

# Increase in extensively-drug resistant *Shigella sonnei* infections in men who have sex with men in the EU/EEA and the UK

23 February 2022

## Summary

On 27 January 2022, the United Kingdom Health Security Agency (UKHSA) reported an increase in extensively-drug resistant *Shigella sonnei* infections. Since then, Austria, Belgium, Denmark, France, Germany, Ireland, Italy, Norway, and Spain have reported cases of shigellosis with sampling dates from 2020 to 2022 and with isolates either closely genetically related by whole genome sequencing (WGS), or with the same or a very similar resistance profile. Most cases were in adult men who have sex with men (MSM). A large proportion of the patients with available information were reported to be infected through sexual transmission.

## Risk assessment

This document assesses the risk of further spread of *S. sonnei* amongst MSM and in the broader population in EU/EEA countries, resulting from the current increase in extensively-drug resistant *S. sonnei* infections.

Sexual contact networks among some MSM in Europe are highly interconnected, sometimes involving high-risk sexual practices often involving anonymous sexual contacts. The probability of new infections in MSM exposed to high-risk sexual practices, and the spread in EU/EEA countries in the coming months is assessed as high, as outbreaks among MSM usually occur over long time periods. If the lifting of restrictions related to the COVID-19 pandemic is also considered, travel and the number of social events will likely increase as well. The impact of such infections is assessed as low in most instances as *S. sonnei* is generally associated with mild disease in healthy adults. However, the impact of the infection could be more severe in immunocompromised adults. In addition, the resistance profile of this strain limits treatment options, whether this is aimed at shortening shedding in mild cases or treating severe cases. Based on these levels of probability and impact, the level of risk for MSM is assessed as moderate.

Opportunities for infection in the non-MSM population increase when transmission among MSM is high. Currently, there have been very few reports of non-MSM cases associated with the ongoing increase of cases of extensively-drug resistant *S. sonnei*. The probability of infections in the broader population, including the probability of foodborne outbreaks associated with infected food handlers, is assessed as very low. The impact of such infections is assessed as low in most instances, due to a generally mild disease in healthy individuals. Consequently, the level of risk for the broader population is assessed as low.

## Options for response

Men who have sex with men should aim to minimise the risk of infection through faecal-oral exposure during sexual activity by practicing safe sex and good hygiene. MSM presenting symptoms of gastrointestinal illness are recommended to get tested for gastrointestinal pathogens and other STIs and to inform the treating physician about the infection risk through sexual activity. Sexual activity should be avoided for at least seven days after symptoms have stopped and faecal-oral contact during sex should be avoided for four to six weeks. Awareness activities targeted at MSM, especially those identified to be at higher risk, e.g. MSM on pre-exposure prophylaxis (PrEP), should also be considered to increase knowledge about the ongoing threat of shigellosis.

People with gastrointestinal symptoms should not handle and prepare food for catering or in private households until fully recovered or stool culture is negative for *Shigella*. In healthcare settings, in addition to standard precautions, contact precautions, including placement in a single room with a dedicated toilet, adequate access to hand hygiene and regular environmental cleaning, should be considered for suspected or confirmed extensively drug-resistant *S. sonnei* cases.

There are very limited options for treatment of extensively-drug resistant *S. sonnei*. Clinicians should be aware of increasing trends of antimicrobial resistance in *Shigella* spp. and ensure susceptibility testing on all clinical isolates, especially from high-risk groups, from patients returning from international destinations, and from MSM, who are at risk of a resistant infection. When antimicrobial treatment is indicated, it should be based on the results of susceptibility testing. Non-specialist physicians should be aware that among young adult males, especially among those with no travel history, the route of acquisition can be sexual.

Timely antimicrobial resistance profiles with sufficient epidemiological information will enable early detection and investigation of treatment failures and will inform national and international treatment guidelines. Reporting of outbreaks with extensively-drug resistant *S. sonnei* and related treatment failures should be strengthened at the national and European level to enable rapid intervention and to prevent the spread of antimicrobial-resistant *S. sonnei*. Timely sharing of data on treatment failure among EU/EEA countries will facilitate a more effective response. The use of EpiPulse is encouraged to implement rapid information sharing at the European level. Any new information linked to this event can be reported in EpiPulse.

ECDC encourages countries to perform whole genome sequencing (WGS) on *S. sonnei* isolates linked to human infections, especially extensively drug-resistant ones. ECDC can provide WGS support for isolates possibly linked to multi-country events.

## Event background

On 27 January 2022, the United Kingdom Health Security Agency (UKHSA) published a press release on the rise of extensively drug-resistant (XDR) *Shigella sonnei* (*S. sonnei*) infections, mainly in gay, bisexual and other men who have sex with men (MSM) [1]. In the press release, the UK reported 47 cases of XDR *S. sonnei* in the four-month period from 1 September 2021 to 10 January 2022, compared with 16 cases of non-XDR *S. sonnei* from 1 April 2020 to 31 August 2021. In the following week, information on this event was posted in the Early Warning and Response System (EWRS). ECDC notified EU/EEA countries and the UK through ECDC's EpiPulse system (event ID: 2022-ARH-00002) on 2 February 2022 and asked Member States to share information on similar cases and/or outbreaks on the EpiPulse platform.

The UK provided updated case numbers and further details on the cases in EpiPulse, including data on the genotypic resistance profile and representative sequences. The UK outbreak strain shows non-susceptibility to penicillins, third generation cephalosporins (carrying the extended spectrum  $\beta$ -lactamase (ESBL) gene *bla*<sub>CTX-M-27</sub>), aminoglycosides, tetracycline, sulphonamides, quinolones and azithromycin. The strains fall within a *S. sonnei* (clade 5) 10-SNP cluster by whole genome sequencing (WGS).

As of 17 February 2022, nine EU/EEA countries (Austria, Belgium, Denmark, France, Germany, Italy, Ireland, Norway, Spain) reported at least 146 confirmed cases of shigellosis in relation to the UK cluster with sampling dates between 2020 and 2022 (Table 1). The definition of confirmed and possible cases is based on the assessment of the countries and/or reporting in EpiPulse. Norway provided a representative sequence from its reported cluster. In individual country clusters, at least 29 isolates have been reported to be genetically closely related by WGS (Table 1). Austria, Belgium, Denmark, Germany, Norway, and Spain reported that all or at least some of the isolates show close genetic relatedness to the UK representative sequences. Ireland reported that its sequences are closely related to the representative sequence from Norway. France reported the identification of the first *S. sonnei* strains clustering with the representative sequences from the UK from September 2020 and have since observed more than 106 isolates (Table 1).

Most cases reported by EU/EEA countries and the UK are adult males. In Denmark, Norway, Spain, and the UK, some of the cases were reported to be MSM and/to have been infected through sexual transmission. For the UK cases with available information, private sex parties or public dark rooms were reported to be the settings where infection was probably acquired. Some cases reported sexual activity during travel to EU/EEA countries that was within the incubation period. Since September 2021, the UKHSA has reported seven hospitalised patients and 16 patients who accessed emergency services. In the same time period, Italy also reported a hospitalised patient. As of 17 February 2022, Luxembourg, Portugal and Sweden reported no isolates with a similar resistance profile and/or matching the representative sequences.

**Table 1. Description of confirmed<sup>1</sup> and possible<sup>1</sup> extensively-drug resistant *Shigella sonnei* cases among MSM by country, EU/EEA countries and the United Kingdom, 2020-2022, as of 17 February 2022**

Country	Confirmed cases <sup>1</sup>	Possible cases <sup>1</sup>	Time of sampling or isolation	Genetic relatedness	Demographic data
Austria	9	-	28 June to 16 November 2021	Isolates closely related within cluster and to the representative sequences from the UK (same sequence type by cgMLST; ST152)	Male, age range: 28-41 years
Belgium	4	>30 <sup>2</sup>	19 July and 2 September 2021 (confirmed cases); since September 2021 (possible cases)	Isolates closely related within the cluster (0-2 AD) and to two of the representative sequences from the UK (3-5 AD and 4-6 AD)	Male, age range: 0-66 years (confirmed cases) <sup>3</sup>
Denmark	1	-	November 2021	Isolate closely related to representative sequences from the UK (2-3 AD by cgMLST)	Adult male
France	106	-	September 2020 to 15 February 2022	All isolates closely related to representative sequences from the UK (genotype 3.6.1.1.2 (MSM5) [2])	102 males, age range: 13-68 years; four females
Germany	3 <sup>4</sup>	-	May to October 2021	Isolates closely related to representative sequences from the UK (2-6 AD)	Two cases are males
Ireland	6	-	Since September 2021	Isolates closely related within cluster and to representative sequence from Norway (within 3 to 7 AD by cgMLST)	-
Italy	3	3	July to September 2021	-	Male, age range: 22-67 years
Norway	6	1	21 September to 16 January 2022	Isolates closely related within cluster (within 3 AD by cgMLST) and to representative sequences from the UK (1 AD); ST152	Male,
Spain	8	22	February 2021 to February 2022	Four isolates sequenced, these are closely related within cluster and to the representative sequences from the UK	Male, age range: 18-56 years
United Kingdom	62	-	4 September 2021 to 26 January 2022	All isolates part of the same 10-SNP cluster by WGS	97% male, median age 34 years

AD, allele difference; cgMLST, core genome multilocus sequence typing; ST, sequence type; WGS, whole genome sequencing.

<sup>1</sup> The definition of confirmed and possible cases is based on the assessment of the countries and/or reporting in EpiPulse.

<sup>2</sup> Cases have a similar drug resistance profile and are MSM.

<sup>3</sup> The cluster includes a case in an infant.

<sup>4</sup> Only two of the three genetically closely related isolates from Germany were reported to have a similar resistance profile to the UK isolates.

## Disease background

*Shigella* species are highly virulent Gram-negative bacteria belonging to *Enterobacteriaceae* family. There are four different species: *S. dysenteriae*, *S. boydii*, *S. flexneri* and *S. sonnei*. *Shigella sonnei* predominates in high-income countries. Transmission occurs via the faecal-oral route through direct person-to-person spread or from contaminated food and water. It is estimated that up to 80% of all infections are transmitted from person to person [3]. The infective dose of *Shigella* is relatively low, with 10–100 organisms sufficient to produce disease [4]. In four outbreaks of *S. sonnei* in Greece, investigations found the attack rates for the broader population vary between 9% to 13% [5].

Symptoms develop after an incubation period of one to three days and range from mild, self-limiting watery diarrhoea to severe dysentery with bloody diarrhoea, high fever, painful stomach cramps and even systemic complications. The duration of clinical disease is five to seven days. Shedding of bacteria may continue for four to six weeks. *Shigella* may also lead to persistent diarrhoea in young children.

Antimicrobial treatment is needed in patients with severe disease, patients requiring hospitalisation, and patients with invasive disease or complications [6]. Antimicrobial treatment reduces the duration of shedding and therefore may be recommended by public health authorities for the control of outbreaks [7].

Complications of *Shigella* infection such as bacteraemia and severe gastrointestinal disease resulting in toxic megacolon and colonic perforation are rarely reported in adults. Other complications due to shigellosis include sepsis, rectal prolapse, arthralgia, seizures, electrolyte imbalance, reactive arthritis (more commonly linked to *S. flexneri*) and the life-threatening haemolytic-uraemic syndrome (most frequently associated with *S. dysenteriae*). Risk factors for complications include immunosuppression and old age. Therefore, high-risk groups along with infants require prompt antimicrobial treatment. Fatal cases have rarely been reported in adults [8].

## Shigellosis in men who have sex with men

Sexual transmission of *Shigella* spp. mainly affects MSM as transmission is through oral-anal contact and, depending on sexual practices, it can be direct (e.g. oral-anal contact (rimming)) or indirect (e.g. oral-penile contact after anal sex or via fingers or sex toys) [9]. MSM affected by outbreaks of sexually-transmitted shigellosis have been reported to have common risk factors, e.g. they are more likely to have multiple sexual partners, to attend on-site sex venues or private sex parties and to use apps to meet sexual partners [9-11]. Use of drugs (chemsex) or alcohol before or during sex and other sexual practices (e.g. group sex, douching, fisting, use of sex toys) have been associated with outbreaks of shigellosis and infections by other sexually transmissible enteric pathogens [9-11]. Cases among MSM are also more likely to be HIV positive and to have co-infections with other pathogens of sexually transmitted infections (STI) [12-16]. Severe *Shigella* spp. disease, including bacteraemia, has been reported in MSM and can be more frequent in people with HIV disease [12-16]. Asymptomatic *Shigella* spp. infections have also been reported among MSM; the risk of onward transmission from this population is not known [17].

*Shigella* spp. isolates from MSM often exhibit antibiotic resistance and they are commonly multidrug-resistant (MDR) or extensively drug-resistant (XDR) [9,18,19]. Individual or combined resistance to first-line oral antibiotics ciprofloxacin and azithromycin has been more common, while third-generation cephalosporin resistant strains have been rarer [20,21]. In recent years, clusters of cases of strains with third-generation cephalosporin resistance and reduced susceptibility to fluoroquinolones have been reported in several countries [19,22,23]. Resistance to third-generation cephalosporins in addition to first-line treatment options such as fluoroquinolones and azithromycin limits the available effective treatment options for severe disease to intravenous last-resort antimicrobial agents, such as the carbapenems [22].

Sporadic cases and outbreaks of shigellosis among MSM including strains carrying *bla*<sub>CTX-M-27</sub> have been reported in several European countries in recent years including international transmission chains. The lineages associated with MSM both as sporadic or as outbreak strains are usually *S. flexneri* and *S. sonnei* [12,18,19,24-26]. In a recent report from the UK, a large decrease in the number of *Shigella* infections was seen since March 2020, after observing an increasing number of infections with *Shigella* spp., especially among presumptive MSM (i.e. non-traveller adult males used as a proxy for MSM in this report) prior to the COVID-19 pandemic [18]. The decline in 2020 was observed for both *S. sonnei* and *S. flexneri* with a more pronounced reduction for *S. sonnei*. *S. flexneri* has been reported more commonly among presumptive MSM since 2019, replacing *S. sonnei*. Among cases in the UK, antibiotic resistance is common and in recent years, around 90% of *Shigella* spp. are MDR or XDR. Resistance to ciprofloxacin and azithromycin was also very high with almost approximately 60% and 40%, respectively in 2020. Resistance to the third-generation cephalosporin ceftriaxone was below 20% with larger yearly variations [18].

## Foodborne transmission

Foodborne transmission of *S. sonnei* is rare in the EU/EEA. In 2020, *Shigella* was reported as a causative agent in five of 3 086 foodborne outbreaks in the EU [27]. One of these, caused by *S. sonnei*, was an outbreak reported in Denmark associated with consumption of imported fresh mint [27]. Foodborne outbreaks of *S. sonnei* have also been linked to imported fresh produce like basil from Southeast Asia in Sweden in 2015 [28], sugar peas from Kenya in Norway in 2009 [29], and baby corn from Thailand in Denmark in 2007 [30]. Similarly, a dispersed outbreak of *S. sonnei* was linked to fresh coriander served in several food outlets in the UK in 2018 [31]; the origin of coriander could not be identified but the phylogenetic analysis showed that the outbreak strain belonged to a clade of strains, some of which were linked to travels to Pakistan. Albeit rarely reported, opportunities for foodborne transmission via infected food handlers exist. Indeed, a foodborne outbreak of *S. sonnei* was reported in a retirement community in the US in 2018 due to an infected food handler who was working while clinically ill [32].

## Disease surveillance for shigellosis in the EU/EEA

For 2020, 28 EU/EEA countries reported 1 884 cases of shigellosis to ECDC, 1 760 of which (93.4%) were confirmed. This represents a drop of shigellosis cases by 64.5% in EU/EEA, largely due to the COVID-19 pandemic and the fact that the UK, which accounted for a large proportion of the reported cases, was no longer reporting after Brexit. Therefore, the reporting in 2019 better reflects the pre-pandemic epidemiological situation in the EU/EEA and the UK. In 2019, 8 230 confirmed cases of shigellosis were reported by 29 EU/EEA countries, including the UK, with an overall EU/EEA notification rate of 1.7 cases per 100 000 population. Three countries accounted for 61.4% of confirmed cases: Germany, France, and the UK, with the UK alone accounting for 39.7% of confirmed cases. The overall male-to-female ratio was 1.4:1. In 2019, 66.2% of male cases were between 25 and 64 years and the respective proportion for females was 57.5%. Travel information was available for 52.3% of the confirmed cases in 2019 and, of these, 48.2% were related to travel, mostly to Egypt, India, Morocco, and Pakistan. In 2019, *Shigella* species were reported for 76.4% of confirmed cases and among speciated isolates, 59.4% were *S. sonnei* followed by *S. flexneri* with 35.4%. For *S. sonnei*, the travel-associated cases dropped by 88.4% from 2019 to 2020. The top five travel destinations for *S. sonnei* cases were Egypt, Indonesia, India, the Republic of Madagascar, and Mexico in 2020. Information on transmission mode was available for 14.3% of *S. sonnei* cases infected within the EU/EEA (including the UK) in 2009-2020. Among the 1 612 cases with information on transmission, 768 cases (47.6%) were estimated to be foodborne, 441 (27.4%) sexually transmitted, 373 (23.1%) from person-to-person transmission and 30 (1.9%) from other types of transmission.

For the period 2017-2020, data on antimicrobial susceptibility was reported to TESSy for 43% (5 070/11 668) of the laboratory-confirmed cases of *S. sonnei* in the EU/EEA. Among the 2 251 isolates tested for penicillins, quinolones and third generation cephalosporins, 172 isolates were non-susceptible to all three classes. Only 12 of these isolates had also been tested for azithromycin and among those, four were non-susceptible. There was an equal gender distribution (49% female, 49% male and 2% missing gender) and 22% of the 172 infections were related to travel, 36% domestically acquired and 42% lacking information on travel status. Information on transmission mode was mainly missing (95%) with only eight cases reported as foodborne and one case with person-to-person transmission.

## ECDC risk assessment for the EU/EEA

This assessment is based on evidence available to ECDC at the time of publication. It follows the ECDC rapid risk assessment methodology, where the overall risk is determined by a combination of the probability and its impact [33].

### What is the risk of further spread of *S. sonnei* amongst MSM and in the broader population in EU/EEA countries resulting from the current increase in extensively-drug resistant *S. sonnei* infections?

#### Risk in men who have sex with men

The apparent cross-border dimension of the increase in extensively-drug resistant *S. sonnei* infections may be explained by the highly interconnected sexual contact networks among some MSM in Europe [34] and opening up the societies after two years in a pandemic mode. The high-risk sexual practices often involving anonymous sexual contacts associated with transmission and outbreaks of *Shigella* spp. in some groups of MSM make partner notification difficult and thus it is of limited use in such outbreaks. The probability of new infections in MSM exposed to high-risk sexual practices, and of the consequent spread in EU/EEA countries in the coming months is assessed as high as outbreaks among MSM usually occur over long time periods and are often linked to travel abroad. As awareness increases, more cases are also likely to be identified and more strains will likely be sequenced leading to higher notification numbers.

Although the UK reported seven hospitalised patients out of 29 interviewed, this most likely represents an overestimation of the true proportion of infected individuals requiring hospitalisation, as the most severe cases are most likely to seek care and be diagnosed. In adults, *S. sonnei* is generally associated with mild disease. Most HIV-positive individuals in EU/EEA settings are receiving antiretroviral treatment and are virally suppressed. However, the resistance profile of this strain limits treatment options, whether this is aimed at shortening shedding in mild cases or treating severe cases. Therefore, the impact of extensively-drug resistant *S. sonnei* infection is assessed as low in most instances (including those with HIV providing they are on effective treatment). However, the impact of *Shigella* spp. could be more severe in immunocompromised MSM.

Based on a high probability of infection and a low impact of such infection, the level of risk for MSM is assessed as moderate.



## Risk in the broader population

Opportunities for infection in the non-MSM population increase when transmission among MSM is high. Transmission in the community could manifest itself as secondary cases among heterosexual or non-sexual contacts of infected cases, foodborne infections after contamination of food items by infected food handlers, and infections transmitted by carers for older people and children (e.g. in long term care facilities or day cares). Currently, there have been very few reports of non-MSM cases associated with the ongoing increase in MSM. However, in previous protracted outbreaks of *S. sonnei*, non-MSM cases were regularly observed [19]. There is the additional concern about potential contribution of XDR *S. sonnei* to the spread of antimicrobial resistance (AMR) in the community by horizontal transfer to other bacterial species through plasmids.

The probability of infections in the broader population, including the probability of foodborne outbreaks associated with infected food handlers, is assessed as very low. This also includes the probability of introduction and sustained transmission into other high-risk groups (e.g. people who inject drugs) as the transmission route is primarily sexual. The probability of infection for family members and other heterosexual partners of MSM is higher than for the broader population but is still assessed as low.

The impact of such infections in the broader population is assessed as low in most instances, due to a generally mild disease in most individuals. However, the resistance profile of this strain limits treatment options, whether this is aimed at shortening shedding in mild cases or treating severe cases.

Based on a very low probability of infection and a low impact of such infection, the level of risk for the broader population is assessed as low. However, such a risk could be higher for family members and other heterosexual partners of MSM.

## Options for response

### Preventing sexual transmission of *Shigella* spp. in men who have sex with men

Men who have sex with men participating in sexual activities with risk of acquisition of *Shigella* spp. should aim to minimise the risk of infection. Faecal-oral exposure during sexual activity should be avoided by proper hygiene measures (i.e. washing of genital and anal areas and of hands before and after sex; latex gloves for fingering or fisting and dental dams during oral-anal sex; not sharing sex toys and ensuring proper cleaning and disinfection after their use and between partners; and changing condoms between anal and oral sex) [35]. The risk of acquisition of other sexually-transmitted infections, including HIV and hepatitis B and C, can also be reduced by condom use.

For those patients presenting symptoms of gastrointestinal illness, it is recommended that they are advised to get tested for gastrointestinal pathogens and to inform the treating physician about the infection risk through sexual activity. Testing for other STIs, including HIV and hepatitis B and C should be considered and discussed during consultations with a healthcare provider. Furthermore, hepatitis A vaccination should be recommended among non-immunised MSM. Sexual activity should be avoided for at least seven days [1] after symptoms have stopped and faecal-oral contact during sex should be avoided for four to six weeks, taking the shedding period into account.

Awareness activities targeting MSM, including through community-based organisations, should also be considered to increase knowledge about the ongoing threat of shigellosis and the need for individual preventive measures. Countries should consider following available national and international guidelines on shigellosis prevention and management among MSM when providing recommendations.

### Infection prevention and control measures

Good personal hygiene is important to prevent *Shigella* spp. infection including handwashing with soap and water, particularly after using the restroom and before starting food preparation. A person with gastrointestinal symptoms should not handle and prepare food in catering establishments and should avoid preparing food for others in private households until fully recovered or stool culture is negative for *Shigella*.

In settings where there may be vulnerable groups, such as healthcare and childcare settings, there should be strict adherence to standard hygiene precautions at all times. Contact precautions should be considered for hospitalised suspected or confirmed extensively drug-resistant *S. sonnei* cases, including single rooms with a dedicated toilet, adequate access to hand hygiene and regular environmental cleaning. Contact precautions are recommended for incontinent patients [36].

## Clinician awareness and antimicrobial stewardship

Clinicians and microbiology laboratories should be made aware of increasing trends of antimicrobial resistance in *Shigella* spp. and ensure susceptibility testing (including ESBL production) on all clinical isolates, especially from high-risk groups, such as immunocompromised, small children and older patients. Susceptibility testing is also essential in patients returning from all international destinations, in particular Asia and Africa and from global travel in MSM, who are at risk of a resistant infection. When antimicrobial treatment is indicated, it should be based on the results of susceptibility testing.

Non-specialist physicians should be aware that among young adult males, especially among those with no travel history, the route of acquisition can be sexual. For this reason, these patient's sexual and travel history should be taken and further tests for other STIs be requested or the patient be referred to a sexual health clinic.

Timely antimicrobial resistance profiles with sufficient epidemiological information will enable early detection and investigation of treatment failures and will inform national and international treatment guidelines. Empirical treatment guidance should be reviewed to consider the emergence and spread of resistance in *S. sonnei*.

Cases and outbreaks of shigellosis should be notified promptly as this may contribute to increased awareness for the disease. Cases should be followed up and interviewed when possible to identify risk factors for infection. This could allow for more targeted recommendations for prevention.

## Surveillance and EU/EEA reporting

Reporting of outbreaks with extensively-drug resistant *S. sonnei* and related treatment failures is essential at the national and European level to enable rapid intervention to prevent the spread of antimicrobial-resistant *S. sonnei*. Close monitoring of surveillance data can rapidly inform about spill-over to the broader population or to specific population groups. Cases among females and among children or an increasing proportion of cases among those under 18 years of age or over 45 years of age would likely indicate community transmission.

Timely sharing of data on treatment failure among EU/EEA countries will facilitate a more effective response. The use of EpiPulse is encouraged to implement rapid information sharing at the European level. Any new information linked to this event can be reported in EpiPulse under the event 2022-ARH-00002, users from the domains Sexually transmitted infections (STI), Antimicrobial resistance and Healthcare-associated infections (ARHAI) and Food- and waterborne diseases (FWD) are invited to participate.

ECDC encourages Member States to perform whole genome sequencing on *S. sonnei* isolates linked to human infections, especially extensively drug-resistant ones. Laboratories not performing sequencing should consider sending isolates for typing/WGS to the reference laboratory in their country.

ECDC can provide WGS support for isolates possibly linked to multi-country events through a laboratory contractor for EU/EEA countries with limited or no WGS capacity (please contact [typing@ecdc.europa.eu](mailto:typing@ecdc.europa.eu)).

## Limitations

With case finding and sequencing of isolates still ongoing at the time of publication of this risk assessment there is substantial uncertainty about the extent of this outbreak in EU/EEA countries. Also, information on the severity of patients is very limited rendering the assessment of the burden of illness from this outbreak challenging.

This assessment is undertaken based on facts known to ECDC at the time of publication.

## Source and date of request

ECDC internal decision, 10 February 2022.

## Consulted experts

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All experts have submitted declarations of interest, and a review of these declarations did not reveal any conflict of interest.

## Disclaimer

ECDC issues this risk assessment document based on an internal decision and in accordance with Article 10 of Decision No 1082/13/EC and Article 7(1) of Regulation (EC) No 853/2004 establishing a European centre for disease prevention and control (ECDC). In the framework of ECDC's mandate, the specific purpose of an ECDC risk assessment is to present different options on a certain matter. The responsibility on the choice of which option to pursue and which actions to take, including the adoption of mandatory rules or guidelines, lies exclusively with the EU/EEA countries. In its activities, ECDC strives to ensure its independence, high scientific quality, transparency and efficiency.

This report was written with the coordination and assistance of an Internal Response Team at the European Centre for Disease Prevention and Control. All data published in this risk assessment are correct to the best of our knowledge at the time of publication. Maps and figures published do not represent a statement on the part of ECDC or its partners on the legal or border status of the countries and territories shown.



## References

1. UK Health Security Agency. Press release: Rise in extremely drug-resistant *Shigella* in gay and bisexual men. [Cited 2022 Feb 14]. 2021. Available from: <https://www.gov.uk/government/news/rise-in-extremely-drug-resistant-shigella-in-gay-and-bisexual-men>.
2. Hawkey J, Paranagama K, Baker KS, Bengtsson RJ, Weill F-X, Thomson NR, et al. Global population structure and genotyping framework for genomic surveillance of the major dysentery pathogen, *Shigella sonnei*. *Nature Communications*. 2021 2021/05/11;12(1):2684. Available at: <https://doi.org/10.1038/s41467-021-22700-4>
3. DuPont HL, Levine MM, Hornick RB, Formal SB. Inoculum size in shigellosis and implications for expected mode of transmission. *The Journal of Infectious Diseases*. 1989 Jun;159(6):1126-8. Available at: <https://pubmed.ncbi.nlm.nih.gov/2656880/>
4. Zaidi MB, Estrada-García T. *Shigella*: A Highly Virulent and Elusive Pathogen. *Curr Trop Med Rep*. 2014;1(2):81-7. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4126259/>
5. Koutsotoli AD, Papassava ME, Maipa VE, Alamanos YP. Comparing *Shigella* waterborne outbreaks in four different areas in Greece: common features and differences. *Epidemiol Infect*. 2006;134(1):157-62. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2870366/>
6. US Centers for Disease Control and Prevention (CDC). CDC Recommendations for Diagnosing and Managing *Shigella* Strains with Possible Reduced Susceptibility to Ciprofloxacin, 2017. [Cited 14 February, 2022]. Available from: <https://emergency.cdc.gov/han/han00401.asp>.
7. Kotloff KL, Riddle MS, Platts-Mills JA, Pavlinac P, Zaidi AKM. Shigellosis. *The Lancet*. 2018 2018/02/24;391(10122):801-12. Available at: <https://www.sciencedirect.com/science/article/pii/S0140673617332968>
8. Morduchowicz G, Huminer D, Siegman-Igra Y, Drucker M, Block CS, Pitlik SD. *Shigella* Bacteremia in Adults: A Report of Five Cases and Review of the Literature. *Archives of Internal Medicine*. 1987;147(11):2034-7. Available at: <https://doi.org/10.1001/archinte.1987.00370110162025>
9. Mitchell H, Hughes G. Recent epidemiology of sexually transmissible enteric infections in men who have sex with men. *Current Opinion in Infectious Diseases*. 2018;31(1) Available at: [https://journals.lww.com/co-infectiousdiseases/Fulltext/2018/02000/Recent\\_epidemiology\\_of\\_sexually\\_transmissible.9.aspx](https://journals.lww.com/co-infectiousdiseases/Fulltext/2018/02000/Recent_epidemiology_of_sexually_transmissible.9.aspx)
10. Caruso E, Wright ER, Respress ET, Evener SL, Jacobson K, Bowen A, et al. Shigellosis Among Gay and Bisexual Men: A Qualitative Assessment to Examine Knowledge, Attitudes, and Practices. *Sexually Transmitted Diseases*. 2020;47(9) Available at: [https://journals.lww.com/stdjournal/Fulltext/2020/09000/Shigellosis\\_Among\\_Gay\\_and\\_Bisexual\\_Men\\_A.4.aspx](https://journals.lww.com/stdjournal/Fulltext/2020/09000/Shigellosis_Among_Gay_and_Bisexual_Men_A.4.aspx)
11. Richardson D, Devlin J, Fitzpatrick C, Pinto-Sander N. Sexually transmitted *Shigella flexneri* and *Shigella sonnei* in men who have sex with men. *Sexually Transmitted Infections*. 2021;97(3):244-. Available at: <https://sti.bmj.com/content/sextrans/97/3/244.full.pdf>
12. Zayet S, Klopfenstein T, Pierron A, Royer P-Y, Toko L, Garnier P, et al. *Shigella sonnei*, an emerging multidrug-resistant sexually transmitted pathogen in Franche-Comté, France. *Emerging Microbes & Infections*. 2021 2021/01/01;10(1):1702-5. Available at: <https://doi.org/10.1080/22221751.2021.1969289>
13. Cresswell FV, Ross S, Booth T, Pinto-Sander N, Alexander E, Bradley J, et al. *Shigella flexneri*: A Cause of Significant Morbidity and Associated With Sexually Transmitted Infections in Men Who Have Sex With Men. *Sexually Transmitted Diseases*. 2015;42(6) Available at: [https://journals.lww.com/stdjournal/Fulltext/2015/06000/Shigella\\_flexneri\\_A\\_Cause\\_of\\_Significant.10.aspx](https://journals.lww.com/stdjournal/Fulltext/2015/06000/Shigella_flexneri_A_Cause_of_Significant.10.aspx)
14. Wilmer A, Romney MG, Gustafson R, Sandhu J, Chu T, Ng C, et al. *Shigella flexneri* serotype 1 infections in men who have sex with men in Vancouver, Canada. *HIV Medicine*. 2015 2015/03/01;16(3):168-75. Available at: <https://doi.org/10.1111/hiv.12191>
15. Serafino Wani RL, Filson SA, Chattaway MA, Godbole G. Invasive shigellosis in MSM. *International Journal of STD & AIDS*. 2016 Sep;27(10):917-9. Available at: <https://journals.sagepub.com/doi/abs/10.1177/0956462415610275?journalCode=stda>
16. Angulo FJ, Swerdlow DL. Bacterial Enteric Infections in Persons Infected with Human Immunodeficiency Virus. *Clinical Infectious Diseases*. 1995;21(Supplement\_1):S84-S93. Available at: [https://doi.org/10.1093/clinids/21.Supplement\\_1.S84](https://doi.org/10.1093/clinids/21.Supplement_1.S84)
17. Braam JF, Bruisten SM, Hoogeland M, de Vries HJC, Schim van der Loeff MF, van Dam AP. *Shigella* is common in symptomatic and asymptomatic men who have sex with men visiting a sexual health clinic in Amsterdam. *Sex Transm Infect*. 2022 Feb 11 Available at: <https://sti.bmj.com/content/early/2022/02/10/sextrans-2021-055274>
18. Public Health England (PHE). Sexually transmitted Shigella spp. in England 2016 to 2020 (2021). [Cited 14 February 2022]. Available from: [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/982595/S\\_P\\_hpr0721\\_shgll20.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/982595/S_P_hpr0721_shgll20.pdf).

19. Fischer N, Maex M, Mattheus W, Van den Bossche A, Van Cauteren D, Laisnez V, et al. Genomic epidemiology of persistently circulating MDR *Shigella sonnei* strains associated with men who have sex with men (MSM) in Belgium (2013–19). *Journal of Antimicrobial Chemotherapy*. 2022;77(1):89-97. Available at: <https://doi.org/10.1093/jac/dkab377>
20. Mook P, McCormick J, Bains M, Cowley LA, Chattaway MA, Jenkins C, et al. ESBL-Producing and Macrolide-Resistant *Shigella sonnei* Infections among Men Who Have Sex with Men, England, 2015. *Emerg Infect Dis*. 2016;22(11):1948-52. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5088027/>
21. Ingle DJ, Easton M, Valcanis M, Seemann T, Kwong JC, Stephens N, et al. Co-circulation of Multidrug-resistant *Shigella* Among Men Who Have Sex With Men in Australia. *Clinical Infectious Diseases: an official publication of the Infectious Diseases Society of America*. 2019 Oct 15;69(9):1535-44. Available at: <https://pubmed.ncbi.nlm.nih.gov/30615105/>
22. Public Health England (PHE). Multi-drug resistant *Shigella sonnei* cluster (CTX-M-27) probably associated with MSM: Information for healthcare professionals. (2019) [Cited 14 February 2022]. Available from: [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\\_data/file/769163/S\\_HGLL-SONN\\_2018275.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/769163/S_HGLL-SONN_2018275.pdf).
23. Ingle Danielle J, Andersson P, Valcanis M, Barnden J, da Silva Anders G, Horan Kristy A, et al. Prolonged Outbreak of Multidrug-Resistant *Shigella sonnei* Harboring blaCTX-M-27 in Victoria, Australia. *Antimicrobial Agents and Chemotherapy*. 64(12):e01518-20. Available at: <https://doi.org/10.1128/AAC.01518-20>
24. Byrne N, Cooney F and Cormican M. Recent outbreak of ciprofloxacin-resistant *Shigella* among MSM in Dublin. *Disease Surveillance Report of HPSC, Ireland. Epi-Insight*. 2017 Feb;18(2). Available from: <http://ndsc.newsweaver.ie/epiinsight/y9rvan81q6z10qkzp9yxn5?a=2&p=51399875&t=17517804>.
25. Bardsley M, Jenkins C, Mitchell HD, Mikhail AFW, Baker KS, Foster K, et al. Persistent Transmission of Shigellosis in England Is Associated with a Recently Emerged Multidrug-Resistant Strain of *Shigella sonnei*. *Journal of Clinical Microbiology*. 2020 Mar 25;58(4) Available at: <https://pubmed.ncbi.nlm.nih.gov/31969425/>
26. Hinic V, Seth-Smith H, Stöckle M, Goldenberger D, Egli A. First report of sexually transmitted multi-drug resistant *Shigella sonnei* infections in Switzerland, investigated by whole genome sequencing. *Swiss Medical Weekly*. 2018 Aug 13;148:w14645. Available at: <https://pubmed.ncbi.nlm.nih.gov/30141522/>
27. European Food Safety Authority (EFSA) and European Centre for Disease Prevention and Control (ECDC), 2021. The European Union One Health 2020 Zoonoses Report. *EFSA Journal* 2021;19(12):6971, 324 pp. Available from: <https://doi.org/10.2903/j.efsa.2021.6971>ISSN:1831-4732©2021.
28. Folkhälsomyndigheten. Shigellainfektion 2015. [Cited 15 February, 2022]. Available from: <https://www.folkhalsomyndigheten.se/folkhalsorapportering-statistik/statistik-a-o/sjukdomsstatistik/shigellainfektion/?p=24397#statistics-nav>.
29. Folkehelseinstituttet. Utbrudd av *Shigella sonnei* i mai 2009. [Cited 15 February, 2022]. Available from: <https://www.fhi.no/globalassets/dokumenterfiler/tema/utbrudd/utbrudd-av-shigella-sonnei-i-mai-2009.pdf>.
30. Lewis H, Ethelberg S, Lisby M, Madsen SB, Olsen KE, Rasmussen P, et al. Outbreak of shigellosis in Denmark associated with imported baby corn, August 2007. *Weekly releases (1997–2007)*. 2007;12(35):3257. Available at: <https://www.eurosurveillance.org/content/10.2807/esw.12.35.03257-en>
31. Mikhail AFW, Pereboom M, Utsi L, Hawker J, Lighthill J, Aird H, et al. Utility of whole-genome sequencing during an investigation of multiple foodborne outbreaks of *Shigella sonnei*. *Epidemiol Infect*. 2021;149:e71-e. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8060841/>
32. Strysko J, Fialkowski V, Marsh Z, Wadhwa A, Collins J, Gharpure R, et al. Notes from the Field: Outbreak of Multidrug-Resistant *Shigella sonnei* Infections in a Retirement Community - Vermont, October–November 2018. *MMWR Morb Mortal Wkly Rep*. 2019;68(17):405-6. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6541310/>
33. European Centre for Disease Prevention and Control (ECDC). Operational tool on rapid risk assessment methodology - ECDC 2019. Stockholm: ECDC; 2019. Available at: <https://www.ecdc.europa.eu/en/publications-data/operational-tool-rapid-risk-assessment-methodologyecdc-2019>.
34. The EMIS Network. EMIS-2017 – The European Men-Who-Have-Sex-With-Men Internet Survey. Key findings from 50 countries. Stockholm: European Centre for Disease Prevention and Control; 2019. Available from: <https://www.ecdc.europa.eu/en/publications-data/emis-2017-european-men-who-have-sex-men-internet-survey>.
35. US Centers for Disease Control and Prevention (CDC). *Shigella* Infections among Gay & Bisexual Men. [Cited 17 February, 2022]. Available from: <https://www.cdc.gov/shigella/msm.html>.
36. Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee, 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. Available from: <https://www.cdc.gov/infectioncontrol/guidelines/isolation/index.html>.