biological	▶ Living with HIV. ▶ Living with HIV and having a high plasma HIV viral load (not taking antiretroviral therapy). ▶ Living with HIV and having a low CD4 count (not taking antiretroviral therapy). ▶ Antimicrobial-resistant <i>Shigella</i> spp. ▶ Having an STI (chlamydia, gonorrhoea, syphilis, acute hepatitis C).
Behavioural	▶ Seroadaptive (HIV) sexual behaviour. ▶ Using HIV pre-exposure prophylaxis. ▶ Using social media to meet sexual partners, access sex parties and source chemsex drugs. ▶ Visiting sex on premises venues. ▶ Using recreational drugs (mephedrone, crystal methamphetamine, GHB/GBH, PDE5 inhibitors, ecstasy, poppers, marijuana and injecting drug use). ▶ Oro-anal sexual behaviour (rimming). ▶ Condomless anal sex. ▶ Fisting (insertive and receptive) and coprophilia. ▶ Multiple non-regular sexual partners. ▶ Attending sex parties. ▶ Group sexual behaviours.

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

men).¹⁷ 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, γ -butyrolactone and γ -hydroxybutyrate, PDE5 inhibitors (sildenafil/tadalafil), ecstasy, poppers and marijuana and injecting drug use was associated with sexually transmitted shigella in MSM.^{7 17 19} Specific sexual behaviours particularly oral-anal sexual contact (rimming), but also condomless anal sex, fisting (insertive and receptive) and coprophilia (deriving sexual excitation from faeces), multiple non-regular sexual partners including attending sex parties and group sex was associated with sexually transmitted shigella in MSM.^{3 16–23}

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 24} 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 15–17 19 21 23} 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.^{1 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 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).¹⁷ 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.¹⁷ 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'. 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.^{24 27} 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

HIV.^{28 29} Most recently, outbreaks of extensively drug-resistant shigella have been described in MSM, highlighting the importance of designing more effective interventions globally for prevention, particularly within the routine delivery of PrEP.¹³ 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.³⁰

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 heterogenous 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.^{7 15 17 19 22} 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.¹⁵ 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.³¹ Those 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 '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 symptomatic 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.^{12 13} 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.³²

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.

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