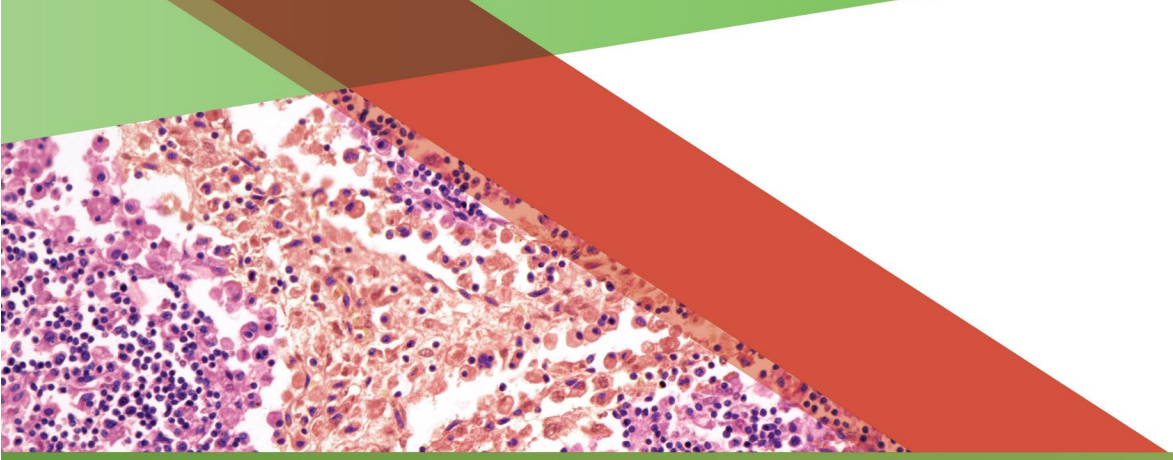

SURVEILLANCE REPORT

Typhoid and paratyphoid fever

Annual Epidemiological Report for 2019

Key facts

- Typhoid and paratyphoid fevers are severe systemic diseases which are relatively rare in the EU/EEA and mainly acquired during travel to countries outside the EU/EEA, particularly South Asia.
- In 2019, 24 EU/EEA countries reported a total of 1 439 cases of typhoid and paratyphoid fever. The EU/EEA notification rate was 0.37 cases per 100 000 population.
- Of the 1 114 cases with available information, 92.4% were related to travel, with Pakistan and India as the two main travel destinations.
- In 2019, 10 countries reported travel-associated cases with an extremely drug-resistant *Salmonella* Typhi (*S.* Typhi). These were related to the typhoid fever outbreak ongoing in Pakistan since 2016. This poses an issue for treatment, as the strain is resistant to all the antimicrobials which are normally used in the treatment of typhoid fever. It only remains susceptible to azithromycin, carbapenems, and tigecycline.
- Cases in the EU/EEA showed clear seasonal trends, with a pronounced peak in September and a small peak in late spring, likely related to travel patterns.
- Although vaccines against typhoid fever are available, it was still more frequently reported than paratyphoid fever, for which no vaccines are yet available.

Introduction

Typhoid and paratyphoid fevers are severe systemic diseases caused by the bacteria *Salmonella* Typhi and *Salmonella* Paratyphi. Humans are the reservoir for these bacteria. Transmission occurs via food or water contaminated with the faeces of an infected person, or via direct person-to-person contact.

After an incubation period of 1–2 weeks, a disease develops which is characterised by high fever, malaise, cough, rash, and an enlarged spleen. Diarrhoea may be present at some stage, but constipation can also be present in adults. When *Salmonella* Typhi is the cause of infection, intestinal perforation and haemorrhage may occur. Bloodstream infections are common, and various organs can be affected by the infection. The case-fatality ratio in untreated typhoid fever is about 10%, while the effects of paratyphoid fever are usually less severe.

Antibiotic therapy has radically changed the prognosis of typhoid fever, though antimicrobial resistance is an increasing problem. Preventive measures include good personal and food hygiene. Effective vaccines are available for typhoid fever, but not for paratyphoid fever.

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Methods

This report is based on data for 2019 retrieved from The European Surveillance System (TESSy) on 19 January 2022. TESSy is a system for the collection, analysis and dissemination of data on communicable diseases.

For a detailed description of the methods used to produce this report, please refer to the 'Methods' chapter in the 'Introduction to the Annual Epidemiological Report' [1].

An overview of the national surveillance systems is available online [2].

A subset of the data used for this report is available through ECDC's online 'Surveillance Atlas of Infectious Diseases' [3].

Typhoid and paratyphoid fevers are reported to TESSy under salmonellosis and separated from non-typhoidal *Salmonella* infections based on the serotype. For 2019, 29 EU/EEA countries reported case-based data for salmonellosis. Bulgaria reported aggregated data, from which cases of typhoid and paratyphoid fevers could not be extracted. Liechtenstein did not report any *Salmonella* data.

Typhoid and paratyphoid fevers are under mandatory notification in all EU/EEA countries. The surveillance systems have national coverage in all but three Member States (France, the Netherlands and Spain). The population coverage is estimated to be 48% in France, and 64% in the Netherlands. The variation in coverage was taken into consideration when calculating the national notification rates. No information on estimated coverage was provided by Spain, thereby preventing the calculation of notification rates.

For 2019, 22 EU/EEA countries reported antimicrobial resistance data for *Salmonella* Typhi and/or Paratyphi. Phenotypic resistance data were reported by 20 countries – 16 as disk zones or minimum inhibitory concentration (MIC) values, and four as interpretation with clinical breakpoints. Two countries reported resistance predicted from whole genome sequencing (WGS).

In addition to reporting to TESSy, information from event-based surveillance for typhoid and paratyphoid fever clusters or outbreaks with a potential EU dimension was collected through the Epidemic Intelligence Information System for Food- and Waterborne Diseases (EPIS-FWD).

Epidemiology

For 2019, 24 EU/EEA countries reported 1 439 confirmed cases of typhoid and paratyphoid fever. Five countries did not report any cases: Cyprus, Estonia, Iceland, Malta, and Slovakia. The EU/EEA notification rate was 0.37 cases per 100 000 population (Table 1). The highest notification rates were reported in France and the United Kingdom (UK)[1] with 0.87 and 0.80 cases per 100 000 population, respectively (Table 1, Figure 1).

Out of the 1 114 cases with available information, 1 029 (92.4%) were related to travel. The probable country of infection was available for 827 (80.4%) of these cases, of which all but one were associated with travel to countries outside the EU/EEA. Pakistan and India were the two main travel destinations, accounting for 45.8% and 29.4% of travel-associated cases with available information, respectively. The number of cases associated with travel to Pakistan more than doubled, from 166 cases in 2018 to 379 in 2019.

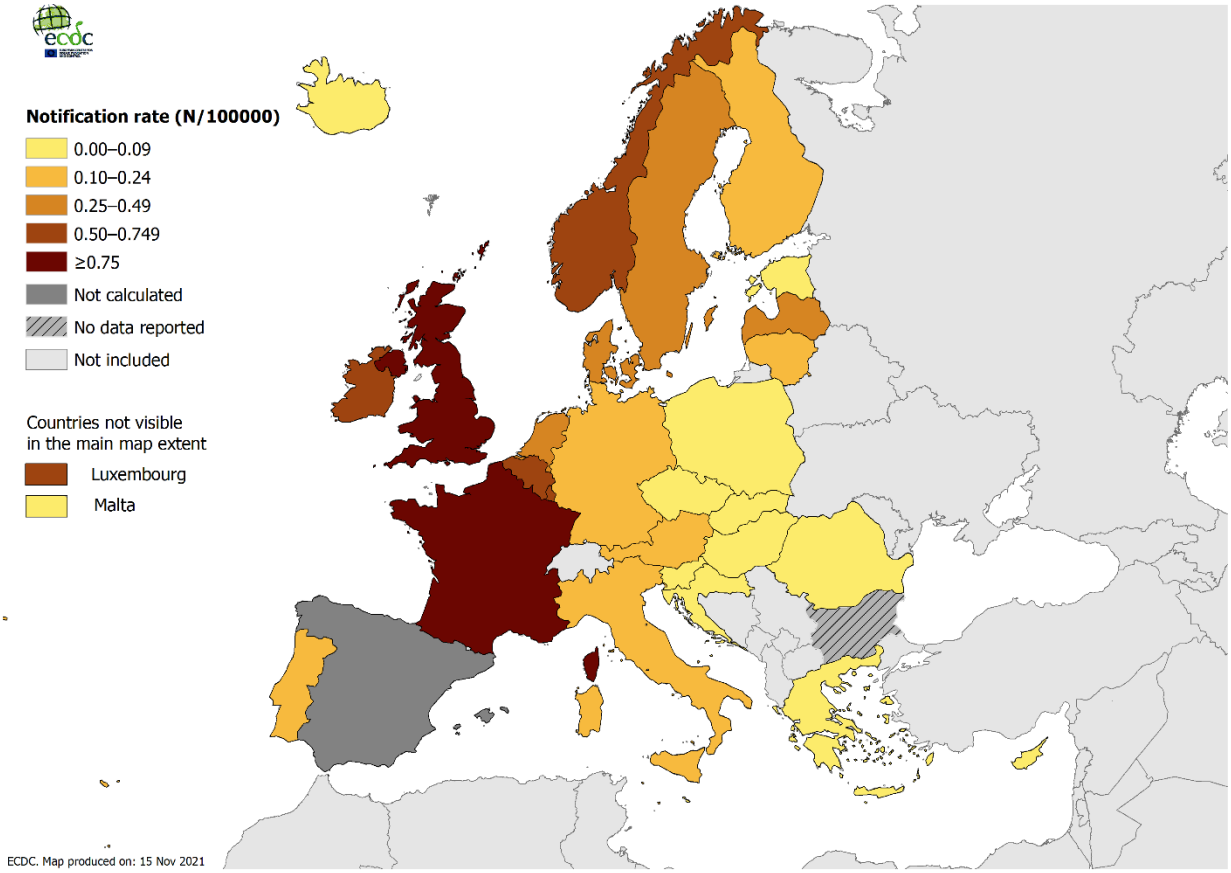
[1] The United Kingdom (UK) is a former Member State of the European Union (EU). The UK withdrew from the EU on 31 January 2020.

Table 1. Distribution of confirmed cases of typhoid and paratyphoid fever and rates per 100 000 population by country and year, EU/EEA, 2015–2019

Country	2015		2016		2017		2018		2019	
	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate
Austria	7	0.08	17	0.20	15	0.17	13	0.15	15	0.17
Belgium	33	0.29	42	0.37	49	0.43	53	0.46	70	0.61
Bulgaria	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Croatia	0	0.00	0	0.00	1	0.02	4	0.10	2	0.05
Cyprus	0	0.00	0	0.00	0	0.00	1	0.12	0	0.00
Czechia	0	0.00	0	0.00	0	0.00	0	0.00	6	0.06
Denmark	18	0.32	24	0.42	23	0.40	24	0.42	22	0.38
Estonia	2	0.15	0	0.00	2	0.15	2	0.15	0	0.00
Finland	7	0.13	5	0.09	15	0.27	14	0.25	6	0.11
France	170	0.53	222	0.69	198	0.62	208	0.65	279	0.87
Germany	102	0.13	95	0.12	120	0.15	87	0.11	120	0.14
Greece	17	0.16	9	0.08	8	0.07	7	0.07	9	0.08
Hungary	0	0.00	3	0.03	1	0.01	0	0.00	2	0.02
Iceland	0	0.00	2	0.60	0	0.00	0	0.00	0	0.00
Ireland	10	0.21	17	0.36	22	0.46	15	0.31	27	0.55
Italy	98	0.16	123	0.20	148	0.24	120	0.20	136	0.23
Latvia	0	0.00	0	0.00	0	0.00	1	0.05	6	0.31
Liechtenstein	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND
Lithuania	2	0.07	3	0.10	1	0.04	3	0.11	3	0.11
Luxembourg	1	0.18	1	0.17	1	0.17	1	0.17	4	0.65
Malta	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Netherlands	45	0.27	56	0.33	62	0.36	66	0.38	67	0.39
Norway	14	0.27	25	0.48	20	0.38	31	0.59	33	0.62
Poland	0	0.00	0	0.00	8	0.02	8	0.02	5	0.01
Portugal	8	0.08	9	0.09	9	0.09	16	0.16	10	0.10
Romania	4	0.02	1	0.01	0	0.00	1	0.01	1	0.01
Slovakia	0	0.00	1	0.02	2	0.04	0	0.00	0	0.00
Slovenia	2	0.10	3	0.15	0	0.00	2	0.10	1	0.05
Spain	34	NR	31	NR	30	NR	35	NR	40	NR
Sweden	27	0.28	16	0.16	37	0.37	32	0.32	42	0.41
United Kingdom	406	0.63	456	0.70	204	0.31	374	0.56	533	0.80
EU/EEA	**1 007**	**0.25**	**1 161**	**0.30**	**976**	**0.25**	**1 118**	**0.29**	**1 439**	**0.37**

Source: country reports
ND: no data reported
NR: no rate calculated.

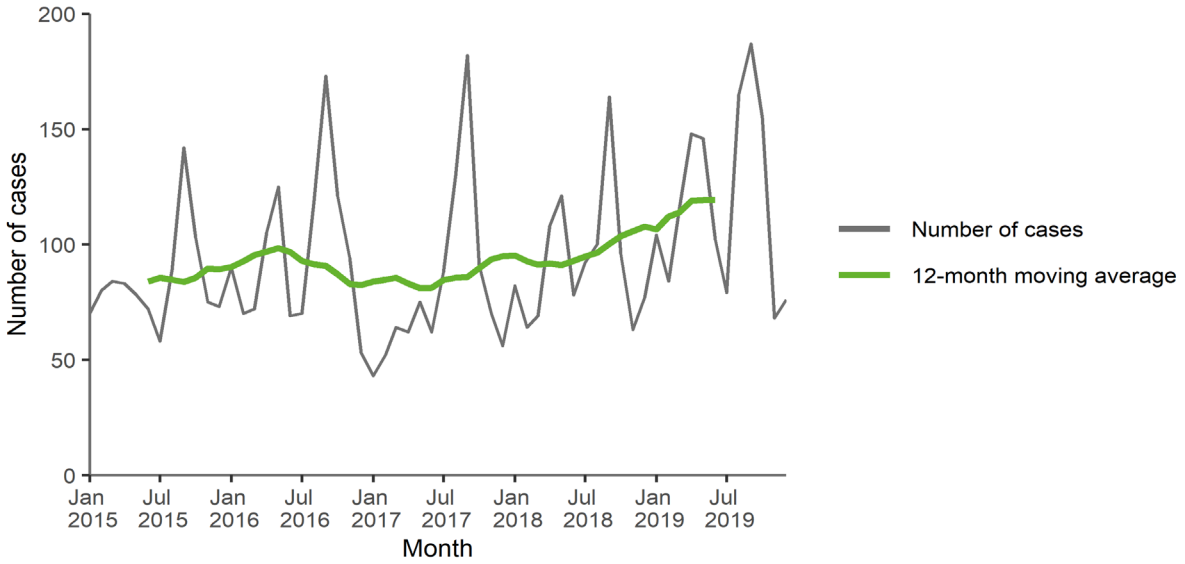
Figure 1. Distribution of confirmed cases of typhoid and paratyphoid fever per 100 000 population by country, EU/EEA, 2019



Source: Country reports from Austria, Belgium, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Sweden, and the United Kingdom. No rates were calculated for Spain.

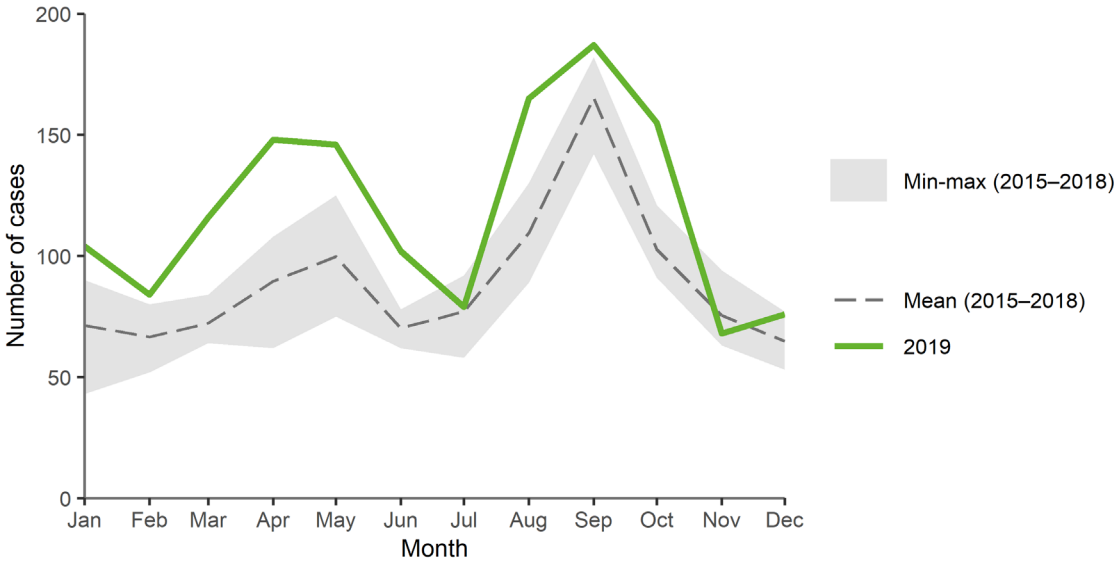
Cases of typhoid and paratyphoid fever in the EU/EEA increased in the period, 2015–2019, with the moving average of monthly cases particularly increasing in 2019 (Figure 2). The disease follows a characteristic seasonal trend in the EU/EEA, with a pronounced peak in late summer to early autumn and a smaller peak in late spring (Figures 2, 3). These peaks were even more pronounced in 2019, with higher peaks in April–May and August–October than observed in the previous four years.

Figure 2. Distribution of confirmed cases of typhoid and paratyphoid fever by month, EU/EEA, 2015–2019



Source: Country reports from Austria, Belgium, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

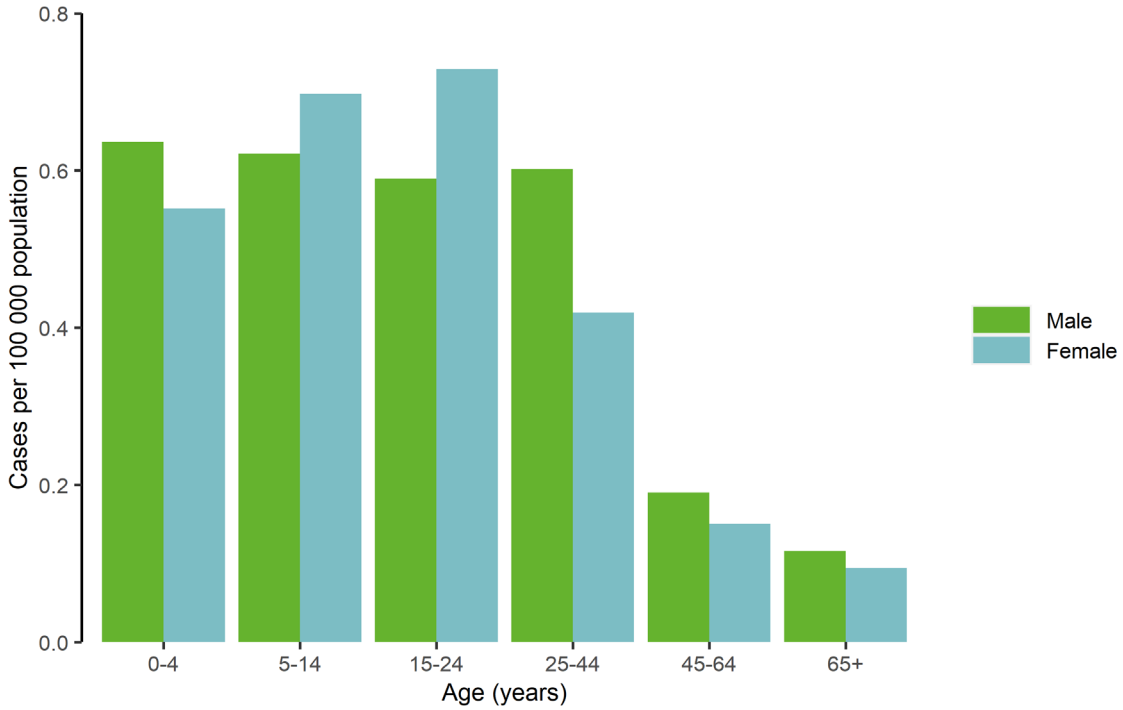
Figure 3. Distribution of confirmed cases of typhoid and paratyphoid fever by month, EU/EEA, 2019 and 2015–2018



Source: Country reports from Austria, Belgium, Cyprus, Czechia, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, and the United Kingdom.

The notification rates for children and adults in the age groups, 0–4, 5–14, 15–24 and 25–44 years were similar, ranging from 0.50 to 0.65 cases per 100 000 population. The rates were much lower in the 45–64 and >65-year age groups (Figure 3). The overall male-to-female ratio was 1.2:1.

Figure 4. Distribution of confirmed cases of typhoid and paratyphoid fever per 100 000 population, by age and gender, EU/EEA, 2019



Source: Country reports from Austria, Belgium, Croatia, Cyprus, Denmark, Estonia, Finland, France, Germany, Greece, Ireland, Italy, Latvia, Lithuania, Luxembourg, the Netherlands, Norway, Poland, Portugal, Romania, Slovenia, Spain, Sweden, and the United Kingdom.

Microbial surveillance

Typhoid fever due to the serotype *S.* Typhi accounted for 69% of typhoid/paratyphoid cases in 2019 (Table 2). Among cases of paratyphoid fever, *S.* Paratyphi A was the most common serotype (22%).

Table 2. *Salmonella enterica* serotype Typhi and *Salmonella* Paratyphi cases, EU/EEA, 2019

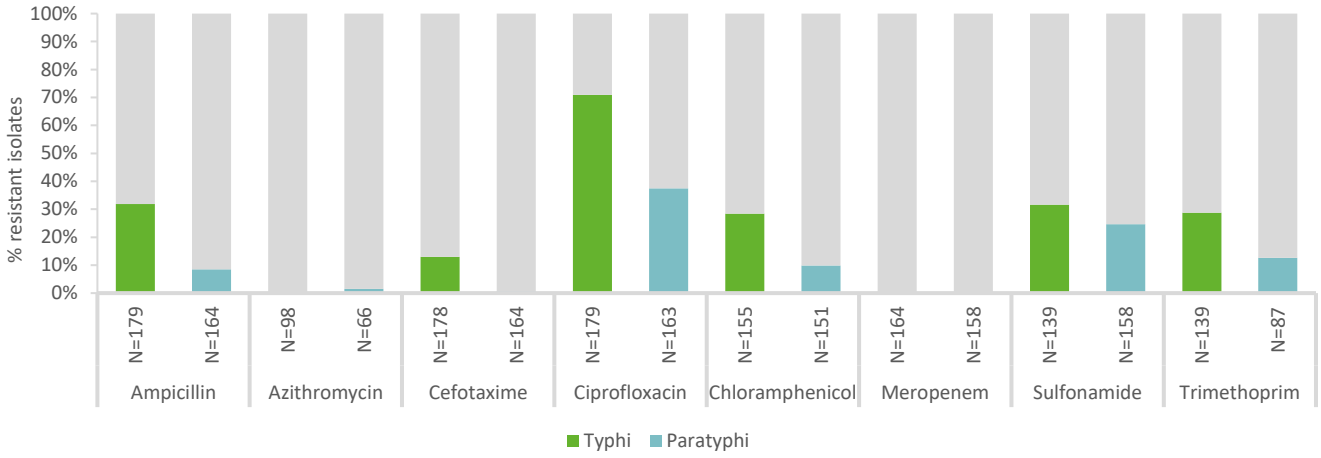
Serotype	Number of cases	Percentage
S. Typhi	990	69%
S. Paratyphi A	318	22%
S. Paratyphi B	91	6%
S. Paratyphi C	11	1%
S. Paratyphi (unspecified)	29	2%
Total	**1 439**	**100%**

Source: Data from TESSy, extracted on 12 September 2022

Figure 5 displays antimicrobial resistance in bacterial isolates from cases of typhoid/paratyphoid fever in 2019 using clinical breakpoints (from 20 countries) or predicted from genetic determinants (from two countries). Resistance was generally higher in *S.* Typhi than in *S.* Paratyphi, with the highest resistance observed to ciprofloxacin – 70.9% in *S.* Typhi and 37.4% in *S.* Paratyphi. No resistance to azithromycin or meropenem was observed in *S.* Typhi, but in *S.* Paratyphi, one isolate (1.2%) was found to be resistant to azithromycin. More than a quarter of all tested isolates of *S.* Typhi were resistant to ampicillin, chloramphenicol, sulfonamides and trimethoprim, and 12.9% were resistant to cefotaxime.

The resistance pattern observed in the extremely drug-resistant (XDR) *S.* Typhi outbreak which started in the Sindh province in Pakistan in 2016 [4] (resistance to ampicillin, chloramphenicol, fluoroquinolones, third and fourth-generation cephalosporins, and trimethoprim-sulfamethoxazole) was identified in bacteria from 19 cases in 10 EU/EEA countries. Of these, nine cases had a travel history to Pakistan, while the travel destinations were unknown for the other cases. Information on age was provided for 13 out of the 19 cases, and among these, six were children aged <15 years old. Ten out of 16 cases with information on the specimen type sampled had bacteraemia, i.e. the bacteria were found in the blood.

Figure 5. Antimicrobial resistance in bacterial isolates from typhoid/paratyphoid infections, EU/EEA, 2019



Source: Country reports from Austria, Belgium, Cyprus, Denmark, Estonia, Finland, Germany, Greece, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Portugal, Romania, Slovenia, Spain, Sweden, and the United Kingdom.

Outbreaks and other threats

The outbreak of XDR *S.* Typhi that started in the Sindh province in Pakistan in November 2016 has still been ongoing in 2019. As of August 2019, 10 365 cases of XDR typhoid fever were reported in the Sindh province since the start of the outbreak [4]. ECDC issued an epidemiological update in October 2019 after the Health Protection Surveillance Centre in Ireland had highlighted an increase in typhoid fever notifications in travellers returning from Pakistan [5]. By then, XDR typhoid fever cases among travellers returning from Pakistan had been identified in at least Australia, Canada, Denmark, Ireland, Taiwan, the UK, and the United States.

Discussion

Globally, it is estimated that between 11 and 21 million cases of typhoid and paratyphoid fever occur annually, with around 130 000 to 160 000 associated deaths [6]. The majority of cases occur in South/South-East Asia, and sub-Saharan Africa. Estimates in 2017 showed the highest incidence in India and Bangladesh, with about 500–700 cases per 100 000 population [7]. A major reduction in the global burden of typhoid/paratyphoid fever has been observed since 1990 [6].

In the EU/EEA, typhoid and paratyphoid fevers are relatively rare infections and most cases are associated with travel during the incubation period. This can be observed in the seasonal pattern of cases, with peaks occurring in September and late spring, which most probably reflects travel during holiday periods, with disease onset after returning home. Pakistan and India were the two main travel destinations among cases, accounting for 45.8% and 29.4% of travel-associated cases with available information, respectively. In the UK, which accounted for 37.0% of all reported cases in 2019 in the EU/EEA, most infections were acquired by people visiting friends or relatives in the Indian subcontinent [8].

An increase of typhoid/paratyphoid fever with more than 300 cases was observed from 2018 to 2019. A large proportion of the increase could be attributed to travel to Pakistan (no increase was observed among travellers to India, which is the second most common travel destination for typhoid/paratyphoid cases). As travel-associated cases from Pakistan of both typhoid fever (*S.* Typhi) and paratyphoid fever (*S.* Paratyphi A) doubled from 2018 to 2019, the increase cannot be solely explained by the outbreak of XDR *S.* Typhi. Possible explanations for this could be changes in travel patterns or a general increase in both typhoid and paratyphoid fever in Pakistan.

The ongoing outbreak of XDR *Salmonella* Typhi in Pakistan, which affects people in Pakistan as well as international travellers, is of concern as the options for treatment are limited. The strain is resistant to all antimicrobials normally used in the treatment of typhoid infections (chloramphenicol, ampicillin, co-trimoxazole, fluoroquinolones, and third-generation cephalosporins). It is only susceptible to azithromycin, carbapenems, and tigecycline, and of those, only azithromycin can be administered orally [9]. The World Health Organization (WHO) has recommended typhoid fever vaccination as a control strategy in the affected areas in Pakistan along with other measures including health education, water quality, sanitation improvements, and the training of healthcare professionals in diagnosis and treatment [6]. Pakistan also became the first country to introduce the WHO-approved typhoid conjugate vaccine (TCV) through its expanded programme on immunisation in 2019 when more than 9.5 million children aged nine months to 15 years were vaccinated [6]. Despite the demonstrated success of several typhoid vaccination strategies, typhoid vaccines remain underused globally [10].

Public health implications

Typhoid and paratyphoid fevers are mainly travel-associated infections in the EU/EEA. Persons planning to stay in high-endemicity countries for prolonged periods should consider vaccination in line with national recommendations before travel. Travellers should also be reminded of the need for proper food hygiene and handwashing practices during travel. Healthcare providers should be made aware of the possibility of XDR *S.* Typhi infection in patients returning from Pakistan.

References

1. European Centre for Disease Prevention and Control (ECDC). Introduction to the Annual Epidemiological Report. Stockholm: ECDC; 2020. Available at: https://www.ecdc.europa.eu/en/annual-epidemiological-reports/methods
2. European Centre for Disease Prevention and Control (ECDC). Surveillance systems overview. Stockholm: ECDC; 2021. Available at: https://www.ecdc.europa.eu/en/publications-data/surveillance-systems-overview-2019
3. European Centre for Disease Prevention and Control (ECDC). Surveillance Atlas of Infectious Diseases. Stockholm: ECDC; 2023. Available at: http://atlas.ecdc.europa.eu/public/index.aspx?Dataset=27&HealthTopic=46
4. World Health Organization Regional Office for the Eastern Mediterranean (WHO/EMRO). Drug resistant *Salmonella* infections in Pakistan: update. Weekly Epidemiological Monitor Vol. 12; Issue No. 34. Cairo: WHO/EMRO; 25 Aug 2019. Available at: https://applications.emro.who.int/docs/epi/2019/Epi_Monitor_2019_12_34.pdf?ua=1
5. European Centre for Disease Prevention and Control (ECDC). Increase of XDR Typhoid fever in travellers returning from Pakistan. Epidemiological update. Stockholm: ECDC; 9 Oct 2019. Available at: https://www.ecdc.europa.eu/en/news-events/increase-xdr-typhoid-fever-travellers-returning-pakistan
6. World Health Organization (WHO). Typhoid vaccines: WHO position paper. Geneva: WHO; Mar 2018. Available at: http://apps.who.int/iris/bitstream/handle/10665/272272/WER9313.pdf
7. Stanaway JD, Reiner RC, Blacker BF, Goldberg EM, Khalil IA, Troeger CE, et al. The global burden of typhoid and paratyphoid fevers: a systematic analysis for the Global Burden of Disease Study 2017. Lancet Infect Dis 2019 Apr;19(4):369–81. Available at: https://www.sciencedirect.com/science/article/pii/S1473309918306856?via%3Dihub
8. United Kingdom Health Security Agency (formerly Public Health England). Enteric fever (typhoid and paratyphoid) England, Wales and Northern Ireland: 2019. London: UKHSA; Feb 2023. Available at: https://www.gov.uk/government/publications/typhoid-and-paratyphoid-laboratory-confirmed-cases-in-england-wales-and-northern-ireland/enteric-fever-typhoid-and-paratyphoid-england-wales-and-northern-ireland-2019
9. Akram J, Khan AS, Khan HA, Gilani SA, Akram SJ, Ahmad FJ et al. Extensively Drug-Resistant (XDR) Typhoid: Evolution, Prevention, and Its Management. Biomed Res Int. 2020 May 2;2020:6432580. Available at: https://www.hindawi.com/journals/bmri/2020/6432580/
10. Date KA, Bentsi-Enchill A, Marks F, Fox K. Typhoid fever vaccination strategies. Vaccine. 2015 Jun 19;33 Suppl 3:C55-61. Available at: https://www.sciencedirect.com/science/article/pii/S0264410X15004818?via%3Dihub