

# INCREASING RESISTANCE IN S.SONNEI

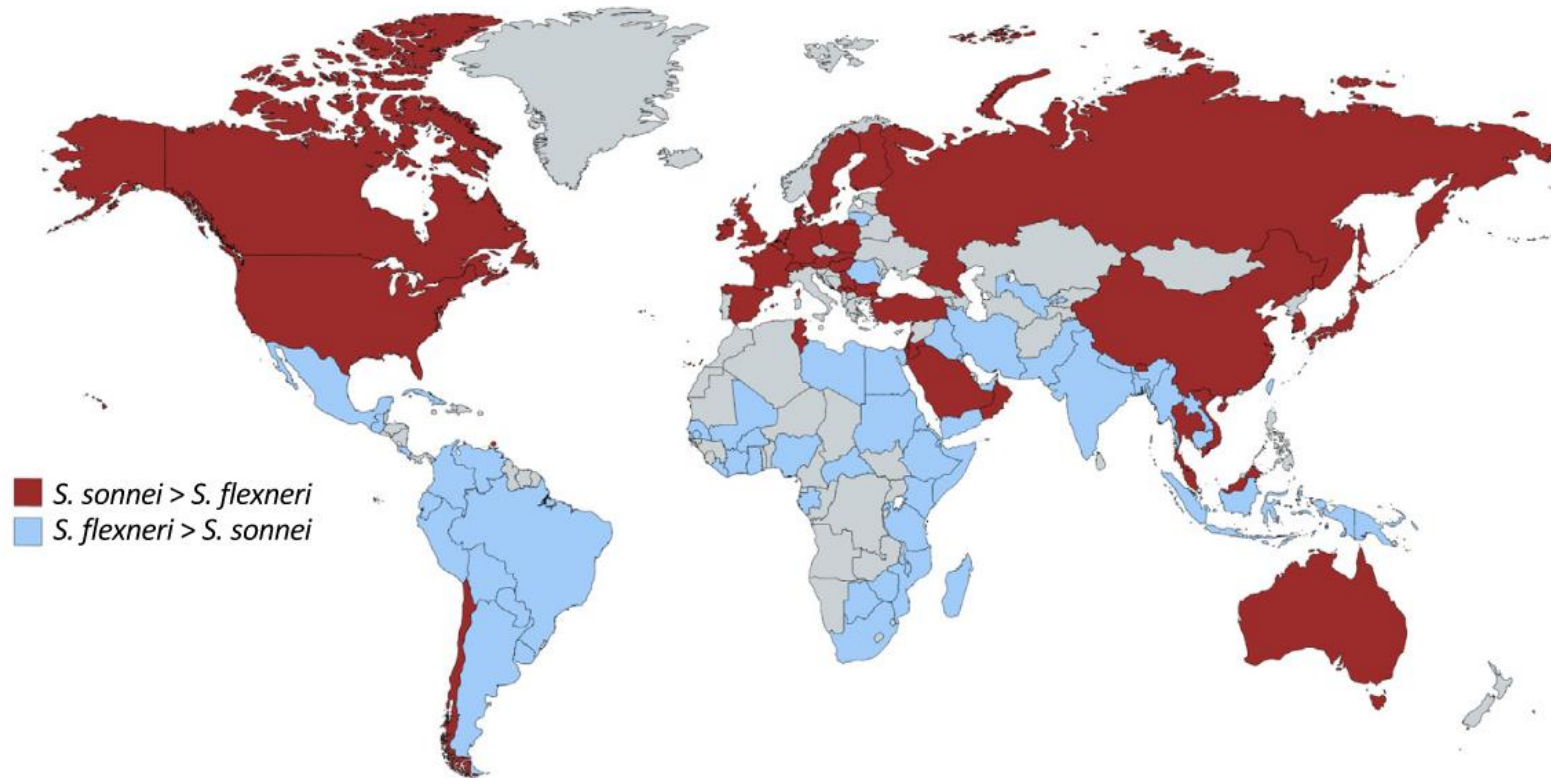
NRC Salmonella & Shigella

Pieter-Jan Ceysens

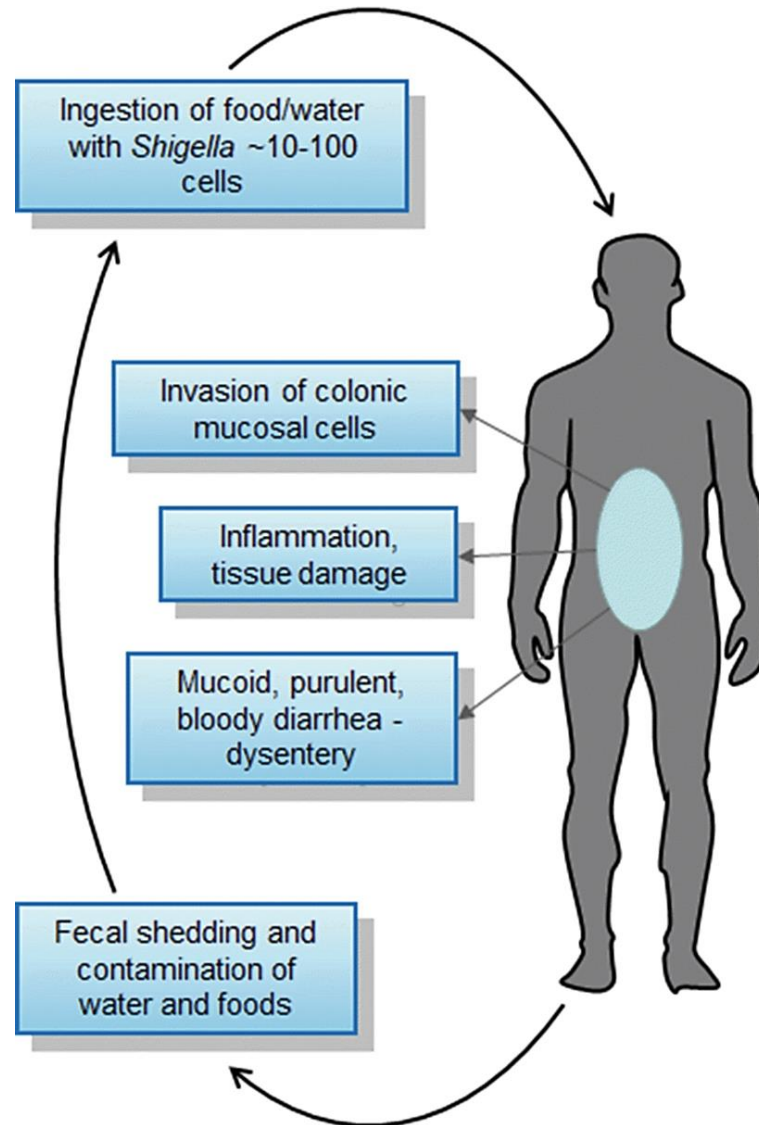
SSID, May 19<sup>th</sup> 2022

## Introduction

*Shigella* are Gram-negative pathogenic Enterobacterales



## Clinical manifestations



### Symptoms

- (bloody) diarrhea
- abdominal pain or cramps
- Fever

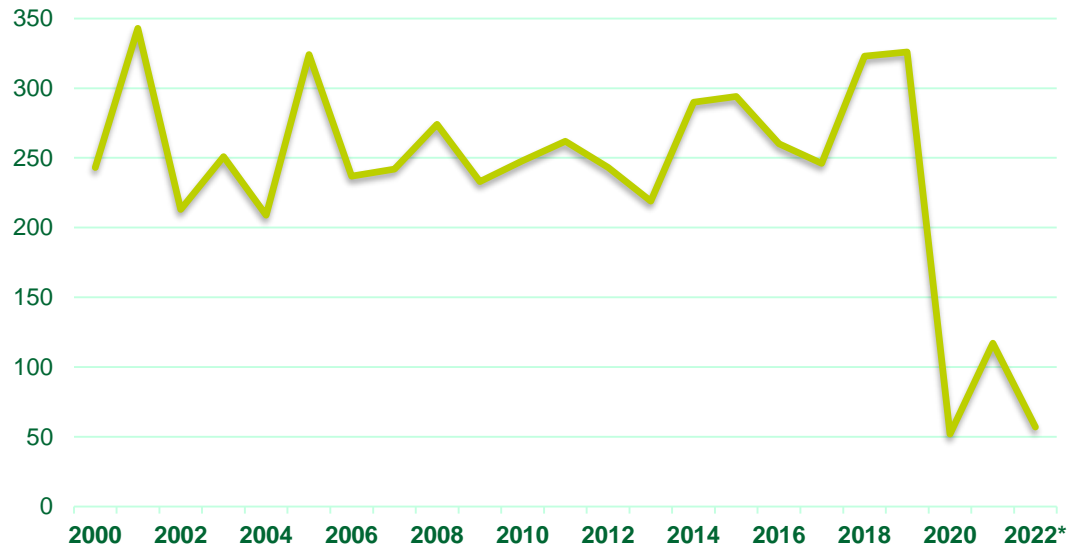
### Complications

- Dehydration
- Seizures
- Rectal prolapse
- Toxin megacolon
- Reactive arthritis

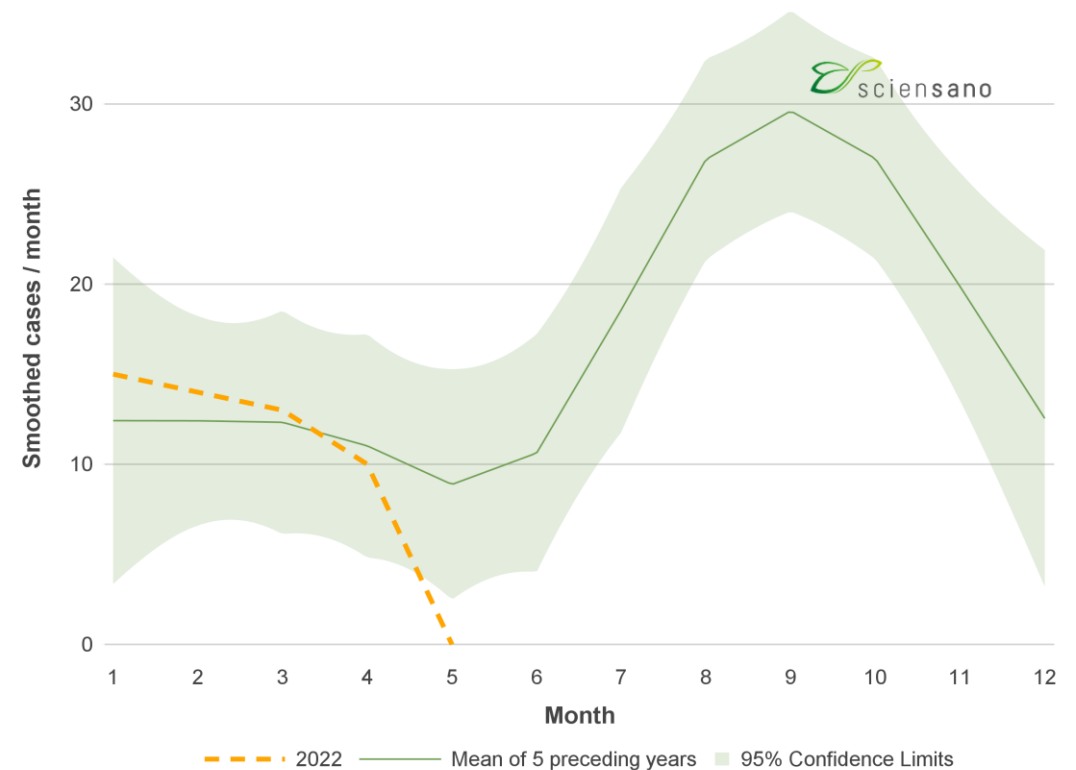
### Recommended treatment

Azithromycin (500mg 3d)

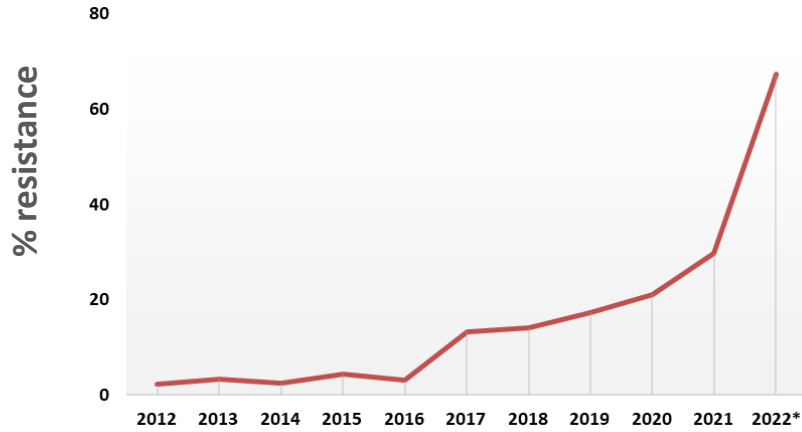
## S. Sonnei: Epidemiology in Belgium



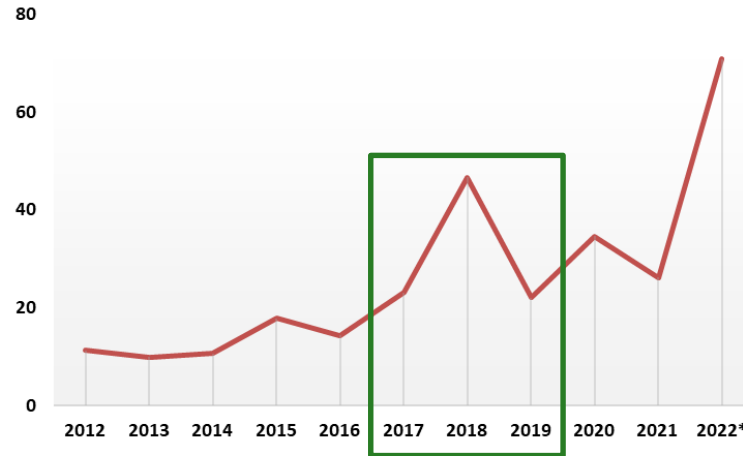
Very stable prevalence,  
until March 2020



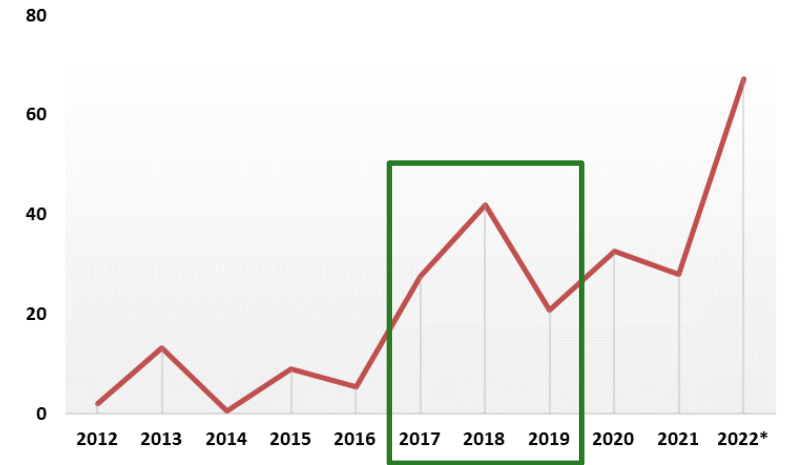
# Strong increase in resistance of *S. sonnei* to oral antibiotics



Cefotaxime



Ciprofloxacin



Azithromycin

Journal of  
Antimicrobial  
Chemotherapy

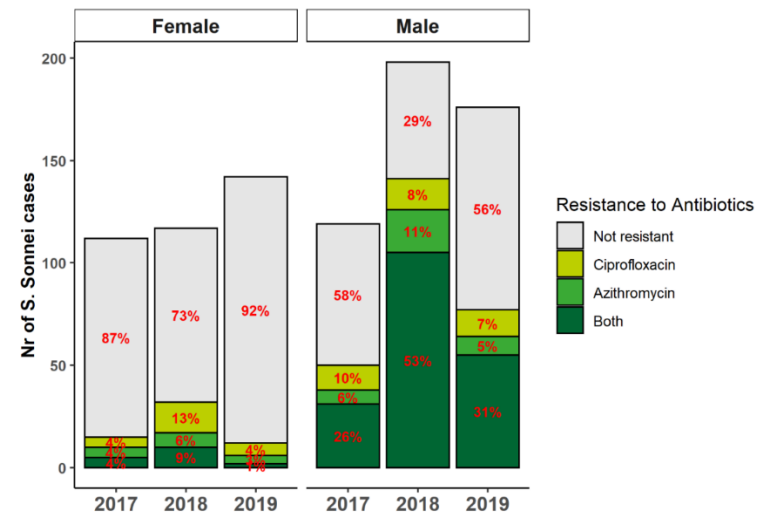
J Antimicrob Chemother  
<https://doi.org/10.1093/jac/dkab377>

## Genomic epidemiology of persistently circulating MDR *Shigella sonnei* strains associated with men who have sex with men (MSM) in Belgium (2013–19)

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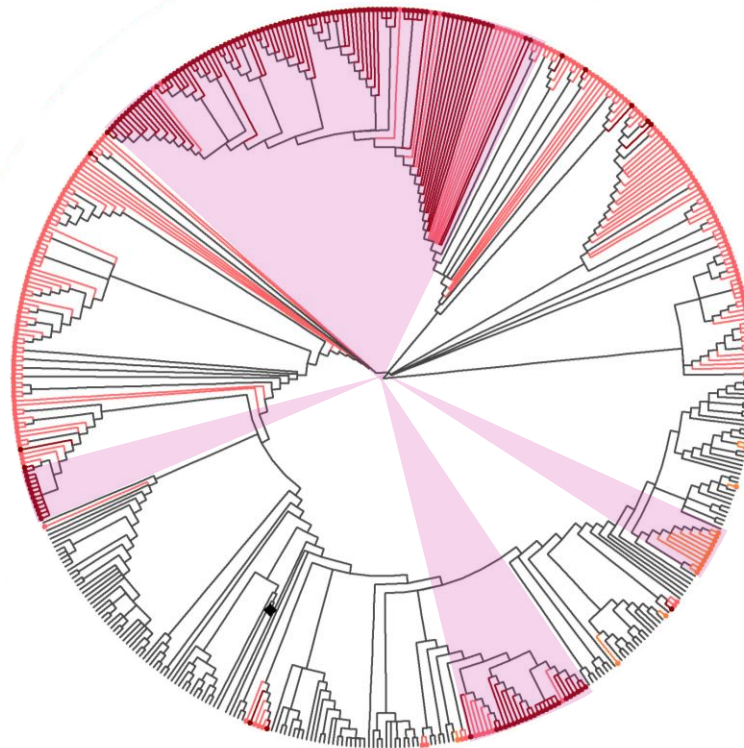
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## Results: Phylogenetic analysis reveals several distinct clusters with double resistance to first-line antibiotics

### Antibiotic resistance

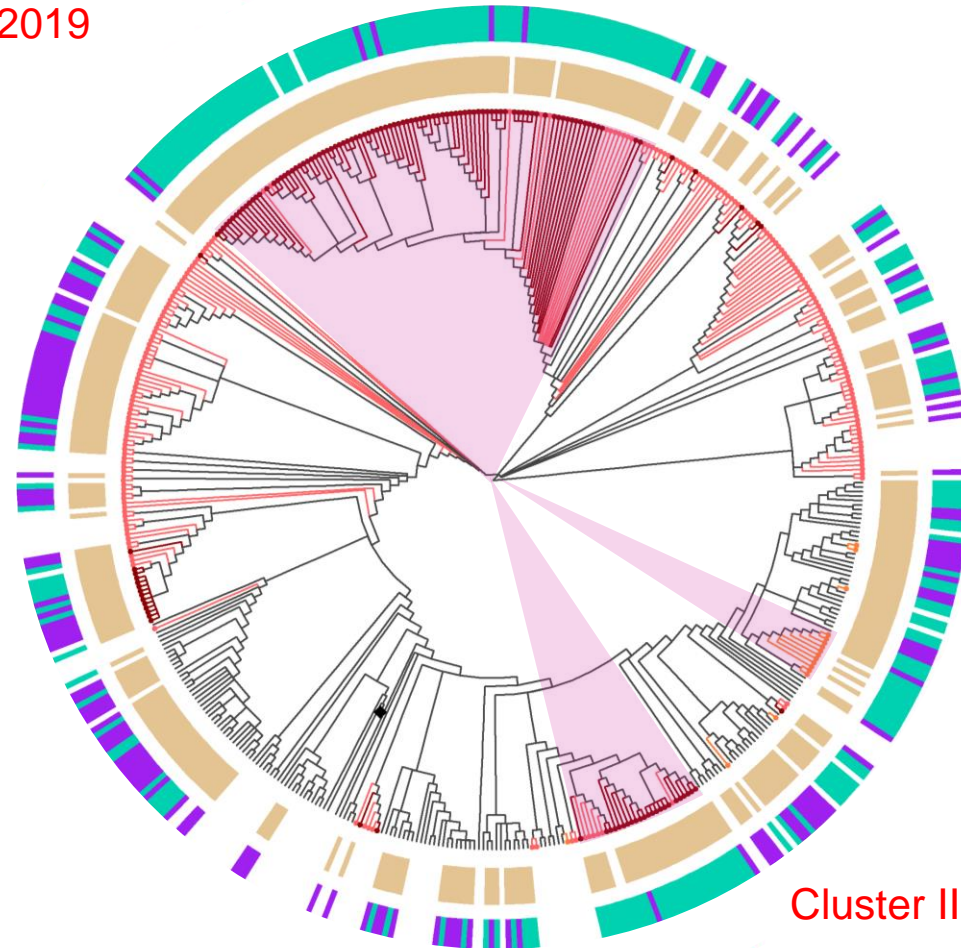
- Both
- Azithromycin
- Ciprofloxacin



# Results: Resistant clusters are predominantly comprised of male cases

Cluster I: 102 cases, 94% ♂  
2015-2019

Gender ■ Male ■ Female



Antibiotic resistance

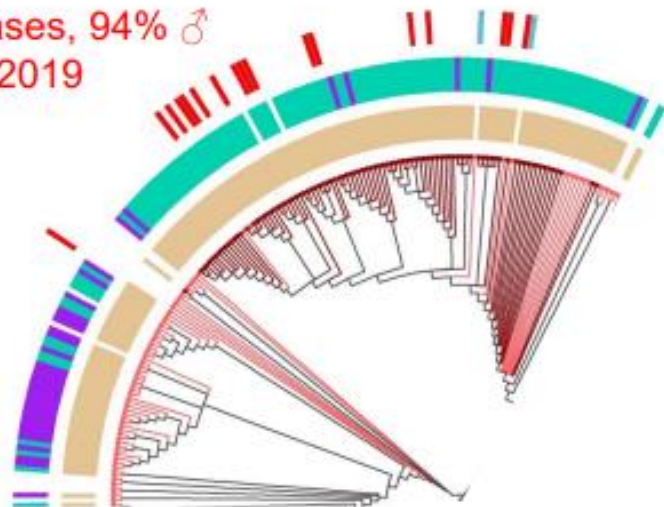
- Both
- Azithromycin
- Ciprofloxacin

NRC Belgium ■ Yes

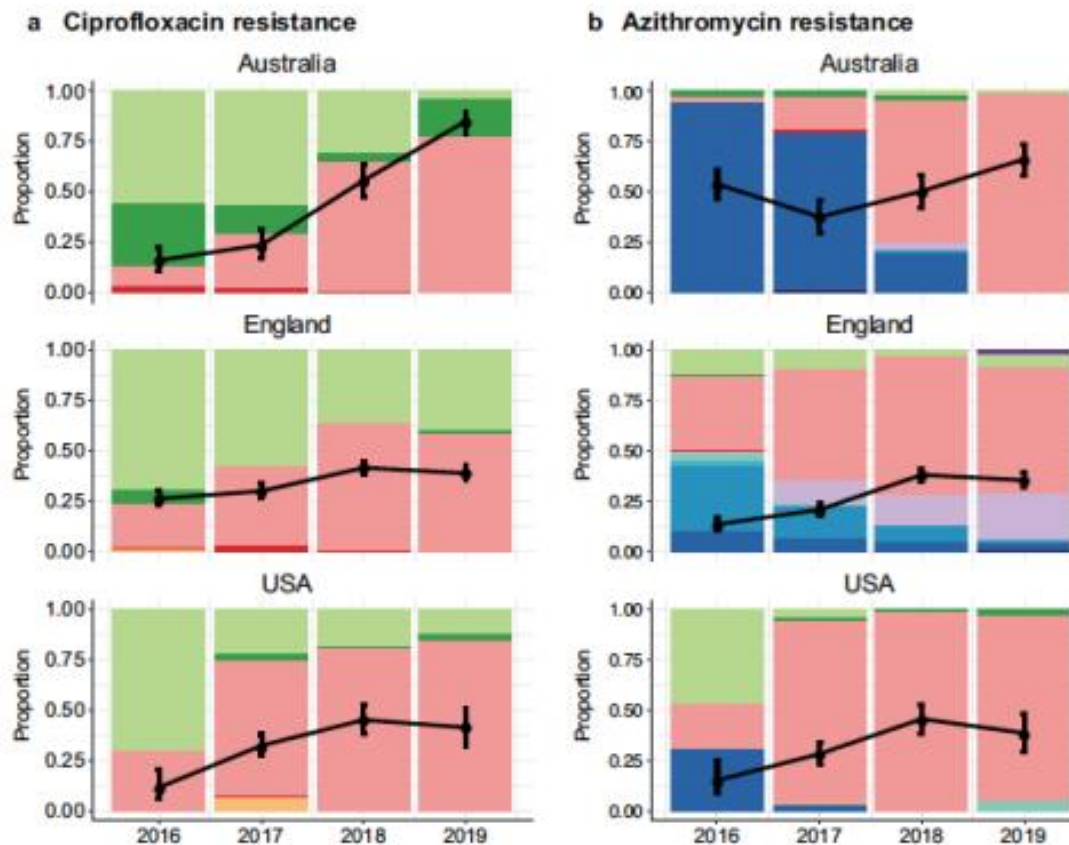
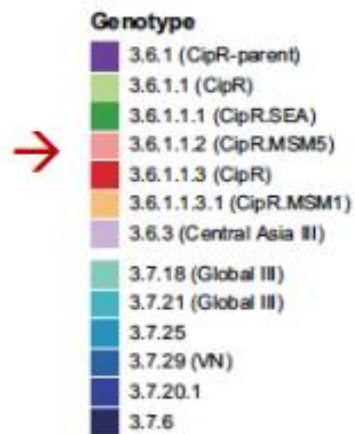
Cluster III: 12 cases, 92% ♂  
2013-2018

Cluster II: 21 cases, 95% ♂  
2015-2019

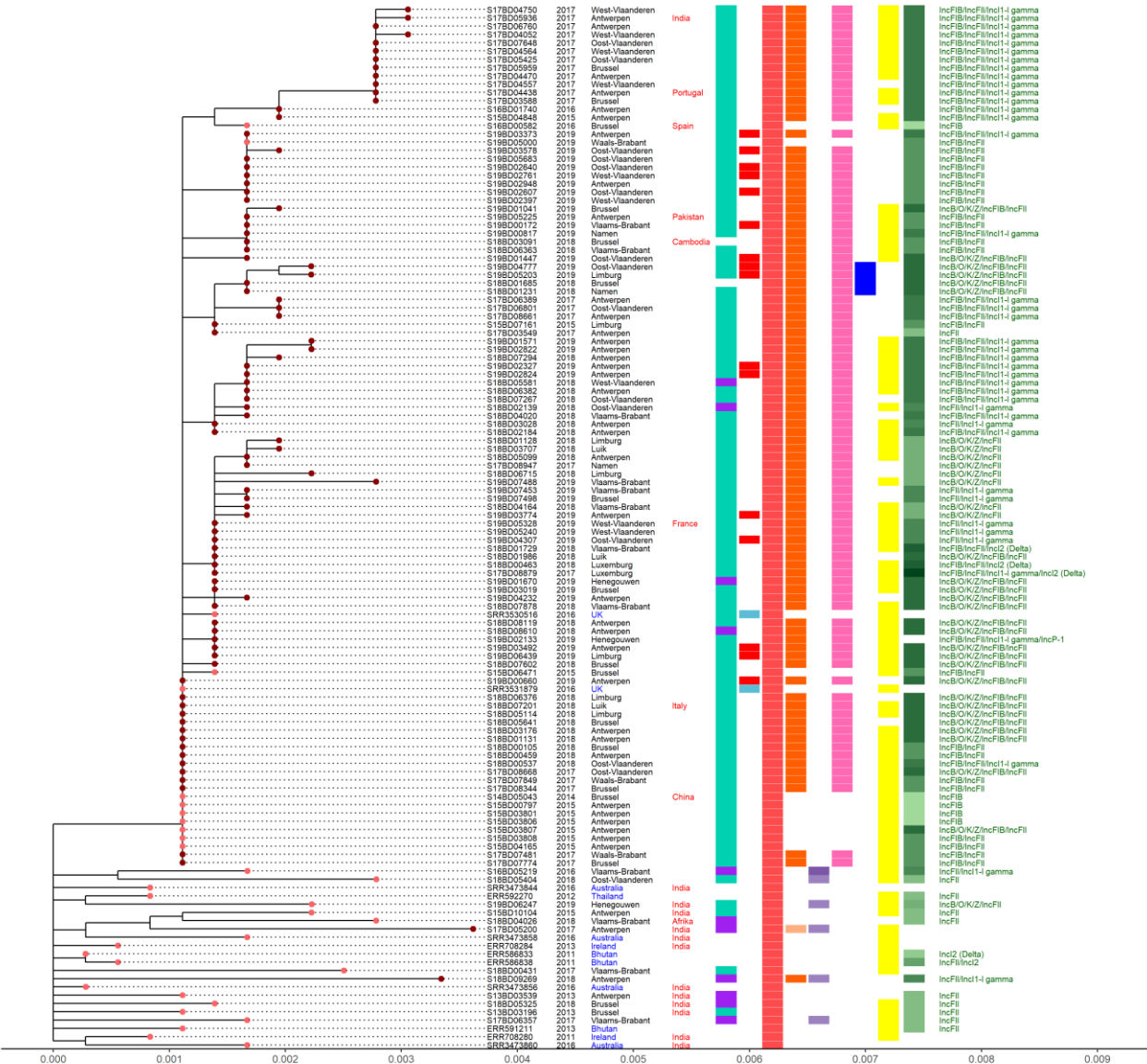
Cluster I: 102 cases, 94% ♂  
2015-2019



Lineage 3.6.1.1.2 dominates globally among MSM







Enormous variety in plasmidome, despite chromosomal relatedness

**Ciprofloxacin resistance** ■ *gyrA* d87g/gyrA s83jparc s80

**SpA** ■ Yes ■ No

**Tn7/Int2** ■ Yes ■ No

**PKSR100 plasmid** ■ Yes ■ No

**MSM Association** ■ MSM Belgium ■ Former MSM UK Clade 7

**Inc plasmids**

- IncFIB/IncFII/IncI1-gamma/IncI2 (Delta)
- IncFIB/IncFII/IncI2 (Delta)
- IncFIB/IncFII/IncB/O/K/Z
- IncFIB/IncFII/IncI1-gamma
- IncFII/IncI1-gamma
- IncFII/IncI2
- IncFII/IncB/O/K/Z
- IncFII
- IncI2 (Delta)
- IncFII/IncI2
- IncFII/IncI1-gamma
- IncFII

**Antibiotic resistance** ● *RSA* & *CipR* ● *CipR*

**Azithromycin resistance** ■ *mphA* ■ *mphA* & *ermB*

**Gender** ■ Male ■ Female

**ESBL genes** ■ *blaCTX-m-55* ■ *blaCTX-m-15*



Public Health  
England

Protecting and improving the nation's health

**Multi-drug resistant *Shigella sonnei*  
cluster (CTX-M-27) probably associated  
with MSM**

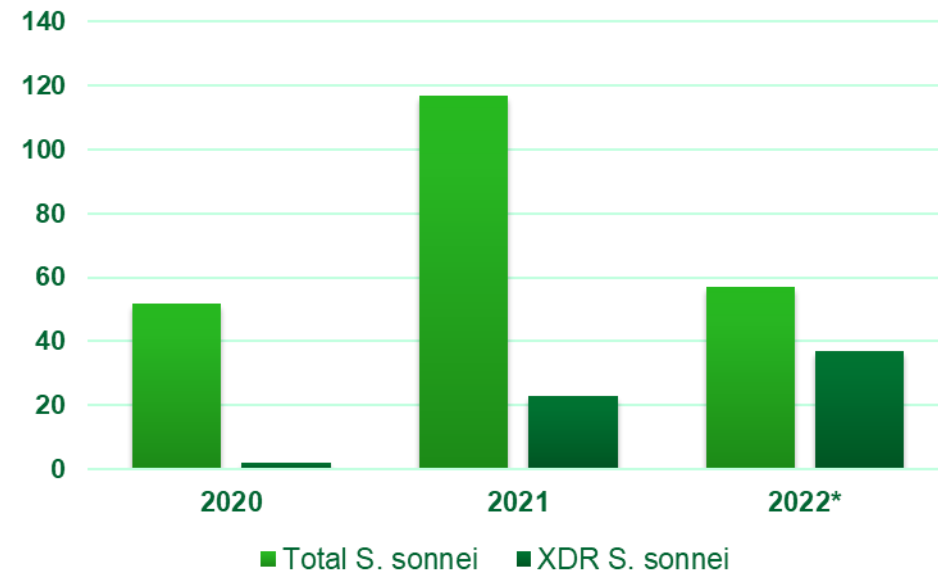
### RESISTANT

- Cephalosporins
- Macrolides
- Fluoroquinolones

### SUSCEPTIBLE

- Carbapenems
- Colistine
- Aminoglycosides

Lineage 3.6.1.1.2 with IncFII plasmid with  
*bla*<sub>CTX-M-27</sub>, *ermA* and *qnrB*



Tree scale: 1000

**blaCTX-M-27**

Present

**Country**

England

Australia

USA

Belgium

**Isolation Year**

2014

2015

2016

2017

2018

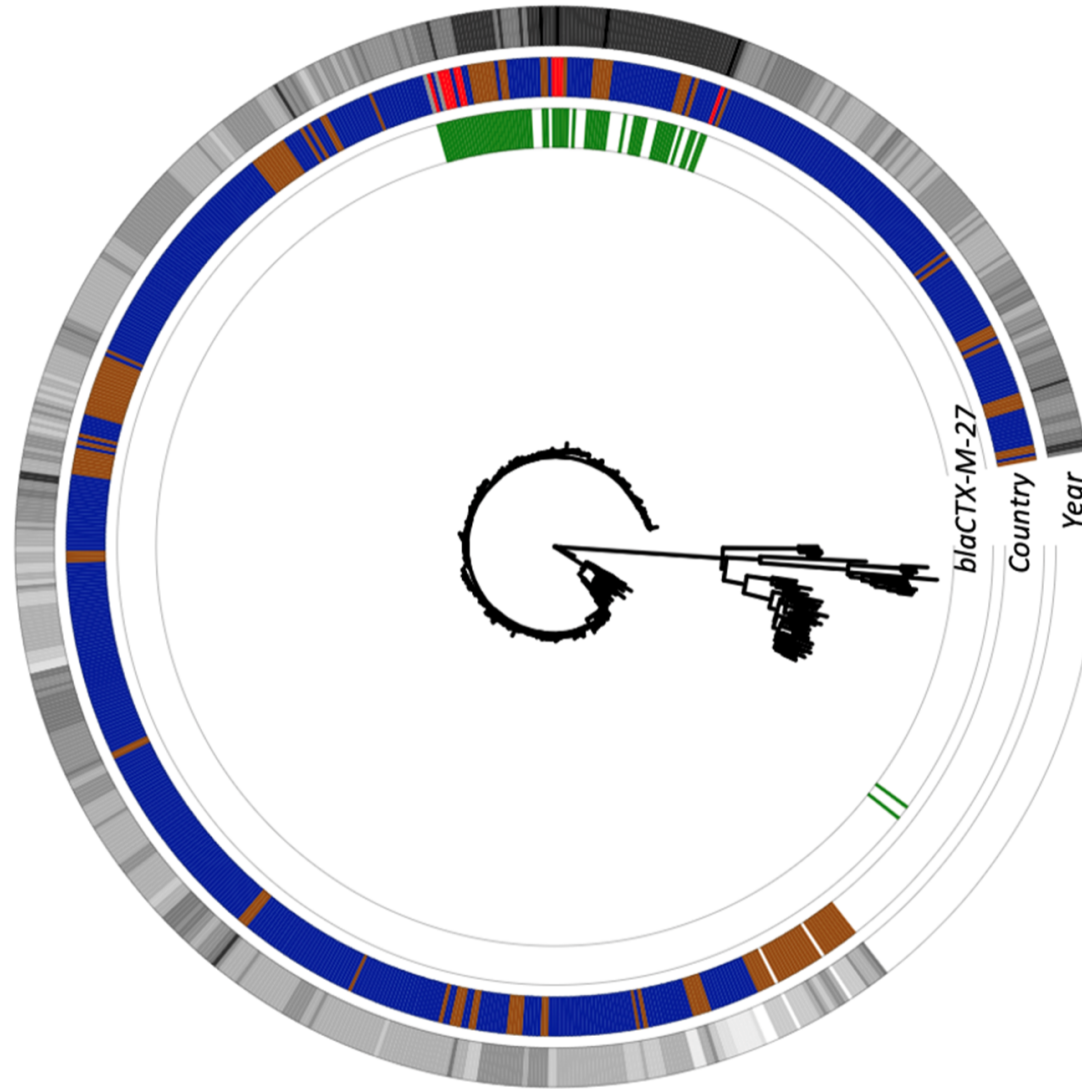
2019

2020

2021

2022

Extremely successful clone globally



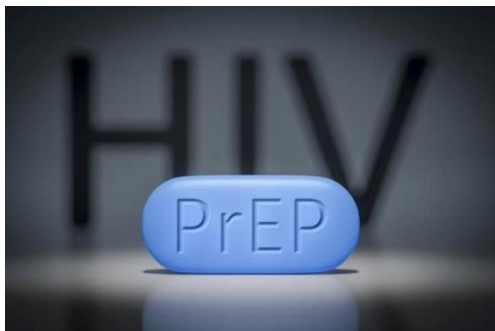
# Sensoa start campagne in homomilieus om te waarschuwen voor darmbacterie shigella

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## Conclusions

- WGS identified several successive/parallel clusters of **multi-drug resistant *S. sonnei*** strains which are circulating in the **MSM-community**
- International emergence of successful clone 3.6.1.1.2
- 70% of *S. sonnei* isolates in 2022 are resistant to main oral drugs (cephalosporins, macrolides & FQ) - Consider revising macrolides as first line
- Similar trend to macrolide resistance in *N. gonorrhoeae* ;



2017-  
Link with recurrent (a)symptomatic treatments of Chlamydia and Gonorrhoea with azithromycin +/- ceftriaxone ?



Figure 20. Evolution of ciprofloxacin (orange) and macrolide (grey) resistance in *N. gonorrhoeae* isolates sent to the NRC for typing, between 2011 and 2020.

## Acknowledgements



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- Margo Maex



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- Valeska Laisnez



- Kate Baker
- Lewis Mason



- Natalie Fischer