

# Typhoid and paratyphoid fever

## Annual Epidemiological Report for 2021

### Key facts

- Typhoid and paratyphoid fevers are relatively rare in the European Union/European Economic Area (EU/EEA) and are mainly acquired during travel to countries outside the EU/EEA, particularly southern Asia.
- For 2021, 19 EU/EEA countries reported a total of 304 laboratory-confirmed cases.
- Since the substantial drop in 2020, which was most likely due to the travel restrictions implemented during the COVID-19 pandemic, the number of case reports has remained low. However, in the second half of 2021, an increase in cases was observed, with the usual seasonal peak in September, albeit at a much lower level than the average for 2017–2020.
- Of the 182 cases with available information, 67.9% were travel-related, which was unusually low. A large part of the domestically-acquired cases were infected in the EU outermost regions.
- Multidrug resistance is an increasing problem, more so with *S. Typhi* than *S. Paratyphi*. However, vaccination against typhoid fever is available and should be considered by those planning to stay in high-endemicity countries for prolonged periods.

### 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 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 sustained fever, headache, malaise, cough, rash, and an enlarged spleen. Diarrhoea may be present at some stage, but constipation can also occur 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. Approximately 3–5% of cases become chronic carriers that shed bacteria via their faeces and urine, sometimes for decades [1]. Chronic carriage and a low infectious dose are potential causes for the easy spread of *S*Typhi. Preventive measures include good personal and food hygiene. Effective vaccines are available for typhoid fever, but not for paratyphoid fever.

### Methods

This report is based on data for 2021 retrieved from The European Surveillance System (TESSy) on 9 October 2022. TESSy is a system for the collection, analysis and dissemination of data on communicable diseases.

For a detailed description of methods used to produce this report, please refer to the 'Methods' chapter [2].

An overview of the national surveillance systems is available online [3].

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A subset of the data used for this report is available through ECDC's online 'Surveillance atlas of infectious diseases' [4].

For 2021, 27 EU/EEA countries reported case-based data on typhoid and paratyphoid fevers. In addition, Bulgaria reported aggregated data for salmonellosis and Luxembourg did not provide data on serotype, thus making it impossible to extract data on cases of typhoid and paratyphoid fevers. No data were reported by the United Kingdom (UK) due to its withdrawal from the EU on 31 January 2020.

It is mandatory to notify typhoid and paratyphoid fevers 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, preventing the calculation of notification rates.

Thirteen EU/EEA countries reported antimicrobial resistance data for *Salmonella* Typhi and/or Paratyphi for 2021. Twelve countries reported phenotypic resistance data as disk zones or minimum inhibitory concentration (MIC) values and one country reported resistance predicted from whole genome sequencing (WGS).

In addition to TESSy reporting, information from event-based surveillance for typhoid and paratyphoid clusters or outbreaks with a potential EU dimension was collected through the Epidemic Intelligence Information System for Food- and Waterborne Diseases (EPIS-FWD). In the summer of 2021, the new European surveillance portal for infectious diseases (EpiPulse) replaced EPIS-FWD.

## Epidemiology

For 2021, 27 EU/EEA countries reported case-based data on typhoid and paratyphoid fevers. Among these, 19 countries reported 304 confirmed cases. Eight countries did not report any cases. The EU/EEA notification rate was 0.10 cases per 100 000 population, which was similar to that in 2020 but a decrease of 67% compared to the period 2017–2019 (Table 1). The highest notification rate was reported in France (0.29 cases per 100 000 population) (Table 1, Figure 1).

Of the 184 cases with available information, 125 (67.9%) were related to travel. The probable country of infection was available for 117 of these, all of which were associated with travel to countries outside the EU/EEA. Pakistan, India and Iraq were the three main travel destinations, accounting for 26.5%, 17.0% and 12.0% of travel-associated cases with available information. Among the 60 cases reported as domestically acquired, France accounted for the highest number of cases (24), the majority of them linked to the French territory Mayotte, (personal communication N. Jourdan da Silva, Sante Publique, France, 12 Feb 2024).

Of 180 cases with known information on specimen type, 66.7% had the bacteria isolated from their blood.

**Table 1. Number of confirmed typhoid and paratyphoid fever cases and rates per 100 000 population by country and year, EU/EEA, 2017–2021**

Country	2017		2018		2019		2020		2021	
	Number	Rate	Number	Rate	Number	Rate	Number	Rate	Number	Rate
Austria	15	0.17	13	0.15	15	0.17	2	0.02	5	0.06
Belgium	49	0.43	53	0.46	70	0.61	34	0.30	20	0.17
Bulgaria	NDR	NRC	NDR	NRC	NDR	NRC	NDR	NRC	NDR	NRC
Croatia	1	0.02	4	0.10	2	0.05	0	0.00	0	0.00
Cyprus	0	0.00	1	0.12	0	0.00	0	0.00	0	0.00
Czechia	0	0.00	0	0.00	6	0.06	1	0.01	1	0.01
Denmark	23	0.40	24	0.42	22	0.38	13	0.22	8	0.14
Estonia	2	0.15	2	0.15	0	0.00	0	0.00	1	0.08
Finland	15	0.27	14	0.25	6	0.11	6	0.11	3	0.05
France	198	0.62	208	0.65	279	0.87	110	0.34	93	0.29
Germany	120	0.15	87	0.11	120	0.14	36	0.04	28	0.03
Greece	8	0.07	7	0.07	9	0.08	3	0.03	2	0.02
Hungary	1	0.01	0	0.00	2	0.02	1	0.01	1	0.01
Iceland	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Ireland	22	0.46	15	0.31	27	0.55	3	0.06	9	0.18
Italy	148	0.24	120	0.20	136	0.23	43	0.07	58	0.10
Latvia	0	0.00	1	0.05	6	0.31	4	0.21	0	0.00
Liechtenstein	NDR	NRC	NDR	NRC	NDR	NRC	NDR	NRC	NDR	NRC
Lithuania	1	0.04	3	0.11	3	0.11	2	0.07	0	0.00
Luxembourg	1	0.17	1	0.17	4	0.65	0	0.00	NDR	NRC
Malta	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Netherlands	62	0.36	66	0.38	67	0.39	10	0.06	27	0.15
Norway	20	0.38	31	0.59	33	0.62	12	0.22	10	0.19
Poland	8	0.02	8	0.02	5	0.01	0	0.00	2	0.01
Portugal	9	0.09	16	0.16	10	0.10	12	0.12	7	0.07
Romania	0	0.00	1	0.01	1	0.01	1	0.01	0	0.00
Slovakia	2	0.04	0	0.00	0	0.00	1	0.02	0	0.00
Slovenia	0	0.00	2	0.10	1	0.05	0	0.00	2	0.09
Spain	30	NRC	35	NRC	40	NRC	7	NRC	8	NRC
Sweden	37	0.37	32	0.32	42	0.41	16	0.15	19	0.18
United Kingdom	204	0.31	374	0.56	533	0.80	NA	NA	NA	NA
<b>EU-EEA</b>	<b>976</b>	<b>0.25</b>	<b>1 118</b>	<b>0.28</b>	<b>1 439</b>	<b>0.37</b>	<b>317</b>	<b>0.11</b>	<b>304</b>	<b>0.10</b>

Source: country reports.

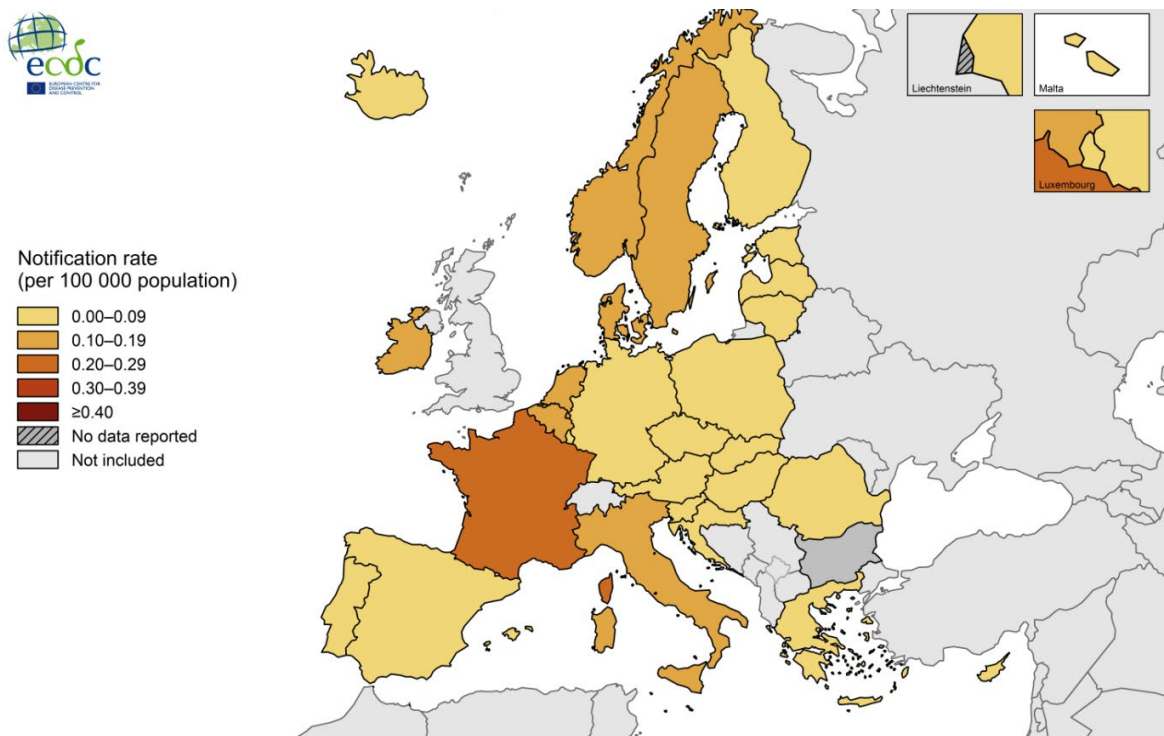
NDR: no data reported.

NRC: no rate calculated.

NA: not applicable.

No data were reported by the United Kingdom for 2020 due to its withdrawal from the EU on 31 January 2020.

**Figure 1. Number of confirmed typhoid and paratyphoid fever cases per 100 000 population by country, EU/EEA, 2021**

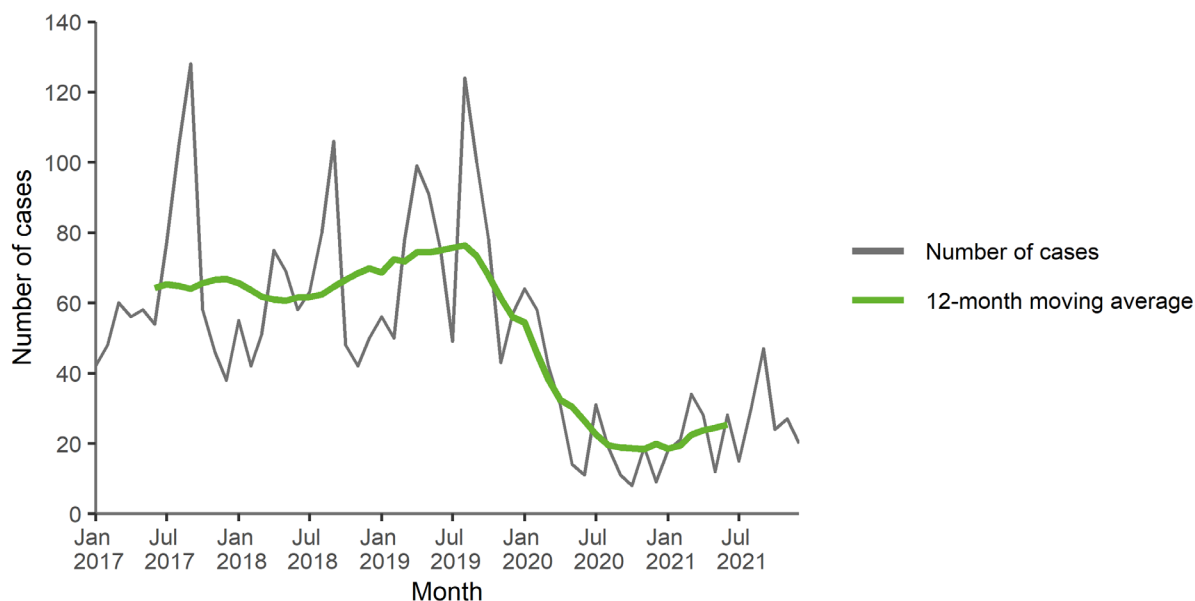


Administration boundaries: © EuroGeographics  
The boundaries and names shown on this map do not imply official endorsement or acceptance by the European Union. ECDC. Map produced on 3 April 2024.

Source: country reports from Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia and Sweden. No rate calculated for Spain.

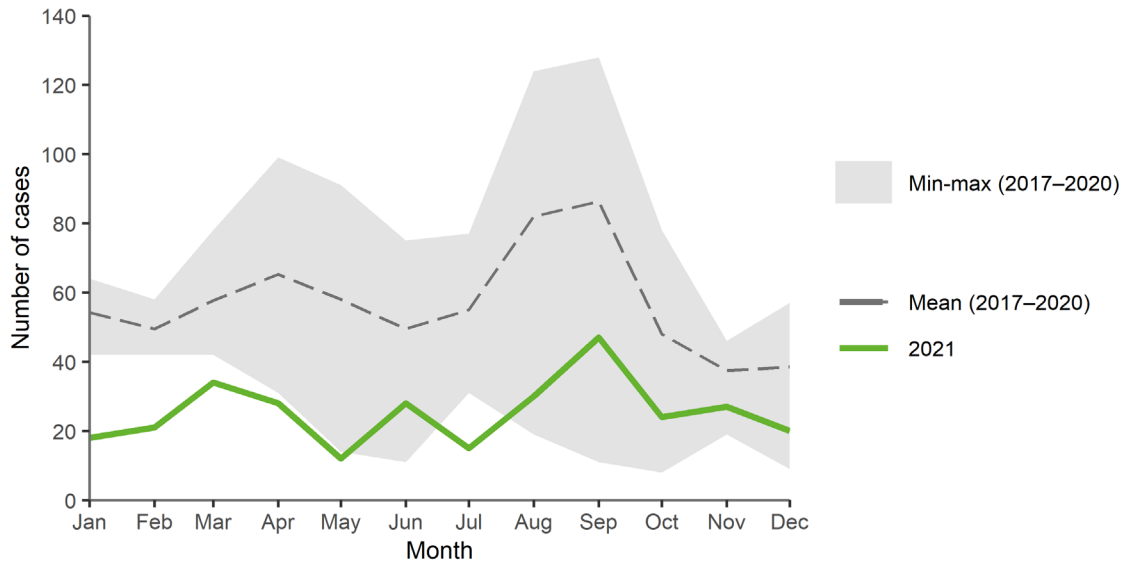
Typhoid and paratyphoid cases remained at a low level in the EU/EEA in 2021 after the substantial drop observed in 2020 due to the COVID-19 pandemic (Figure 2, Figure 3). In the second half of the year, an increase was observed, with the usual seasonal peak in September, albeit at a much lower level compared to the average for 2017–2020 (Figure 3).

**Figure 2. Number of confirmed typhoid and paratyphoid fever cases by month, EU/EEA, 2017–2021**



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

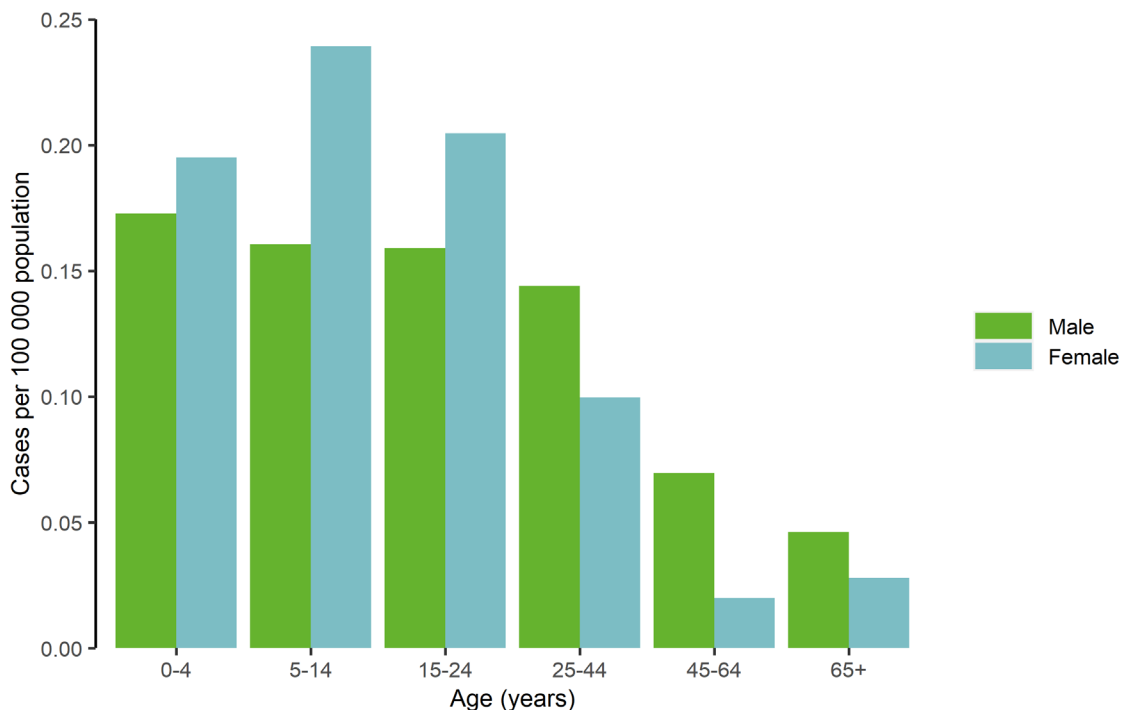
**Figure 3. Number of confirmed typhoid and paratyphoid fever cases by month, EU/EEA, 2021 and 2017–2020**



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

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 0.12 to 0.20 cases per 100 000 population, while rates in the age groups 45–64 and >65 years were substantially lower, at 0.04 cases per 100 000 population (Figure 3). By gender, female cases were more common among children and young adults, while male cases were more common in those aged 25 years and above. The overall male-to-female ratio was 1.1:1.

**Figure 4. Number of confirmed typhoid and paratyphoid fever cases per 100 000 population, by age and gender, EU/EEA, 2021**



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, Slovakia, Slovenia, Spain, Sweden.

## Microbial surveillance

### Serovars

Typhoid fever accounted for 72.3% of typhoid/paratyphoid cases (Table 2). Among paratyphoid fever cases with known serotype, *S. Paratyphi* B was more common than *S. Paratyphi* A and *S. Paratyphi* C in 2021

**Table 2. *Salmonella enterica* serotype Typhi and *Salmonella* Paratyphi cases, EU/EEA, 2021**

Serotype	Number of cases	Percentage
Typhi	224	72.3
Paratyphi A	28	9.0
Paratyphi B	42	13.6
Paratyphi C	4	1.3
Paratyphi (unspecified)	12	3.9
<b>Total</b>	<b>310</b>	<b>100.0</b>

Source: TESSy data, extracted 23 October 2023

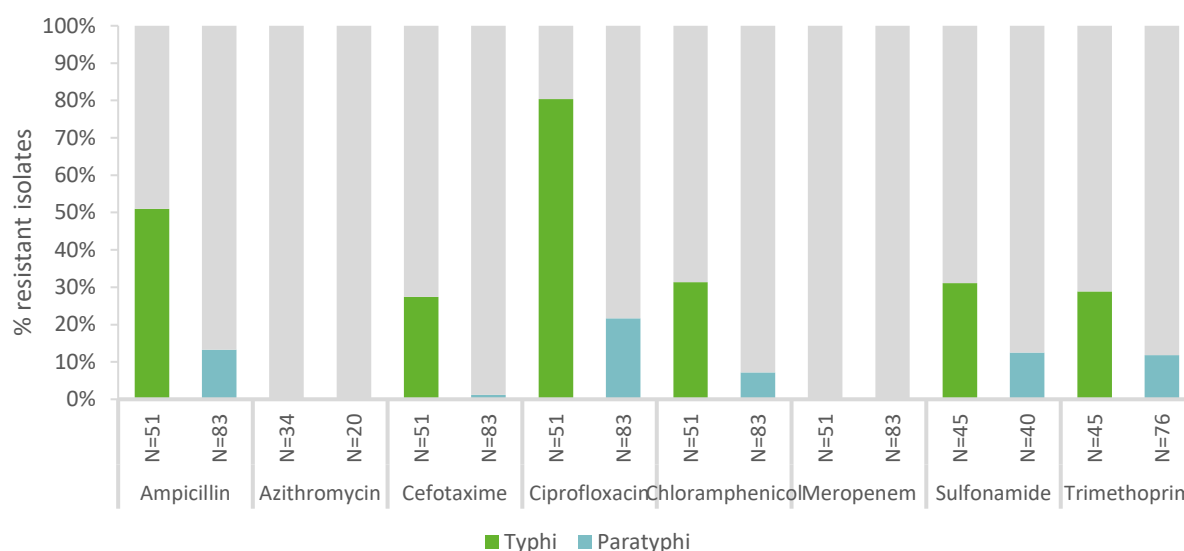
### Antimicrobial resistance

Resistance to clinically important antimicrobials was observed in both *S. Typhi* and *S. Paratyphi* in 2021, with higher resistance in *S. Typhi*. Resistance to ciprofloxacin was most common, where 80.4% and 21.7% of isolates were resistant in *S. Typhi* and *S. Paratyphi*, respectively (Figure 5). Resistance to ampicillin, sulfamethoxazole, trimethoprim and chloramphenicol was observed in about 30% of *S. Typhi* isolates but in 15% or less of *S. Paratyphi*. Resistance to cefotaxime was observed in 27.5% of *S. Typhi* isolates but only in 1.2% of *S. Paratyphi*. Of the *S. Typhi* confirmed to be ESBL-producing (with resistance to third and fourth generation cephalosporins), all were of the type CTX-M-15. No resistance was observed to azithromycin or meropenem.

Four isolates from three EU/EEA countries displayed the same resistance pattern as the extremely drug-resistant (XDR) *S. Typhi* in the outbreak ongoing in Pakistan since 2016 [5] (resistance to ampicillin, chloramphenicol, fluoroquinolones, third- and fourth-generation cephalosporins, and trimethoprim-sulfamethoxazole). Travel status was missing for two of the cases, while the other were reported to have travelled, although there was no information available on destination. All isolates were from blood samples and the cases were aged 15–33 years.

Six other isolates from two countries, also all isolated from blood, displayed resistance to fluoroquinolones and third- and fourth-generation cephalosporins. Two of these were related to travel to Iraq, three were lacking information on travel status and one was reported as domestically acquired.

**Figure 5. Antimicrobial resistance in isolates from typhoid/paratyphoid infections by serotype, EU/EEA, 2021**



Source: Country reports from Austria, Belgium, Denmark, Ireland, Italy, Malta, the Netherlands, Norway, Portugal, Spain and Sweden.

## Outbreaks and other threats

In 2021, there were no typhoid or paratyphoid fever events reported by any EU/EEA country through either FWD-EPIS or EpiPulse. The outbreak of XDR *S. Typhi* that started in the Sindh province in Pakistan in November 2016 was still ongoing in 2021, with 2 274 cases reported [5]. This was a decrease compared to the peak in 2019 when 9 731 cases were reported in the same area. Based on the AMR data provided by countries, travel-related cases with this XDR strain were detected in at least three EU/EEA countries in 2021 (see above).

## Discussion

Typhoid and paratyphoid fevers are severe systemic diseases which are endemic in several parts of the world. It is estimated that between 11 and 21 million cases of typhoid and paratyphoid fever occur globally each year, with around 130 000 to 160 000 associated deaths [6]. The majority of cases occur in South/South-East Asia, and sub-Saharan Africa.

In the EU/EEA, typhoid and paratyphoid fevers are relatively rare infections and most cases are associated with travel during the incubation period. In France, the country with the highest notification rate in 2021, studies have shown that the majority of travel-related infections in children were acquired when visiting friends or relatives [7].

The seasonal pattern of typhoid and paratyphoid fever in the EU/EEA, with peaks usually observed in September and late spring, most likely reflects travel during holiday periods, with disease onset after returning home. In 2021, when the COVID-19 pandemic was still ongoing, global tourism arrivals were reduced by 69% compared to 2019 [8]. Consequently, during the first half of the year, case counts were below the average for 2017–2020, but an increase in cases was observed in the second half of the year.

Pakistan, India and Iraq were the three main travel destinations among cases in 2021, accounting for 26.5%, 17.0% and 12.0% of travel-associated cases with available information. Among the domestically-acquired cases, a significant proportion were infected in the French outermost region of Mayotte in the Indian Ocean, where typhoid fever is endemic.

Typhoid and paratyphoid infections can cause very severe disease. The type of sample from which the bacteria is isolated can serve as an indication of the severity and in 2021, 68% of the cases had a bloodstream infection (in contrast to only 2% of non-typhoidal salmonellosis, source TESSy). Antimicrobial treatment is then necessary to avoid worsening symptoms or a fatal outcome. As resistance developed to first line treatments for typhoid fever (penicillins, chloramphenicol and co-trimoxazole), fluoroquinolones (mainly ciprofloxacin) became the first-line therapy. However, resistance, or non-susceptibility to ciprofloxacin, soon emerged, particularly in South and South-East Asia [9]. In 2018, South Asia was the region with the highest consumption (defined as Defined Daily Dose per 1 000 population and day) of fluoroquinolones in humans [10]. In 2021, ciprofloxacin resistance was observed in 80% of *S. Typhi* cases and 22% of *S. Paratyphi*, and resistance to other antimicrobials used in treatment, including third- and fourth-generation cephalosporins, was about 30% in *S. Typhi*. Four of the 51 *S. Typhi* cases for which AMR data was provided carried a strain with the XDR pattern observed in the *S. Typhi* outbreak in Pakistan and all were isolated from blood. As there are very few antimicrobials left with which to treat this strain, and only one of them (azithromycin) can be administered orally [11], vaccination against typhoid fever may be considered for travellers to Pakistan, particularly if staying for longer periods, or in areas with poor sanitation. Despite the demonstrated success of several typhoid vaccination strategies, typhoid vaccines remain underused globally [12].

## Public health implications

Typhoid and paratyphoid fevers are mainly travel-associated infections in the EU/EEA. Those 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 hand-washing practices during travel. Healthcare providers should be made aware of the possibility of XDR *S. Typhi* infection in patients returning from Pakistan.

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