

Protecting and improving the nation's health

Epidemiology of *Shigella* in adults in the South East, 2011 to 2015:

Continued increase in cases in men who have sex with men

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Public Health England 133-155 Waterloo Road Wellington House London SE1 8UG

Tel: 020 7654 8000 www.gov.uk/phe Twitter: @PHE uk

Facebook: www.facebook.com/PublicHealthEngland

Prepared by: Jacquelyn McCormick, Piers Mook and Paul Crook, Field Epidemiology Services. For queries relating to this document, please contact jacquelyn.mccormick@phe.gov.uk

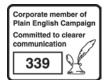
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Contents

Contents	3
Executive summary	4
Aim	5
Context	5
Data sources	8
Epidemiology	9
Conclusion	21
Appendix 1. Data management	22
References	23
About Field Epidemiology Services	24

Executive summary

Shigella are bacteria spread by the faecal oral route which can cause bloody diarrhoea. In the past, Shigella infections in adults in the UK were primarily associated with travel to low-income countries, with endemic transmission due to poor sanitation, however, in the past decade outbreaks have been documented in men who have sex with men (MSM) due to transmission during sexual activity.

Previous investigation of MSM cases in the UK described cases as having high numbers of sexual partners, high levels of condomless sex, attending sex parties, sex under the influence of recreational drugs (chemsex) and high levels of HIV positivity. Recent investigation of a *S. sonnei* cluster has revealed low levels of awareness of *Shigella* among MSM cases.

The overall number of *Shigella* cases in adults in the South East Public Health England Centre has increased over the past four years (n=145 in 2012 to n=186 in 2015). This increase is attributable to cases with no known travel history. *S. sonnei* (59% in 2015) is the most commonly reported species among adults, followed by *S. flexneri* (37% in 2015). The proportion of *S. sonnei* cases is increasing. Among *S. flexneri* cases, serotype 2a (43%) overtook 3a (12%) as the most common serotype in 2015.

The number of cases of *Shigella* in adults without a known travel history has increased from 81 cases in 2014 to 107 cases in 2015. Cases reported in 2015 are more likely to be male: 87% (compared to 56% in 2011), a male to female ratio of 6.6:1 (compared to 1.3:1 in 2011).

The increase in the male to female ratio is likely to represent an increase in transmission among MSM and it is likely that *Shigella* is now endemic in this group in parts of the South East. There were 78 excess male cases without a known travel history in 2015, nearly a ten-fold increase from eight cases in 2011. The underlying serotype of male cases has also been changing. While in 2013, there was a preponderance of *S. flexneri* 3a, more recently we have seen increases in *S. flexneri* 2a and *S. sonnei*.

Although local work has been undertaken, further work is needed to reduce transmission of *Shigella* in MSM. MSM need to be aware of how to avoid *Shigella* infection and of the symptoms. PHE is planning to repeat a campaign to raise awareness and it is recommended that local action is taken by commissioners and sexual health clinics to raise awareness using materials already available on the PHE website. Sexual health clinics and health protection teams managing cases should take further opportunities to provide advice to cases on how to prevent spread.

Aim

The aim of this report is to update stakeholders on the epidemiology of *Shigella* in adults in the South East Public Health England Centre (PHEC).

Context

Shigella

Shigella is a gram negative bacteria that cause a highly infectious intestinal disease with symptoms ranging from watery diarrhea to bloody diarrhea, fever and abdominal pain. In certain cases, infection with *Shigella* can result in severe invasive disease and life threatening complications such as toxic megacolon and haemolytic uraemic syndrome. Mild and asymptomatic infection can also occur. Persons with mild infections usually recover quickly without antibiotic treatment and the infection can be easily limited by following hygienic measures such as frequent hand washing^{1,2}.

The incubation period of *Shigella* is between 12 and 96 hours and the infectious period is primarily during the diarrhoeal illness. Humans are the only significant reservoir of *Shigella* infection with transmission occurring faeco-orally through ingestion of contaminated food or water, or through close personal or sexual contact with an infected person. The infectious dose of *Shigella* is low, with possible infection following the ingestion of as few as 10 organisms. Moreover, the bacteria can survive for up to 20 days in favourable environmental conditions, enhancing the probability of transmission through contact with contaminated fomites.

Shigella sonnei, which is common in Europe and is endemic in England and Wales, is usually associated with mild illness. Shigella boydii, Shigella dysenteriae and Shigella flexneri have historically been usually associated with travel to developing countries and cause more severe disease^{1,2}.

Public health management

Shigella is a notifiable disease. Health Protection Teams and Environmental Health Officers (EHOs) routinely follow-up all cases of *S. boydii, S. dysenteriae* and *S. flexneri* in order to identify cases and contacts in risk groups that require clearance. Advice is also given on how to prevent further spread.

Epidemiology

In the past, *Shigella* infections in adults in the UK were primarily associated with travel to low-income countries, with endemic transmission due to poor sanitation, however, there has been a change in the epidemiology of shigellosis since 2009, marked by the emergence of an outbreak of *Shigella flexneri* 3a in men who have sex with men (MSM), thought to be associated with sexual transmission^{3,4}

The most recent national surveillance data suggest further intensification of *Shigella* transmission associated with sex between MSM has occurred since the 2009 outbreak⁵. The emergence of three distinct national outbreaks of *S. flexneri* 3a, *S. flexneri* 2a, and *S. sonnei* suggests at least three separate introductions of this pathogen into the MSM population over the past decade. These outbreaks have coincided with increased diagnoses of gonorrhoea, lymphogranuloma venereum (a form of chlamydia causing systemic infection) and infectious syphilis, particularly in those co-infected with HIV.

The recent cluster of verotoxin-producing *Escherichia coli* 0117:H7 among MSM also indicates that the risk of transmission is not restricted to *Shigella*, but to other highly infectious bacteria transmitted via the faeco-oral route.

We have previously reported a national outbreak and investigation of *S. flexneri* 3a occurring in MSM between 2009 and 2011³. Most of these cases were white, UK-born MSM, many were HIV-positive, and they reported being part of dense sexual networks involving high numbers of casual and regular partners. This outbreak was associated with (i) low awareness about the risk of enteric infections, (ii) chemsex (sexual activity while under the influence of [typically] stimulant drugs), and (iii) meeting sex partners and locating sex parties through social and sexual networking applications (iv) condomless sex⁶.

The use of whole genome sequencing (WGS) on *Shigella* isolates has been introduced in 2015, which has led to the identification of new clusters of genetically similar *Shigella* infections that would not otherwise be detected. In late 2015 WGS identified a number of clusters of *S. sonnei* with high proportions of adult males with no travel history which had specific antibiotic resistance profiles. Further investigation into one of these clusters centred in London has identified a number of cases to be MSM who report a variety of high risk sexual exposures during the incubation period and low awareness of *Shigella*. The *S. sonnei* in this cluster had high levels of antimicrobial resistance (Extended-spectrum beta-lactamase (ESBL) producing) typically only seen before in *Shigella* infections associated with travel and therefore imported⁷. The potential spread of antibiotic resistance found in these clusters may have implications in the treatment of enteric pathogens in the immunocompromised.

Response

PHE conducted an awareness campaign in early 2014 with the Terence Higgins Trust (THT), which included the production of posters and leaflets which are available via the PHE website⁸. A further campaign is planned for 2016 to improve awareness among MSM as well as among medical practitioners.



As an example of local work, the PHE South East health protection staff have worked with partners in Surrey and Sussex including:

- working with the local genitourinary medicine Claude Nicholl Unit to introduce questions regarding bowel habit changes as part of the sexual history, and emphasising the need to take stool specimens where appropriate
- engaging Brighton's THT outreach team to increase awareness, as they already provide condoms and advice to MSM who engage in sex on premises, attend saunas and cruising areas
- working with EHOs to increase skills in asking sexual risk questions by placements with sexual health advisors based at the Claude Nicholl Unit
- work to standardise the management of Shigella under the 'Single case plan', so both Health Protection Teams and EHOs are clear on their roles and the need for good communication links for each

Data sources

The PHE Gastro Data Warehouse (GDW) was the only data source used to produce this report. GDW reports on samples processed at the PHE Gastrointestinal Bacteria Reference Unit (GBRU). It is known that not all positive cultures are sent to GBRU for referencing; 49% of *Shigella* samples reported by laboratories in the South East from 2011 to 2015 through the laboratory reporting system were also on GDW. Please see the Appendix 1 for more information on how data was analysed.

This report only includes laboratory confirmed cases of *Shigella* aged 16 to 60 years resident in the South East PHEC. If case residence was unknown, original reporting laboratory was used as proxy. Residence information is often missing (only 54% of reports have a valid postcode).

Epidemiology

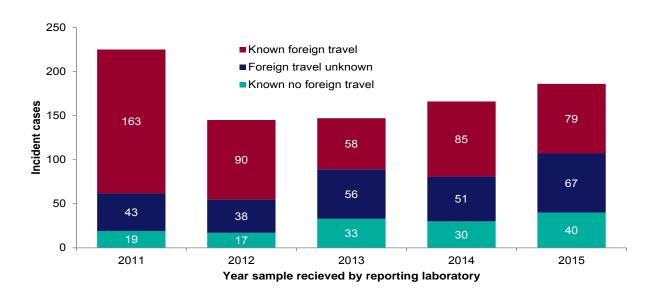
All cases

Overall the numbers of *Shigella* in the South East PHEC decreased from 225 cases in 2011 to 145 cases in 2012, with a subsequent year-on-year increase to 2015, with 186 cases (Figure 1).

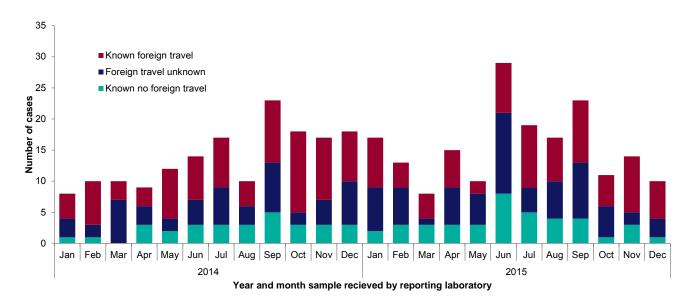
Figure 1. Cases aged 16 to 60 years diagnosed with *Shigella* infection, by foreign travel status, South East PHEC

Data source: Gastro Data Warehouse (GDW)

A) 2011 to 2015, by year



B) 2014 to 2015, by year and month



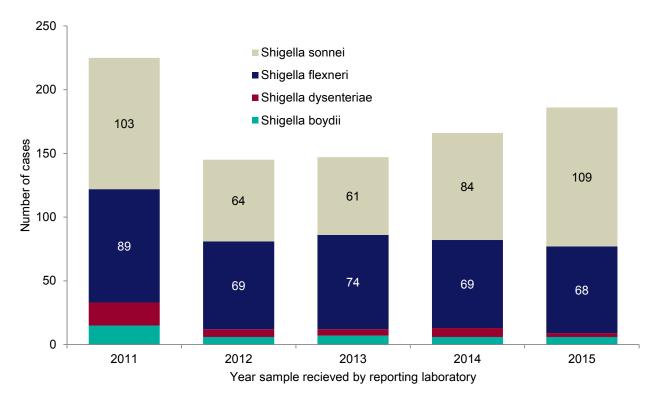
PCR testing was introduced in some laboratories in 2014 and 2015; this is a more sensitive test and is therefore more likely to detect *Shigella*. This may have resulted in an increase in the number of *Shigella* cases reported in 2014 and 2015.

S. flexneri and *S. sonnei* were the most commonly reported species each year between 2011 and 2015, 37% and 59% in 2015 respectively. The number of *S. sonnei* cases decreased from 2011 (103 cases) to 2012 (64 cases), but subsequently increased to 109 cases in 2015 (Figure 2). The proportion of all reported *Shigella* cases that are *S. sonnei* has increased from 51% to 59% from 2014 to 2015.

Numbers of *S. flexneri* cases have decreased from 2011 (89 cases) to 2015 (68 cases), with a steady number of cases reported since 2012. *S. dysenteriae* and *S. boydii* were less common, these species represent a combined total of 9% of cases between 2011 and 2015 (Figure 2). Numbers of *S. dysenteriae* and *S. boydii* decreased from 2011 to 2012 and the number of reported cases has remained steady.

Figure 2. Cases aged 16 to 60 years diagnosed with *Shigella* infection, by species, South East PHEC 2011 to 2015





Foreign travel

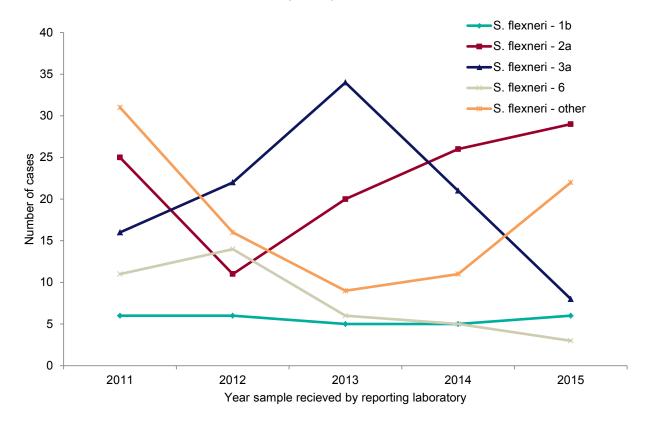
The travel status of 29% cases is not explicitly known. The number of *Shigella* cases known to be associated with foreign travel reduced by 52% between 2011 (163 cases) and 2015 (79 cases) (Figure 1).

No known foreign travel

There was no clear trend in the number of cases not known to be associated with foreign travel between 2011 (62 cases) and 2014 (81 cases) (Figure 1), however this number has increased to 107 in 2015. The proportion of cases where there is no information on foreign travel constitutes 66% of cases where there is no known foreign travel.

Among cases in adults diagnosed without a known history of foreign travel there was a marked rise in *S. flexneri* 3a in 2013 and a subsequent decline in 2014 and 2015. After two years of increases, *S. flexneri* 2a replaced 3a as the most common serotype in 2014 and this has persisted into 2015 (Figure 3).

Figure 3. Cases aged 16 to 60 years diagnosed with *Shigella flexneri*, no known history of travel outside the UK, by serotype, South East PHEC 2011 to 2015 Data source: Gastro Data Warehouse (GDW)

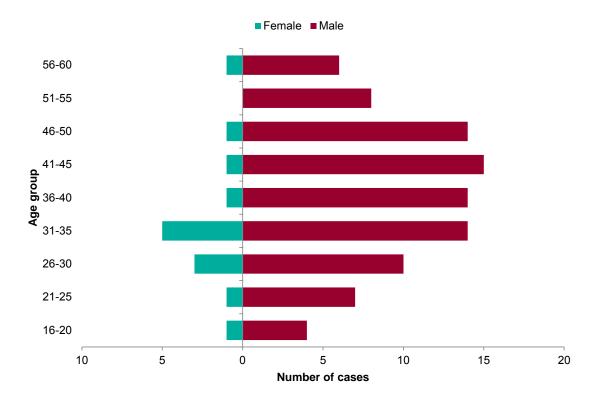


Excess of adult males without a known history of foreign travel

In 2015 the number of *Shigella* cases was highest among males aged 41 to 45 years, with the majority of cases between males aged 31 to 50 years (Figure 4).

Figure 4. Age and sex distribution of cases aged 16 to 60 years diagnosed with *Shigella* infection, with no known history of travel outside the UK, South East PHEC, 2015

Data source: Gastro Data Warehouse (GDW)



There is a clear excess of adult male cases of *Shigella* in those without a known history of foreign travel among cases where sex is known. This has increased notably in recent years and these increases persisted in 2015.

- in 2015 there were 78 excess adult male cases of *Shigella* (compared to females), nearly a ten-fold increase from 2011 (n=8) (Figure 5)
- the proportion of male cases has increased from 2011 (56%) to 2015 (87%)
 (Table 1)
- the ratio of male to female cases increased year-on-year between 2011 (1.3:1 male to female cases) and 2015 (6.6:1) (Table 1)

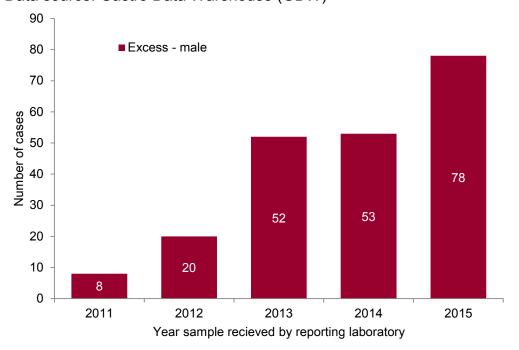
Table 1. Sex ratio and excess male cases aged 16 to 60 years diagnosed with *Shigella* infection, with no known history of travel outside the UK, where sex is known, South East PHEC, 2011 to 2015, sex ratios greater than 2.0 shaded red¹

Data source: Gastro Data Warehouse (GDW)

Shigella species	Serotype	Sex, sex ratio, excess male cases	2011	2012	2013	2014	2015	Total
S. flexneri	1b	Male	1	3	4	3	1	12
		Female	0	0	1	0	0	1
		Ratio	∞	∞	4.0	∞	∞	12.0
		Excess male	1	3	3	3	1	11
	2a	Male	2	1	11	14	19	47
		Female	3	3	0	2	2	10
		Ratio	0.7	0.3	∞	7.0	9.5	4.7
		Excess male	-1	-2	11	12	17	37
	3а	Male	6	10	29	14	5	64
		Female	3	1	1	0	0	5
		Ratio	2.0	10.0	29.0	∞	∞	12.8
		Excess male	3	9	28	14	5	59
	6	Male	1	3	2	0	1	7
		Female	1	4	1	0	0	6
		Ratio	1.0	0.8	2.0	-	∞	1.2
		Excess male	0	-1	1	0	0	1
	Other	Male	5	3	5	7	10	30
		Female	3	2	1	1	2	9
		Ratio	1.7	1.5	5.0	7.0	5.0	3.3
		Excess male	2	1	4	6	8	21
	NA	Male	18	16	18	27	56	135
S. sonnei		Female	14	5	13	8	8	48
		Ratio	1.3	3.2	1.4	3.4	7.0	2.8
		Excess male	4	11	5	19	48	87
S. boydii	NA	Male	1	1	1	1	0	4
		Female	1	2	1	1	2	7
		Ratio	1.0	0.5	1.0	1.0	0.0	0.6
		Excess male	0	-1	0	0	-2	-3
S. dysenteriae	NA	Male	1	0	0	0	0	1
		Female	2	0	0	1	0	3
		Ratio	0.5	-	-	0.0	-	0.3
		Excess male	-1	0	0	-1	0	-2
All	NA	Male	35	37	70	66	92	300
		Female	27	17	18	13	14	89
		Ratio	1.3	2.2	3.9	5.1	6.6	3.4
		Excess male	8	20	52	53	78	211

¹ Sex ratio is the ratio of male to female cases, excess male cases is the difference between the number of male and female cases.

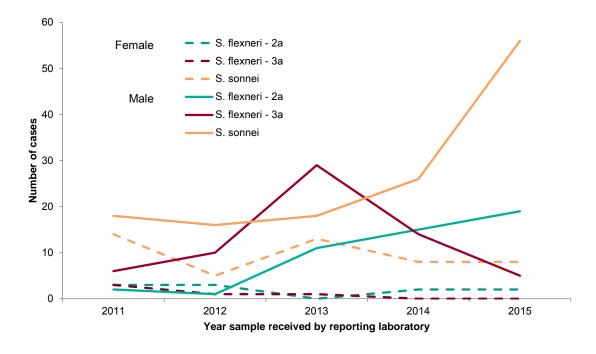
Figure 5. Excess male cases aged 16 to 60 years diagnosed with *Shigella* with no known history of travel outside the UK, by sex, South East PHEC, 2011 to 2015 Data source: Gastro Data Warehouse (GDW)



The most notable recent increases in adult male cases have been in *S. flexneri* 2a and *S. sonnei* cases (Figure 6).

Figure 6. Cases aged 16 to 60 years diagnosed with *Shigella flexneri* serotypes 2a and 3a and *Shigella sonnei*, with no known history of travel outside the UK, by sex, South East PHEC 2011 to 2015

Data source: Gastro Data Warehouse (GDW)



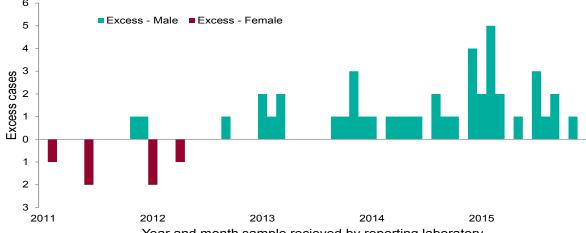
The number of male *S. flexneri* 2a cases increased in 2013 (11 cases) and 2014 (15 cases) compared to recent years (mean of 2 cases between 2011 and 2012). Higher numbers of male *S. flexneri* 2a were reported in 2015 (19 cases) (Figure 6). High numbers of excess male cases of *S. flexneri* 2a were reported in late 2014 and early 2015 (Figure 7).

The number of male *S. sonnei* cases increased in 2014 (26 cases) compared to recent years (mean of 17 cases between 2011 and 2013). Relatively high numbers of male *S. sonnei* cases were reported in 2015 (56 cases), more than a two-fold increase from 2014 (Figure 6). The number of excess male cases of *S. sonnei* increased in 2015 (Figure 7).

Figure 7. Excess male and female cases aged 16 to 60 years, with no reported history of travel outside the UK, by sex, South East PHEC, 2011 to 2015

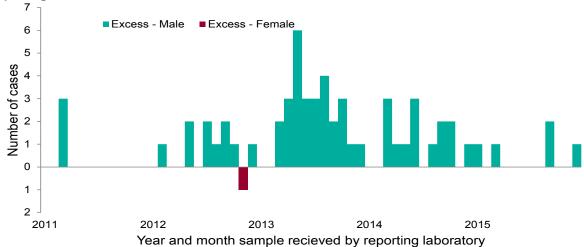
Data source: Gastro Data Warehouse (GDW)

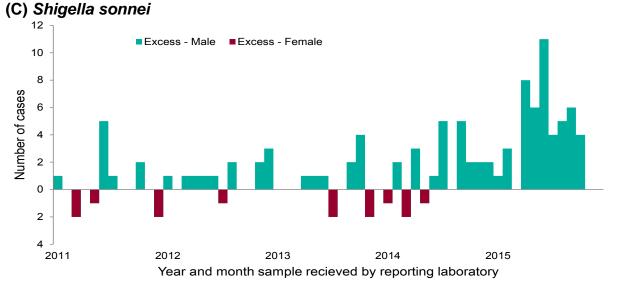
(A) Shigella flexneri 2a



Year and month sample recieved by reporting laboratory

(B) Shigella flexneri 3a



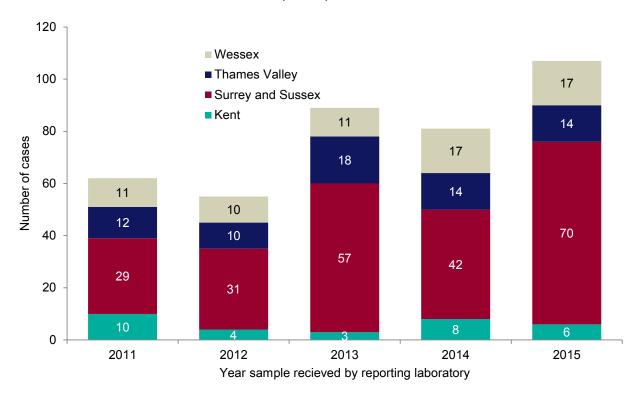


Breakdown by of cases with no known foreign travel by Health Protection Team

The epidemiology differs across different Health Protection Teams (HPTs) in the South East PHEC. The largest number of cases of *Shigella* with no known travel in those aged 16 to 60 years is in Surrey and Sussex, which comprises 65% of cases with no known travel in the South East in 2015 (Figure 8). There has been an increase in the number of cases in Surrey and Sussex from 29 cases in 2011 to 70 cases in 2015. The number of cases has also increased in Wessex from 11 in 2011 to 17 in 2015. There is no discernible trend in the number of cases in Thames Valley or Kent.

Figure 8. Cases aged 16 to 60 years diagnosed with *Shigella* infection with no known history of travel outside the UK, by Health Protection Team, South East PHEC, 2011 to 2015

Data source: Gastro Data Warehouse (GDW)



There has been an increase in the number of excess male cases of *S. flexneri* 2a in cases in Surrey and Sussex from no cases in 2011 to 11 in 2015 (Figure 9). Numbers are too small to determine a trend in Kent, Wessex and Thames Valley.

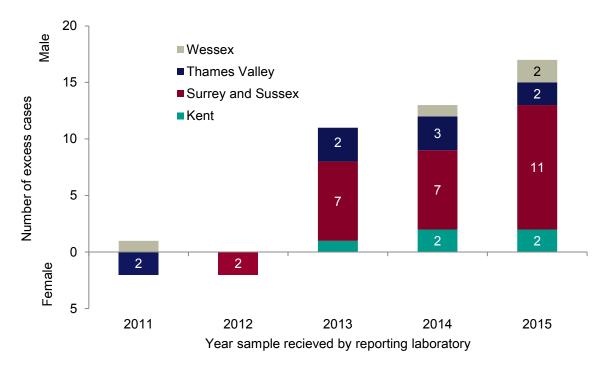
The increase of excess male *S. flexneri* 3a cases with no known foreign travel in 2013 was predominately due to Surrey and Sussex (21 cases), with small numbers of excess male cases in Kent, Wessex and Thames Valley (Figure 9). The large number of cases in Surrey and Sussex is likely due to the large population of MSM living in Brighton and surrounding areas (Figure 10).

Surrey and Sussex has had a large increase in the number of *S. sonnei* excess male cases with no known foreign travel, from five cases in 2011 to 34 cases in 2015 (Figure 9). The number of excess male cases has also increased in Wessex from two cases in 2011 to 8 cases in 2015. Thames Valley has a small number of excess male cases in 2015 (2 cases) after having excess female cases from 2011 to 2012. There is no discernible trend in Kent.

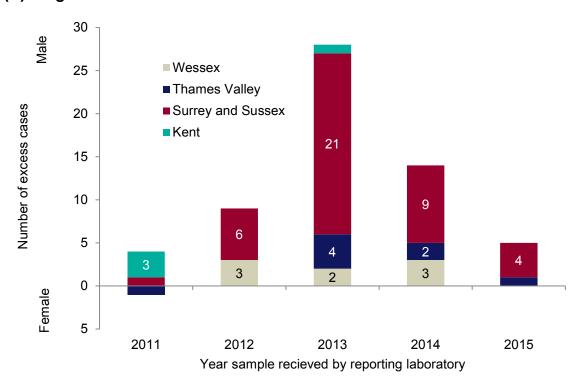
Figure 9. Excess male and female cases aged 16 to 60 years, with no reported history of travel outside the UK, by Health Protection Team, South East PHEC, 2011 to 2015

Data source: Gastro Data Warehouse (GDW)

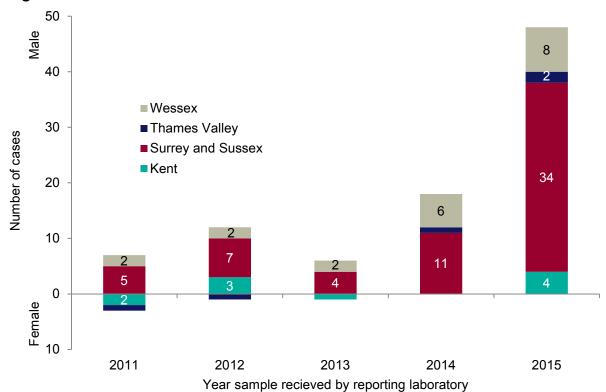
(A) Shigella flexneri 2a



(B) Shigella flexneri 3a



(C) Shigella sonnei



Breakdown by of male cases with no known foreign travel by local authority

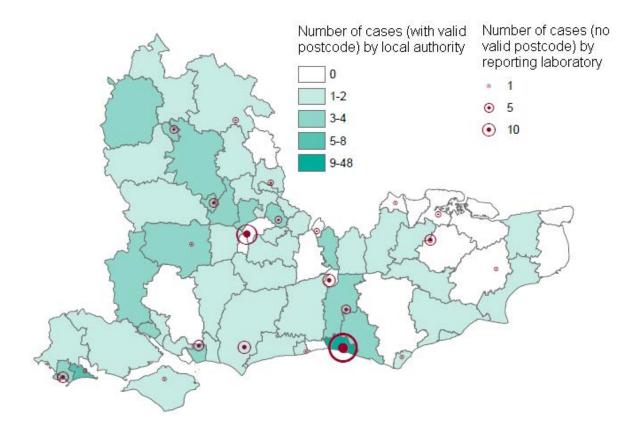
The spread of adult male cases with no known travel history is displayed in Figure 10. Please note that 42% of male cases with no known foreign travel do not have valid postcode so their local authority of residence is unknown and they will be assigned to the laboratory of testing.

Of cases with no valid postcode, the laboratory at Brighton Hospital has reported the highest number of Shigella infections during this period (45 cases).

In 2011 to 2015, Brighton and Hove had the largest number of cases of diagnosed Shigella infection in males with no known foreign travel with valid UK (48 cases) (Figure 10). Eighteen local authorities across the South East did not have any cases of diagnosed Shigella in males with no known foreign travel during this period with valid postcodes, half of which are in Kent.

Figure 10. Thematic map of male cases of diagnosed *Shigella* infection aged 16 to 60 years, with no reported history of travel outside the UK, by local authority of residence where known, or by reporting laboratory where local authority of residence is unknown, South East PHEC, 2011 to 2015

Data source: Gastro Data Warehouse (GDW)



Conclusion

Overall numbers of *Shigella* have gradually increased in the South East PHEC over the past four years, after a decrease in 2012 which was most likely due to a decline in the number of people being infected abroad. The subsequent increase is attributable to an increase in the number of cases with no known travel.

The numbers of cases in the South East PHEC without a known travel history in 2015 was higher than from 2011 to 2014. There has been a clear rise in the number of excess adult male *Shigella* cases, which points to a likely increase in transmission among MSM. In 2015, there was an excess of 78 adult male cases without a known travel history, and adult males represented 87% of all non-travel *Shigella* cases. Among adult males, the most notable increases have been in *S. flexneri* 3a cases in 2013, *S. flexneri* 2a in 2014 and 2015 and *S. sonnei* cases in 2015. This is consistent with the national picture.

The majority of cases in the South East were in Surrey and Sussex, many of whom live in or were diagnosed in Brighton. This is likely due to the large MSM population in Brighton. The trends in cases with no known foreign travel in Surrey and Sussex of *S. flexneri* 2a, *S. flexneri* 3a and *S. sonnei* are in keeping with national trends that have been ascribed to sexual transmission between MSM. There is a clear excess of male cases in Kent, Thames Valley and Wessex, however numbers of cases are smaller and trends of *S. flexneri* 2a, *S. flexneri* 3a and *S. sonnei* are harder to interpret.

Further interagency work is required to monitor and respond to the burden of illness in MSM, to improve our understanding of risk taking behaviour and to develop targeted health messages in a format that will reach the most at risk MSM.

In order to reduce transmission in this group, work is needed to raise awareness among MSM at a national and local level, regarding how to prevent acquisition and recognise symptoms as being sexually transmitted. This follows recommendations from previous investigation of MSM cases which highlighted a low level of awareness. Materials are available on the PHE website for this purpose. Health protection teams and clinicians can also take opportunities to provide information to cases on how to prevent further spread.

Appendix 1. Data management

- 1. Data source: Gastro Data Warehouse (GDW).
- 2. Date data extracted: data extracted 22 January 2016.

3. Inclusion criteria:

- a. Laboratory confirmed Shigella infection cases reported to GDW.
- b. Cases resident in the South East PHEC, if case residence unknown, original reporting laboratory in the South East PHEC.
- c. Cases with sample date between 01/01/2011 to 31/12/2015 (inclusive).
- d. Cases aged between 16 and 60 years.

4. Exclusion criteria:

- a. Records were de-duplicated based on first name and surname; if a given individual was reported more than once within a 14 day period the record with the earliest sample date was preserved and other records excluded.
- b. Records with missing date of birth were excluded.

5. Modifications:

- a. Sample receipt date was used if sample date was missing.
- **6. Caveats:** not all positive cultures are sent to the Gastrointestinal Bacteria Reference Unit (GBRU), therefore the data held in GDW is a subset of the true number of positive results reported in PHE South East. Cases where sex is unknown (n=5 from 2011 to 2015 among those with no known foreign travel) are excluded from figures and calculations when data is presented by sex.

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About Field Epidemiology Services

The Field Epidemiology Service (FES) supports Public Health England Centres and partner organisations through the application of epidemiological methods to inform public health action.

FES does this in two main ways, firstly by providing a flexible expert resource, available, as and when needed, to undertake epidemiological investigations for key health protection work and secondly through the expert analysis, interpretation and dissemination of surveillance information to PHE Centres, local health partners, service providers and commissioners of services.

Within the FES network, excellence and innovation is encouraged, we foster academic collaborations and take active part and lead in research, development and training.

You can contact your local FES team at fes.seal@phe.gov.uk

If you have any comments or feedback regarding this report or the FES service, please contact fes.seal@phe.gov.uk