



# Defining travel-associated cases of enteric fever

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## KEYWORDS

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**Summary** There is no internationally recognized case-definition for travel-associated enteric fever in non-endemic countries. This study describes the patterns of case reporting between 2007 and 2011 as travel-associated or not from the surveillance data in England, Wales and Northern Ireland (EWNI), before and after a change in the time component of the case-definition in January 2011. It examines in particular the role of a time frame based on the reported typical incubation period in defining a case of travel-associated enteric fever. The results showed no significant differences in the distribution of cases of enteric fever in regards to the interval between the onset and UK arrival in 2011 compared to 2007–2010 ( $p=0.98$  for typhoid and paratyphoid A); the distribution for paratyphoid B was also similar in both time periods. During 2007–2010, 93% (1730/1853) of all of the cases were classified as travel-associated compared to 94% (448/477) in 2011. This difference was not statistically significant. Changing the time component of the definition of travel-associated enteric fever did not make a significant difference to the proportion of travel-associated cases reported by investigators. Our analysis suggests that time might be subordinate to other considerations when investigators classify a case as travel-associated.

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## Introduction

Enteric fevers (otherwise known as typhoid and paratyphoid fevers, which in this study are referred to as 'typhoid' and 'paratyphoid') are exclusively

human diseases transmitted via the fecal–oral route and caused by *Salmonella enterica* subspecies *enterica* serovar Typhi and Paratyphi A, B, and C. Unlike other *Salmonella* spp., they primarily cause a systemic illness with fever, headache, stomach pain, loss of appetite and nausea; diarrhea might be present in some cases, but not all. The illness varies in severity; paratyphoid has been reported in the literature to be typically

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milder than typhoid, although more recent studies have suggested that there is little difference between their clinical presentations [1,2], and both could be serious and life-threatening unless treated promptly with antibiotics. The incubation periods for enteric fevers are dependent on the infectious dose and the vehicle in which the organisms are ingested as well as on host factors [3,4]. Typical ranges quoted in the literature are 8–14 days and 10–20 days for typhoid and 1–10 days for paratyphoid [5] although the range might be wider, and the extreme range for typhoid is quoted as 3–60 days [5,6].

Enteric fevers occur in parts of the world where hygiene and sanitation are poor. The latest estimates for the number of typhoid and paratyphoid cases occurring globally were 21.7 million and 5.4 million, respectively, in 2000 [7]. The regions of high incidence are Africa, parts of South and South-East Asia, South America and several Asian regions of the former USSR [8]. Enteric fever in the United Kingdom [2] and other countries in western Europe [9–12], the United States [13], Canada [14], Australia [15], New Zealand [16], Japan [17] and Singapore [18] is most often associated with travel to or arrival from an endemic country. In many published studies on travel-associated enteric fever, “travel-associated” is not explicitly defined, or where it is defined, the time interval between travel and the onset of symptoms used in the definition differs across countries, with the maximum varying between three weeks and three months (Table 1).

National enhanced surveillance of enteric fever in England, Wales and Northern Ireland (EWNI) began in May 2006, and all of the cases in which *Salmonella* Typhi or Paratyphi has been isolated from a blood (optimally) or fecal sample are eligible for inclusion. All of the isolates are confirmed and typed by the *Salmonella* Reference Service at Public Health England, Colindale. The protocol and questionnaire for the surveillance were developed by a multidisciplinary collaborative steering group drawn from laboratory and epidemiological specialists and practitioners in Public Health England (PHE) (formerly the Health Protection Agency), the Local Authorities Coordinators of Regulatory Services and the National Travel Health Network and Centre (NaTHNaC). The questionnaires are completed by Local Authority environmental health officers or the local PHE staff, depending on the local arrangements, and coordinated nationally by the Travel and Migrant Health Section (TMHS) at the PHE Centre for Infectious Disease Surveillance and Control in Colindale. Between 2007 and 2011, questionnaires were

submitted to TMHS for 86% of laboratory-confirmed cases.

Until 2011, a travel-associated case of enteric fever was defined in the national surveillance questionnaire as onset within three weeks of arrival in or return to the UK from abroad. This definition was based on the typical maximum incubation period quoted for typhoid [25] and expert consensus from the steering group. For simplicity, the identical definition was used for typhoid and paratyphoid despite their reportedly different incubation periods because, at the time of completion of the questionnaire, the causative organism might not be known. Analysis of the data collected between 2007 and 2010 demonstrated that investigators did not always adhere to the three-week cut off period for defining a travel-associated case of enteric fever, particularly in cases in which there had been travel to a known endemic country outside the defined time frame. The vast majority of cases between 2007 and 2010 had an onset of illness up to one month after arrival in or return to the UK from abroad. In the light of these findings, the definition of a travel-associated case was changed in January 2011 to cases that had an onset of illness within one month after arrival in or return to the UK from abroad. For analysis purposes, a month was defined as 28 days.

This study retrospectively describes the patterns of reporting of cases as travel-associated or not, before and after the change in definition of a travel-associated case, to examine how much weight investigators gave to the time frame of the definition and to consider the appropriateness of the change in definition. The general epidemiology of enteric fevers in EWNI is beyond the scope of this study and is available elsewhere [2].

## Methods

The data from national surveillance are managed with a Microsoft Access 2007 database and were analyzed for this study using Microsoft Excel 2007. In cases in which a questionnaire could not be completed, information on the travel history might be obtained from the laboratory request form (for the country of travel only) or directly from the local PHE Health Protection Teams. The investigators completing questionnaires are asked to classify a case as travel-associated or not (based on the definitions as described above) and to complete information about the onset date of illness and dates of any travel. The time (in days) between overseas travel and the onset date was calculated for all of the

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