Supplementary Materials:

Supplementary Materials for

Distinguishable Epidemics Within Different Hosts of the Multidrug Resistant Zoonotic Pathogen *Salmonella* Typhimurium DT104

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Materials

Data

A description of the number, country of origin, and purpose for selection of all isolates used in this study is presented in Table S1. The majority of animal isolates (70%) are of bovine origin (Tables S2 – S5), which reflects the primary animal reservoir (*20, 31*). Sequence data are deposited in the European Nucleotide Archive, under study accession numbers ERP000244, ERP000270, and ERP000994. Sequence data of the Japanese strains can be obtained from the DNA Data Bank of Japan, accession number DRA000942.

Whole genome sequencing

All isolates were sequenced using multiplex libraries on the Illumina HiSeq platform using 100 bp paired end reads (Table S1), unless otherwise stated. To create a high quality DT104 reference sequence, *S.* Typhimurium DT104 genomic DNA was fragmented by sonication, and several libraries were generated in pUC18 using size fractions ranging from 1.0 to 2.5 kb. The high quality finished DT104 genome was sequenced to a depth of 9x coverage from M13mp18 (insert size 1.4–2 kb) and pUC18 (insert size 2.2–4.2 kb) small insert libraries, using dye terminator chemistry on ABI3700 automated sequencers. End sequences from larger insert plasmid (pBACe3.6, 12–30 kb insert size) libraries were used as a scaffold. The sequence was assembled, finished, and annotated as described previously (*32*). The finished chromosome and plasmid sequences have been submitted to the European Molecular Biology Laboratory (accession numbers HF937208 and HF937209, respectively).

Scottish *S.* Typhimurium DT104

The surveillance programme that generated the Scottish animal and human *Salmonella* Typhimurium DT104 (hereafter, DT104) data used in this study is described in Mather *et al* (*11*). *Salmonella* is a reportable human and livestock pathogen in the UK, and all suspected *Salmonella* isolates identified at medical and veterinary diagnostic laboratories in Scotland are forwarded to the Scottish *Salmonella Shigella* and *Clostridium difficile* Reference Laboratory (SSSCDRL) for confirmation and typing. Both human and animal DT104 isolates were subject to the same microbiological and typing procedures. Serotyping of the isolates and phage typing was accomplished according to internationally standardized methods (*33-35*). Antimicrobial susceptibility was assessed using a modified breakpoint method, involving solid agar plates containing a pre-determined concentration of antimicrobial (Table S7), and isolates were classified as non-resistant or resistant (*36*). There were four sets of isolates selected from the collection held at the SSSCDRL. The total number of isolates submitted to the SSSCDRL over the period 1990 – 2004 (figure from the supplementary material of (*11*)), and the number of isolates sequenced per year in this study are represented in Figure S7, demonstrating the coverage of the epidemic represented by the sequenced isolates.

1. Scottish domestically-acquired DT104 isolates – diversity of antimicrobial resistance

As described in Mather *et al* (*11*), 2,439 animal isolates and 2,761 human isolates were collected over the epidemic period 1990 – 2004. Phenotypically, there were 52 profiles identified in human DT104 isolates during this time period, and 35 profiles in animal isolates. Twenty-two of these profiles were held in common by both animals and humans; overall, there were 65 unique

profiles (*11*). Human isolates were derived from domestically-acquired infections of DT104, from cases with no history of recent foreign travel.

We selected a subset of 156 of these DT104 isolates for sequencing. The selection process was the same for both human and animal isolates, as follows: All isolates with phenotypic AMR profiles observed only once or twice during the study period were selected for sequencing. For profiles observed three to nine times, two random isolates for each of these profiles were selected for sequencing. For each of the profiles comprised of ten or more isolates, with the exception of the most prevalent profile, three random isolates were selected for each. For the most prevalent profile, demonstrating phenotypic resistance to ampicillin, chloramphenicol, spectinomycin, streptomycin, sulphonamides, and tetracycline (ApClSpStSuTe), nine isolates were randomly selected. For any of the selected isolates which on retrieval from storage proved to be non-viable, additional DT104 isolates were randomly selected which were of the same profile; if no further isolates of the same profile were available, additional DT104 isolates from the most numerous profiles (ApClSpStSuTe and ApClSpStSuTe+trimethoprim) were randomly selected. A list of these isolates is presented in Table S2. All isolates of *Salmonella* at the SSSCDRL, once characterized, were inoculated on Dorset egg slopes for long-term storage. The isolates selected for sequencing were plated onto cysteine lactose electrolyte-deficient (CLED) agar and incubated overnight at 37ºC. A single colony from each culture was subcultured separately into 5 mL Brain Heart Infusion (BHI) broth, and incubated overnight at 37ºC. DNA was extracted using the Puregene Core Kit B (Qiagen). Nine (9) isolates were removed from further analysis following sequencing due to sample contamination or poor sequence quality.

2. Scottish domestically-acquired DT104 isolates – diversity within the main resistance profile: ApClSpStSuTe

To assess the diversity within isolates demonstrating the main resistance pattern, conferring resistance to ampicillin, chloramphenicol, spectinomycin, streptomycin, sulphonamides, and tetracycline, an additional 47 animal isolates and 47 human isolates were selected for sequencing. These were selected stratified by year so that, along with the ApClSpStSuTe isolates selected in the first round of selection, the number of these isolates was proportional to the number of isolates demonstrating the ApClSpStSuTe profile that were submitted in each year from each host population (Fig. S7). DNA was extracted as described above, and isolates sequenced (see Table S3). One human isolate was subsequently found to be contaminated and so was removed from all further analysis.

3. Scottish domestically-acquired DT104 isolates – post-epidemic

Twenty-four DT104 isolates (12 from animals, 12 from humans) were randomly selected from the post-epidemic period 2005 – 2011. DNA was extracted as described above, and isolates sequenced (Table S3). Two human isolates were subsequently found to be contaminated or had poor sequence quality and so were removed from all further analysis.

4. Travel-associated DT104 isolates reported to the SSSCDRL

Over the period 1990 – 2004, there were 135 reported human infections of DT104 from patients with a recent history of foreign travel. To assess how these isolates fit within the DT104 phylogeny generated with the Scottish isolates, 28 isolates were selected across the diversity of countries that the patients reported visiting (Table S3). DNA was extracted as described above,

and isolates were sequenced. One isolate was subsequently found to be contaminated and so was removed from all further analysis.

Japanese *S.* Typhimurium DT104

To provide context to the Scottish DT104 isolates, five human and five animal DT104 isolates were sequenced at the Laboratory of Bacterial Genomics, Pathogen Genomics Center, at the National Institute of Infectious Diseases in Tokyo, Japan. The Illumina GAIIx machine, with 81 base paired end reads, was used to obtain whole genome sequences. These isolates were from the period 1994 – 2012. Phenotypic susceptibility was assessed through disc diffusion, using Clinical and Laboratory Standards Institute (CLSI) criteria and breakpoints (*37, 38*). Resistance to ampicillin, chloramphenicol, streptomycin, sulphonamides, tetracycline, nalidixic acid, ciprofloxacin, kanamycin, cefotaxime, trimethoprim/sulphamethoxazole, gentamicin and fosfomycin was assessed. The phenotypic resistance patterns and year of isolation for these isolates are presented in Table S4.

Canadian *S.* Typhimurium DT104

To provide context to the Scottish DT104 isolates, 51 human isolates of DT104 from Canada were sequenced (Table S4). These isolates were from across Canada, over the period 1999 – 2002, and collected through the Canadian Integrated Program for Antimicrobial Resistance Surveillance (*39*). Phenotypic susceptibility was assessed using the Sensititer Automated Microbiology System (Trek Diagnostic Systems Ltd, Westlake, OH) method (*40*), and isolates were classified as resistant or non-resistant to each antimicrobial, according to CLSI breakpoints (*41*). Resistance to amoxicillin-clavulanic acid, ampicillin, amikacin, gentamicin, kanamycin, streptomycin, ceftiofur, ceftriaxone, cefoxitin, nalidixic acid, ciprofloxacin, sulphamethoxazole, trimethoprim-sulphamethoxazole, tetracycline and chloramplenicol was assessed.

English and Welsh *S.* Typhimurium DT104

To provide context to the Scottish DT104 isolates, 12 human isolates and 12 isolates from other animals were sequenced using the Illumina MiSeq platform and 150 bp paired end reads. The human isolates were provided by Public Health England (PHE; formerly the Health Protection Agency), and were isolated between 1991 – 2005. The isolates from other animals were provided by the Animal Health and Veterinary Laboratories Agency (AHVLA), and were isolated between 1996 – 2004 (then the Veterinary Laboratories Agency). Phenotypic susceptibility of the animal isolates (AHVLA) was assessed using disc diffusion (Table S8); isolates were classified as resistant or susceptible according to the zone sizes in Table S8 (*42*). Phenotypic susceptibility of the human isolates (PHE) was assessed using a modified breakpoint technique (*43*) (Table S9). The phenotypic resistance patterns and year of isolation for these isolates are presented in Table S5. One animal isolate was subsequently found to be contaminated and so was removed from all further analysis.

Methods

Genomic analysis

Mapping

Following sequencing, the DT104 isolates, the *S.* Typhimurium LT2 and *S.* Typhimurium SL1344 reference sequences (accession numbers AE006468 and FQ312003, respectively) were mapped to the finished *S.* Typhimurium DT104 chromosome and plasmid (accession numbers

HF937208 and HF937209, respectively) using SMALT v0.5.8. (*44*). Prophage sequences, which are known to be highly variable (*45, 46*), the multidrug resistance region of *Salmonella* Genomic Island 1 and the virulence plasmid were then excluded from single nucleotide polymorphism (SNP) calling, leaving a core genome of 4,686,262 base pairs. Genome-wide identification of SNPs and small insertions or deletions in the core genome, compared to the reference genome, were called. The minimum base call quality to call a SNP was set at 50, and the minimum mapping quality to call a SNP was set at 30 (*47*). Recombination events were detected and removed as outlined in Croucher *et al*. (*48*). RAxML v7.0.4 was used to reconstruct a phylogenetic tree from the SNPs called from the core genome (*49*), using a general time-reversible model with a gamma correction for among site variation. Support for nodes was assessed using 100 random bootstrap replicates. The tree was visualized using the Interactive Tree of Life (*50, 51*).

The mutation rate was calculated using the SNP alignment of the 359 typical Scottish and non-Scottish DT104 isolates, using the BEAST v1.7.4 software package (*18*). A proportion of invariant sites was included, as well as a discrete gamma distribution to model rate variation among sites. The isolation dates of samples in years were used to calibrate the time scale of the tree, and an uncorrelated lognormal relaxed molecular clock was used to accommodate rate variation among lineages (*52*). The exponential growth coalescent tree prior was used (*53, 54*), with a general time-reversible nucleotide substitution model. Four independent Markov Chain Monte Carlo (MCMC) analyses were run for 25 million states, sub-sampled once every 10,000 states. LogCombiner (*18*) was used to remove 10% as burn-in, resample every 50,000 states, and to combine those sub-samples from the four runs. The mutation rate was estimated to be 3.4 x 10^{-7} substitutions/site/year (95% highest posterior density [HPD] interval: 3.1 x 10^{-7} – 3.7 x 10^{-7}).

Assembly

The raw Illumina data were used to create a *de novo* draft assembly of the genome of each sample using the VELVET v0.7.03 algorithm (*55*), creating multi-contig draft genomes.

Identification of antimicrobial resistance determinants

The 147 Scottish isolates of DT104 from humans and other animals selected to investigate the diversity of observed phenotypic resistance profiles were interrogated for antimicrobial resistance determinants. An antimicrobial resistance determinant is defined as either a gene that has been previously identified to be associated with AMR, or a SNP that has been previously identified to be associated with AMR in *Salmonella*, such as those in DNA gyrase subunit A and quinolone resistance. The presence or absence of acquired resistance genes and SNPs associated with resistance were identified in the following way: A non-redundant pan-resistance pseudomolecule was created as a 'sub-reference sequence', consisting of the DT104 reference chromosome and plasmid, and other resistance genes and related regions that have been previously found to be involved in resistance to the 13 antimicrobials for which there were phenotypic data. These included unique regions of different SGI1 variants found in the literature (*17, 56-58*), as well as resistance genes reported to be found in *Salmonella* (*59, 60*), and other genetic regions, mainly plasmids, from which most of these genes were found (Table S10). After re-mapping the Illumina reads per sample with SMALT (*44*) to the resulting new pseudomolecule composed of both the DT104 reference sequence and the pan-resistance sub-reference sequence, resistance genes and related determinants within the samples that are not

present in the DT104 reference genome were detected. To identify further resistance determinants that were not included in the pan-resistance pseudomolecule, the accessory genome regions of the draft genomes were searched using BLAST.

A list of every gene identified, known to be relevant for antimicrobial resistance, was compiled for each isolate. Antimicrobial resistance genes that were believed to be pseudogenes, either due to truncation or interruption by another gene, were included, as they provide an indication of the evolutionary history of the isolate with respect to AMR. The *gyrA*, *gyrB*, *parC* and *parE* genes were inspected for SNPs that have been previously described as conferring resistance to quinolone antimicrobials (*59*). Venn diagrams of the number of resistance determinants and number of genotypic resistance profiles, and of the number of phenotypic resistance profiles in the original 5,200 domestically-acquired DT104 isolates from 1990 – 2004 (*11*) were generated using the VennDiagram package (*61*) of R (*62*). The same methods were used to interrogate all isolates for the presence or absence of the same resistance determinants. Table S11 details the number of antimicrobial resistance determinants and number of unique resistance profiles for the 133 typical DT104 isolates.

It is worth noting that four resistance phenotypic profiles of the original 65 observed (*11*) were not represented in the sequencing analysis, due to non-viability of the archived isolate or contamination; of these, three were from humans. There were also two phenotypic resistance profiles of the original 35 observed in the animal isolates that that are not represented in the sequencing analysis, due to non-viability of the archived isolate or contamination, but which are represented in the sequenced human isolates. Similarly, two phenotypic resistance profiles of the original 52 observed in the human isolates are not represented in the sequencing analysis, due to non-viability of the archived isolate or contamination, but which are represented in the sequenced animal isolates.

To evaluate whether or not differential sampling bias could be, in part, responsible for our observation of a greater diversity of resistance determinants and profiles in the human isolates, we performed a rarefaction analysis using the vegan package (*63*) of R (*62*) on the dataset of 147 isolates. This examines the number of genotypic profiles (species richness) for a certain number of isolates, and evaluates whether or not there is additional, unsampled diversity. The diversities cannot be directly compared, as these particular isolates are a highly non-random subset of the overall sample collection from humans and animals (n=5,200). While the number of genotypic resistance profiles cannot be compared statistically, the greater diversity in the human isolates confirms that observed in the phenotypic resistance profiles. What be observed in Fig. 3D is that we have sampled the animal isolates as thoroughly, if not more so, than the human isolates, and thus suggests that our results cannot be accounted for by sampling bias.

Bayesian phylogenetic inference

The BEAST v1.7.4 software package (*18*) was used for Bayesian ancestral state reconstruction, using discrete phylogenetic diffusion models (*19*). Four models were set up, allowing for either bidirectional (both human-to-animal and animal-to-human transmission), or unidirectional transmission, and for the bidirectional models, either symmetric (equal two-way) or asymmetric (allowing unequal) transmission. The models therefore represented: 1) bidirectional asymmetric diffusion, 2) bidirectional symmetric diffusion, 3) unidirectional human-to-animal diffusion, 4)

unidirectional animal-to-human diffusion. The data for these models were the alignment of variable sites (SNPs) of the 248 Scottish DT104 isolates, 135 (54%) human and 113 (46%) animal, and the discrete trait representing the host population from which the isolates were obtained. A proportion of invariable sites was included, as well as a discrete gamma distribution to model rate variation among sites. These isolates were sampled from 1990 – 2011 (see Tables S2 and S3), excluding the 14 atypical DT104 isolates. The exponential growth coalescent tree prior was used (*53, 54*), with a general time-reversible nucleotide substitution model. Other tree priors were explored and compared using Bayes factors estimated through path sampling (*64*); the exponential prior was the preferred model. The isolation dates of samples in years were used to calibrate the time scale of the tree, and an uncorrelated lognormal relaxed molecular clock was used to accommodate rate variation among lineages (*52*). A conditional reference prior was specified on the overall rate scalar (clock rate) in the continuous-time Markov chain (CTMC) model for the phylogenetic diffusion of the discrete host population trait (*65*). We used stochastic mapping techniques to estimate both the transitions (Markov jumps) and the waiting times (Markov rewards) of the host trait diffusion process throughout the evolutionary history (*66, 67*). Markov jumps estimates provide expectations for the unobserved human-to-animal and animal-to-human transitions along each branch of the tree; Markov rewards estimates provide corresponding expectations for the amount of time that is spent in each state, human or animal. Log marginal likelihoods obtained by path sampling and the resulting log Bayes factors revealed strong evidence against both the unidirectional scenarios. For these marginal likelihood estimations, we treated trees, independently estimated from the sequence data, as a discrete set of possibilities (*68*); the analysis for all four models integrated over the same empirical tree distribution. The best fitting model was the asymmetric bidirectional model (Table S12); four independent Markov Chain Monte Carlo (MCMC) analyses were run for 50 million states, sub-sampled once every 10,000 states, using BEAGLE (*69*) in conjunction with BEAST (*18*). LogCombiner (*18*) was used to remove 10% as burn-in, resample every 50,000 states, and to combine those sub-samples from the four runs. The maximum clade credibility tree from the resulting 3,600 trees was summarized with TreeAnnotator and visualized with FigTree (*18*). The posterior median number of unobserved animal-to-human transitions along branches was 39 (95%HPD: 27 – 55), and the median number of unobserved human-to-animal transitions within branches was 27 (95%HPD: 17 – 36). Of the entire evolutionary time represented by Fig. 2A, the Markov rewards indicated the model spent a median of 400 (95%HPD: 318 – 521) years in the animal state, and a median of 666 (95%HPD: 545 – 771) years in the human state. To quantify and test the degree of host admixture we used a modified Association Index (AI) (*19*). Briefly, for each tree in our posterior distribution, we calculate the association value following Wang *et al* (*70*), which quantifies the association between phylogeny and host traits. We calculate the same value for a number of permutations (n = 10), in which traits are randomly associated with the tree tips, and take the ratio of the association value for the real traits and the corresponding mean value for the permutations. Finally, we report the posterior distribution for this ratio by summarizing the AI for each tree in the posterior sample. A general deviation from the permuted distributions implies low AI values and suggests host structure in the phylogeny whereas AI values close to 1 suggest host admixture or no more clustering by host as expected from random association. The AI was 0.66 (95%HPD: 0.57 – 0.76), which rejects the null hypothesis (AI = 1), and indicates that clustering within the phylogenetic trees is not randomized.

We also conducted additional analyses with two different subsets of the data, with two independent MCMC analyses each. The majority of animal isolates are from cattle, reflecting the main animal reservoir of DT104 (*20, 31*). Thus, we performed the same analysis examining the 135 Scottish human isolates, and the 83 Scottish cattle isolates. We also conducted the same analysis dividing the animal isolates into their respective species, excluding species which were represented less than five times in the 113 animal isolates, giving 83 bovine, seven ovine, eight porcine, and six poultry isolates (n=104). In both cases, as the number of animal isolates decreased in the dataset, the dominance of the human ancestral state in the evolutionary history increased, as one would expect. In the cattle-only model, compared to the model with the full dataset, there were higher human Markov rewards, lower cattle Markov rewards, and fewer cattle-to-human Markov jumps. In the model sub-dividing the animal species, compared to the full model there were higher human Markov rewards, although similar animal Markov rewards, fewer animal-to-human Markov jumps and more human-to-animal Markov jumps. These results substantiate our conclusions based on the more conservative analysis including all animal and human isolates.

Comparing phenotypic resistance profiles and the genomic backbone of *S.* Typhimurium DT104

Each isolate in the dataset that was submitted to the SSSCDRL, as well as the reference DT104 sequence (accession HF937208), was included in this comparison. The 275 isolates from the SSSCDRL included those acquired domestically in Scotland, and those submitted from Scottish patients with a recent history of foreign travel; only these isolates were included, as the same microbiological and antimicrobial susceptibility testing methods were used to characterize these isolates. A molecular phylogenetic tree was generated as described in the Mapping section, by mapping the isolates to the reference sequence, calling SNPs from the core genome, and using RAxML (*49*) to draw the phylogenetic relationships. The distribution of the main phenotypic profile, ApClSpStSuTe, throughout the molecular phylogenetic tree of the same 275 isolates was visualized by plotting this specific trait on the tree using the Interactive Tree of Life (*50, 51*) (Fig S3A). All phenotypic resistance profiles, the combinations of phenotypic resistance to the 13 antimicrobials assessed, were also plotted against the tree (Fig. S3B).

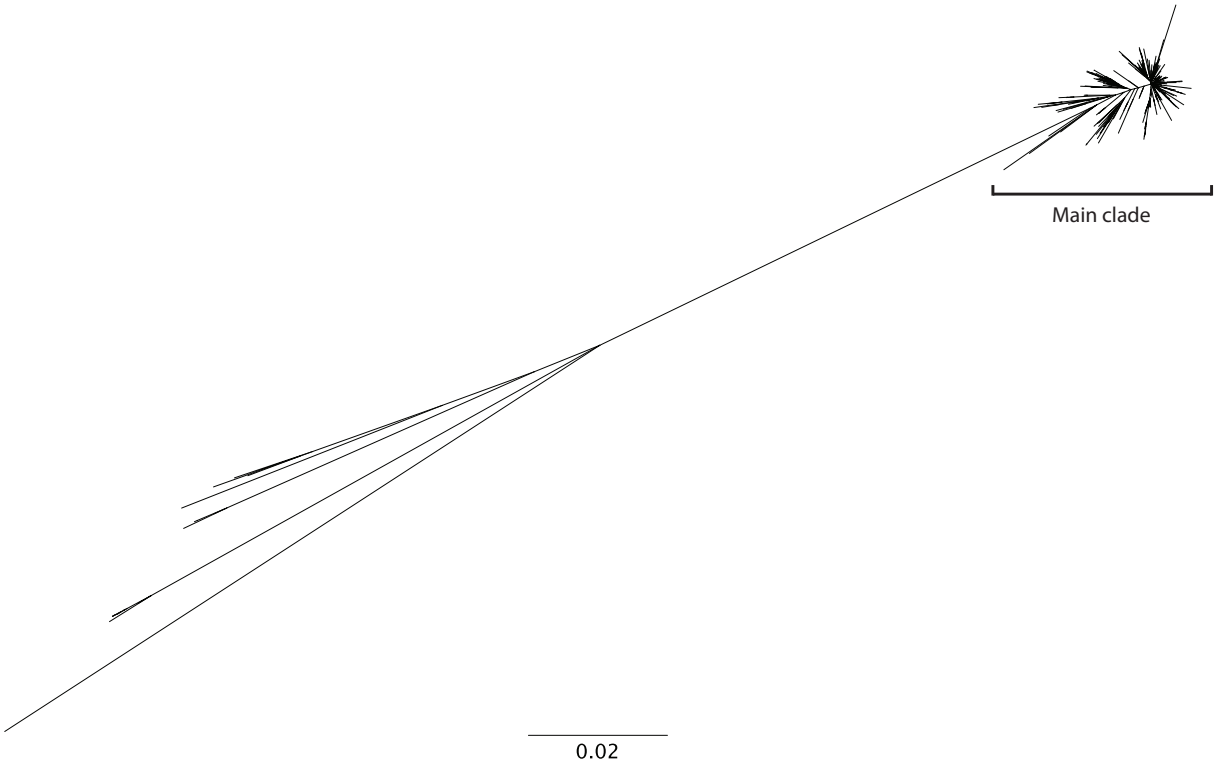


Fig. S1.

Maximum likelihood phylogeny of all 373 *Salmonella* Typhimurium DT104, from Scotland and elsewhere, demonstrating a main clade and a subset of 14 isolates. Scale bar represents number of substitutions per single nucleotide polymorphism site per year.

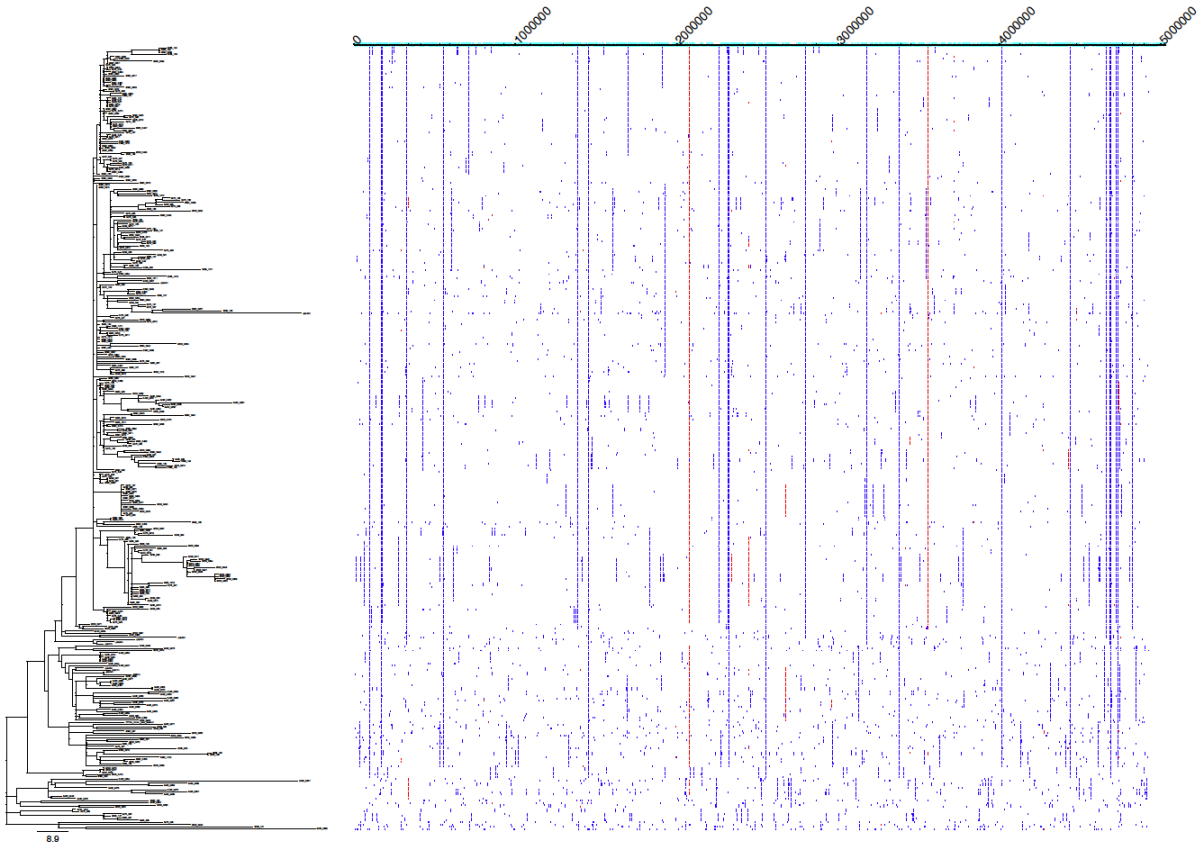


Fig. S2

Single nucleotide polymorphisms (SNPs; blue) and homoplastic SNPs (red) across the genome of *S.* Typhimurium DT104 in the 359 typical DT104 isolates. Non-synonymous SNPs found in >5 isolates primarily were found in genes encoding membrane proteins; genes related to peripheral metabolism, amino acid transport, transcription regulation, catabolic pathways, or disulphide bond formation; genes of unknown function; flagellin; DNA gyrase A; degenerate phage genes; virulence-related genes; or pseudogenes of various classes.

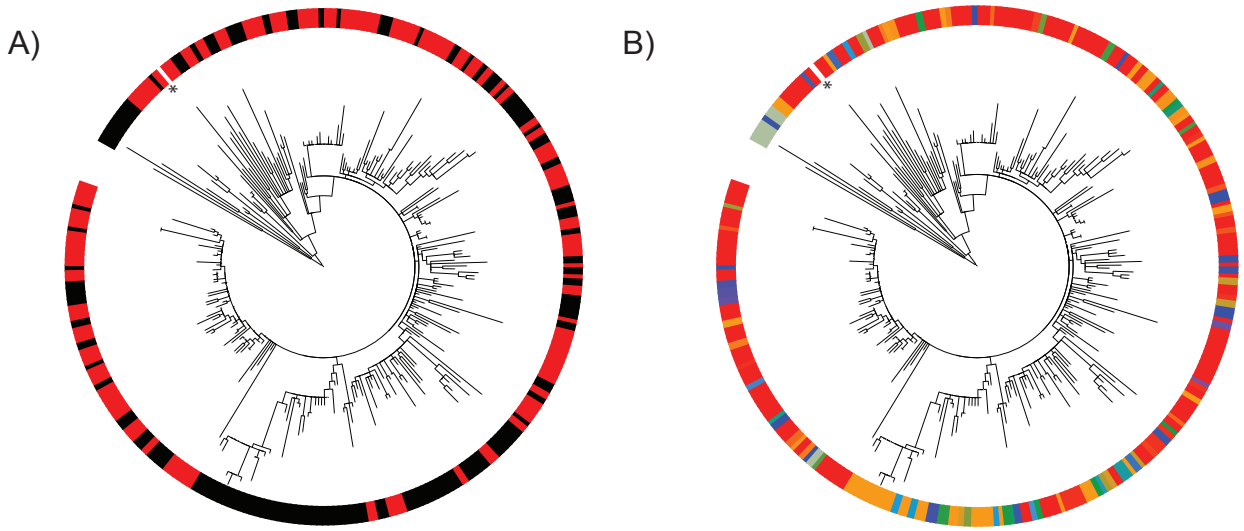


Fig. S3

Maximum likelihood phylogenetic tree, mid-point rooted, using single nucleotide polymorphisms of 275 *Salmonella* Typhimurium DT104 isolates processed by the Scottish *Salmonella Shigella* and *Clostridium difficile* Reference Laboratory, with A) isolates exhibiting resistance to the ApClSpStSuTe phenotypic resistance profile (red), putatively conferred by *Salmonella* Genomic Island 1, and other phenotypic resistance profiles (black), and B) all phenotypic resistance profiles colored individually. The asterisk indicates the location of the reference isolate HF937208.

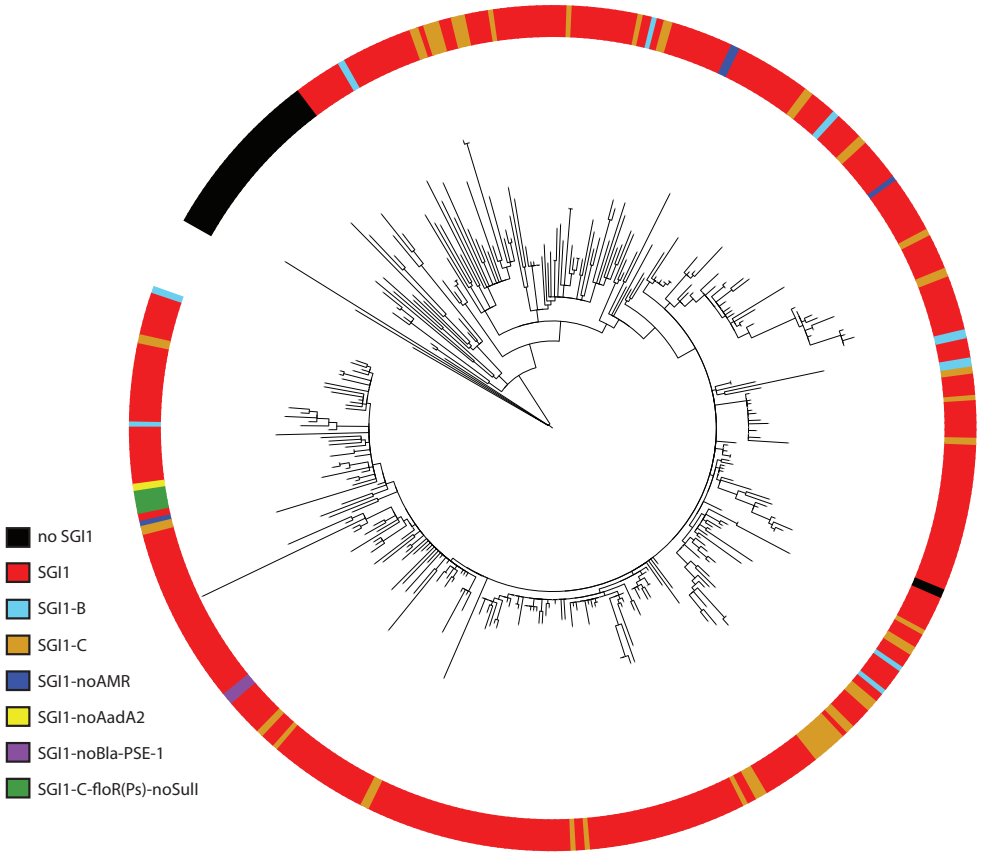


Fig. S4.
Phylogeny of Scottish and global *Salmonella* Typhimurium DT104, rooted on *S.* Typhimurium SL1344. The colored ring indicates the putative *Salmonella* Genomic Island 1 variant within each isolate; (Ps) indicates a pseudogene.

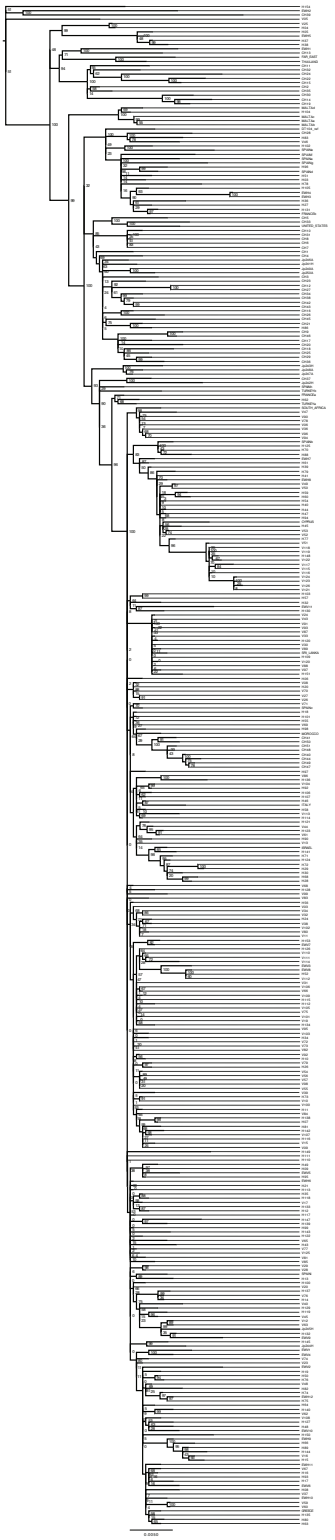


Fig S5. Phylogeny from Fig. 1 of Scottish and non-Scottish *Salmonella* Typhimurium DT104, rooted on *S.* Typhimurium SL1344, with bootstrap values.

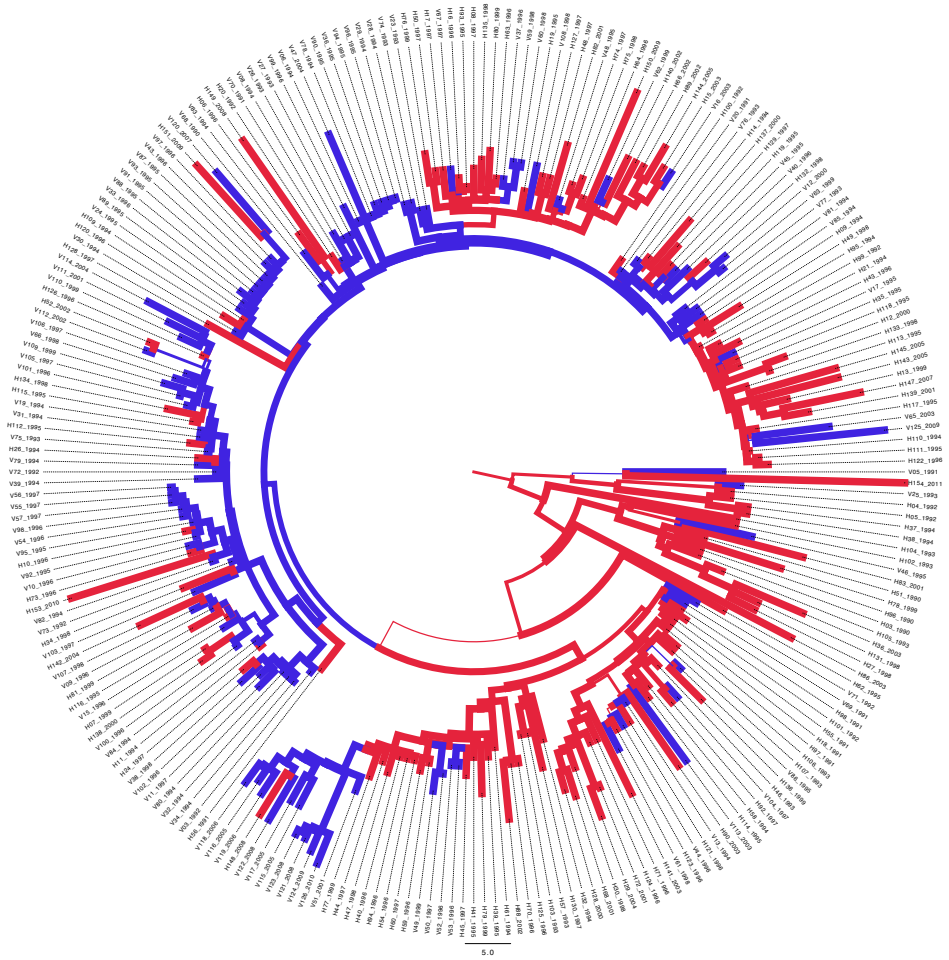
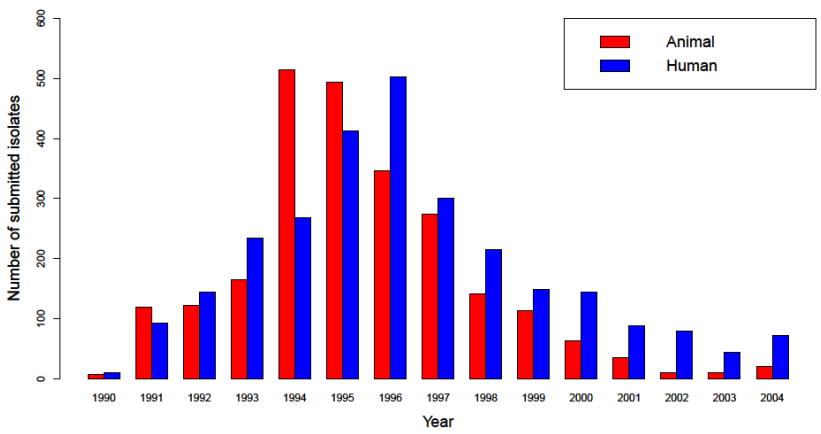


Fig. S6

Bayesian maximum clade credibility phylogenetic tree and most probable ancestral state reconstruction of host population for *Salmonella* Typhimurium DT104 in Scotland of Fig. 2A. Branches with a reconstructed state (host population) posterior probability are colored red for human, blue for animal; branch width is scaled by the posterior probability of reconstructed state.

A)



B)

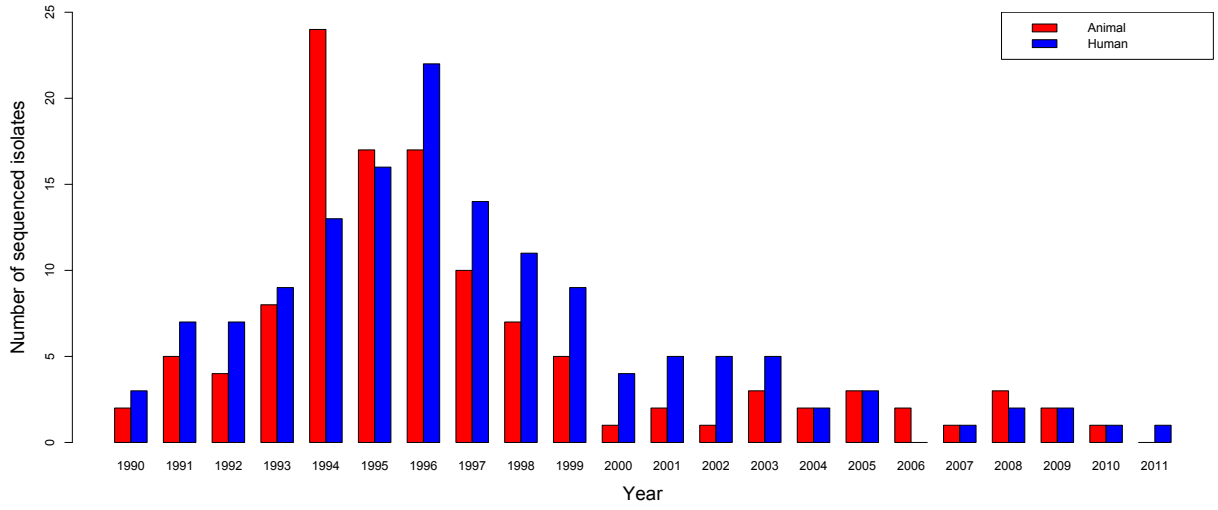


Fig. S7

A) Number of *S.* Typhimurium DT104 domestically-acquired isolates submitted per year to the Scottish *Salmonella Shigella* and *Clostridium difficile* Reference Laboratory, 1990 – 2004 (reproduced from (*11*)), and B) the number of sequenced domestically-acquired (*n*=262) *S.* Typhimurium DT104 isolates, 1990 – 2011, by year of isolation in the study dataset.

Table S1. Number of *Salmonella* Typhimurium DT104 isolates per country, the reason for selecting the isolates, and the sequencing information for the isolates included in the study.

Country of detection	Country of origin	Host	No. isolates	Purpose	Sequencing
Scotland	Scotland	Humans, animals	147	To cover the observed phenotypic AMR profiles	Illumina GAII, 76bp paired end
Scotland	Scotland	Humans, animals	93	To investigate the diversity within the predominant phenotypic AMR pattern*	Illumina HiSeq, 100bp paired end
Scotland	Scotland	Humans, animals	22	To investigate the post-epidemic period, 2005-2011	Illumina HiSeq, 100bp paired end
Scotland	Various foreign countries§	Humans	27	To provide context to the Scottish DT104	Illumina HiSeq, 100bp paired end
Canada	Canada	Humans	51	To provide context to the Scottish DT104	Illumina HiSeq, 100bp paired end
Japan	Japan	Humans, bovids	10	To provide context to the Scottish DT104	Illumina GAIIx, 81bp paired end
England/ Wales	England/ Wales	Humans, animals	23	To provide context to the Scottish DT104	Illumina MiSeq, 150bp paired end

* demonstrating resistance to ampicillin, chloramphenicol, streptomycin, spectinomycin, sulphonamides, tetracycline

§ see Table S3 for details

Table S2. Human and animal isolates of *S.* Typhimurium DT104 from Scotland, submitted to the Scottish *Salmonella Shigella* and *Clostridium difficile* Reference Laboratory, showing antimicrobial resistance (AMR) phenotypic profile and resistance determinants, in the subset of 147 isolates used to assess the diversity of resistance. Ap = ampicillin, Cl = chloramphenicol, Sp = spectinomycin, St = streptomycin, Su = sulphonamides, Te = tetracycline, Ka = kanamycin, Cp = ciprofloxacin, Na = nalidixic acid, Gm = gentamicin, Ne = netilmicin, Tm = trimethoprim, Fz = furazolidone. Genes marked as (Ps) are believed to be pseudogenes, either through truncation (Ps) or interruption by another gene (Ps-2f).

Isolate	Isolated from:	AMR phenotypic profile	Year of isolation	Resistance determinants identified*
H01	Human	ApStSuTe	1991	*tetA(A), tetR(A), bla(TEM-1b), strA, strB, sulII*
H02	Human	ApStSuTe	1992	*tetA(A), tetR(A), bla(TEM-1b), strA, strB, sulII*
H03	Human	pansusceptible	1990	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H04	Human	pansusceptible	1992	
H05	Human	pansusceptible	1992	
H06	Human	ApClSpStSuTe	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H07	Human	ApClSpStSuTe	1999	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H08	Human	ApClSpStSuTe	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H09	Human	ApClSpStSuTe	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H10	Human	ApClSpStSuTe	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H11	Human	ApClSpStSuTe	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H12	Human	ApClSpStSuTe	2000	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H13	Human	ApClSpStSuTe	1999	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H14	Human	ApClSpStSuTe	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H15	Human	ApClSpStSuTeTm	2003	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
H16	Human	ApClSpStSuTeTm	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
H17	Human	ApClSpStSuTeTm	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
H18	Human	ApClSpSuTe	1991	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H19	Human	ApClSpSuTe	1995	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H20	Human	ApClFzSpStSuTe	1992	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H21	Human	ApClFzSpStSuTe	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H22	Human	Te	1993	*tetA(A), tetR(A)*
H23	Human	Te	1995	*tetA(A), tetR(A)*
H24	Human	ApClGmNeSpStSuTe	1997	*aadA2, sulI*
H26	Human	ApClKaSpStSuTe	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H27	Human	ApClKaSpStSuTe	1998	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H28	Human	SpStSu	2000	*aadA2, sulI*

H29	Human	SpStSu	2004	*aadA2, sulI*
H30	Human	SpStSu	1998	*aadA2, sulI*
H31	Human	SuTeTm	1991	*tetD, tetC, tetA, tetR2*
H32	Human	ApSu	1994	*bla(PSE-1), sulI*
H34	Human	ApSu	1998	*aadA2, sulI*
H35	Human	ApSpStSuTe	1995	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H36	Human	ApSpStSuTe	2003	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H37	Human	SuTm	1994	*sulII, strA(Ps-2f), dfrA14, strB*
H38	Human	SuTm	1994	
H39	Human	ApClNaSpStSuTe	1995	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
H40	Human	ApClNaSpStSuTe	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
H41	Human	ApClNaSpStSuTe	1995	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
H43	Human	ApClNaSpStSuTeTm	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
H44	Human	ApClNaSpStSuTeTm	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, dfr1, bla(TEM-1b), sulII, DgyrA(87)N*
H45	Human	ApClNaSpStSuTeTm	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB, DgyrA(87)N*
H46	Human	ApSpStSu	1993	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H47	Human	ApClKaNaSpStSuTeTm	1998	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB, DgyrA(87)N*
H48	Human	ApClKaSpStSuTeTm	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H49	Human	ApClKaSpStSuTeTm	1998	*aadA2, sulI*
H50	Human	ApClCpNaSpStSuTe	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, SgyrA(83)F*
H51	Human	ApClStSuTe	1990	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H52	Human	ApClStSuTe	2002	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H54	Human	Na	1996	*DgyrA(87)N*
H55	Human	ApClFzSpStSuTeTm	1991	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H56	Human	ApClSpSu	1991	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H57	Human	ApStSu	1993	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H58	Human	ApStSu	1994	*bla(PSE-1), sulI*
H59	Human	ApClKaNaSpStSuTe	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
H60	Human	ApClKaNaSpStSuTe	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph3'(I), DgyrA(87)N*
H61	Human	ApClNaStSuTe	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
H62	Human	ApClFzNaSpStSuTe	1995	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H63	Human	ApNaSu	1996	*bla(PSE-1), sulI, DgyrA(87)G*
H64	Human	ApClSuTeTm	1996	*bla(PSE-1), floR, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*

H66	Human	ApSuTm	2002	*bla(PSE-1), sulI, sulII, strA(Ps-2f), dfrA14, strB*
H67	Human	StSuTe	1996	*tetA(A), tetR(A), strA, strB, sulII*
H68	Human	StSuTe	2001	*aadA2, sulI*
H69	Human	ClFzSuTeTm	1996	*cat, aadA5, sulI, tetR2, tetA, tetC, dfrA17*
H70	Human	ApKaSu	1996	*bla(PSE-1), sulI, aph3'(I)*
H71	Human	SpSt	1996	*aadA2, sulI*
H72	Human	SpSt	2001	*aadA2, sulI*
H73	Human	SpStSuTe	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H74	Human	SpStSuTm	1997	*floR(Ps), aadA2, sulII, strA(Ps-2f), dfrA14, strB*
H75	Human	SpStSuTm	1998	*floR(Ps), aadA2, sulII, strA(Ps-2f), dfrA14, strB*
H76	Human	ApCpNaSpStSuTm	1999	*aadA2, sulI, SgyrA(83)F*
H77	Human	KaNaSpStSuTm	1999	*aadA2, sulI, sulII, aph3'(II), ble, sph, dfrA12, DgyrA(87)N*
H78	Human	NaSpStSu	1999	*aadA2, sulI, DgyrA(87)N*
H79	Human	NaSpStSu	1999	*aadA2, sulI, DgyrA(87)N*
H80	Human	ApCpNaSpStSuTe	1999	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)G*
H81	Human	ApCpSpStSuTe	1999	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H82	Human	ApClSpStSuTm	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
H83	Human	ApSuTe	2001	*bla(PSE-1), sulI*
H86	Human	Ap	2003	*bla(PSE-1), sulI*
H88	Human	ApClStSuTeTm	2002	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
H89	Human	ApClStSuTeTm	2002	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
H90	Human	StSu	2003	*aadA2, sulI*
H92	Human	ApClSpStSuTe	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H93	Human	ApClSpStSuTeTm	1995	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
H94	Human	ApClNaSpStSuTe	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
H95	Human	ApClSpStSuTeTm	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
V01	Bovine	ApStSuTe	1994	*tetA(A), tetR(A), bla(TEM-1b), strA, strB, sulII*
V02	Porcine	ApStSuTe	1990	*tetA(A), tetR(A), bla(TEM-1b), strA, strB, sulII*
V03	Bovine	pansusceptible	1992	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V05	Bovine	pansusceptible	1991	
V06	Ovine	ApClSpStSuTe	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V08	Bovine	ApClSpStSuTe	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V09	Bovine	ApClSpStSuTe	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V10	Bovine	ApClSpStSuTe	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V11	Bovine	ApClSpStSuTe	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V12	Poultry	ApClSpStSuTe	2000	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*

V13	Bovine	ApClSpStSuTe	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V15	Poultry	ApClSpStSuTeTm	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V16	Bovine	ApClSpStSuTeTm	2003	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
V17	Bovine	ApClSpStSuTeTm	1995	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V19	Ovine	ApClFzSpStSuTe	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V20	Bovine	ApClFzSpStSuTe	1991	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V21	Bovine	Te	1991	
V22	Porcine	Te	1994	*tetA(A), tetR(A)*
V23	Bovine	ApClGmNeSpStSuTe	1993	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, tetA(A), tetR(A), strA, strB, aac3(IV), hygBr*
V24	Ovine	ApClGmNeSpStSuTe	1995	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V25	Bovine	ApKaStSuTe	1993	*tetA(A), tetR(A), bla(TEM-1b), strA, strB, sulII, aph3'(I)*
V26	Bovine	ApClGmKaNeSpStSuTe	1993	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, strA, strB, aac3(IV), hygBr*
V27	Bovine	ApClGmKaNeSpStSuTe	1993	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V28	Equine	ClSpStSuTe	1994	*floR, aadA2, sulI, tetG, tetR*
V29	Equine	ClSpStSuTe	1994	*floR, aadA2, sulI, tetG, tetR*
V30	Bovine	ApClSpStTe	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V31	Bovine	ApClSpSt	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V32	Bovine	ApClKaSpStSuTe	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V33	Bovine	ApClKaSpStSuTe	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V34	Bovine	ApClSpStSu	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V35	Porcine	KaSpStSuTe	1994	*tetD, tetC, tetA, tetR2*
V36	Bovine	SpStSu	1995	*aadA2, sulI*
V37	Bovine	SpStSu	1996	*aadA2, sulI*
V38	Bovine	SpStSu	1998	*aadA2, sulI*
V39	Porcine	ApClGmKaNeSpStSuTeTm	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aac3(IV), hygBr*
V40	Porcine	ApClGmKaNeSpStSuTeTm	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
V41	Bovine	SuTeTm	1994	*tetD, tetC, tetA, tetR2*
V42	Bovine	SuTeTm	1994	*sulII, strA(Ps-2f), dfrA14, strB, tetD, tetC, tetA, tetR2*
V43	Bovine	ApSu	1996	*bla(PSE-1), sulI*
V44	Bovine	ApSu	1996	*bla(PSE-1), sulI*
V45	Bovine	ApClNeSpStSuTe	1995	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V46	Ovine	ApSpStSuTe	1995	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V47	Bovine	ApSpStSuTe	2004	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V48	Bovine	SuTm	1995	
V49	Bovine	ApClNaSpStSuTe	1999	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*

V50	Bovine	ApClNaSpStSuTe	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
V51	Bovine	ApClNaSpStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
V52	Poultry	ApNaSpStSuTe	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
V53	Poultry	ApNaSpStSuTe	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
V54	Bovine	ApClGmNaSpStSuTe	1996	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, strA(Ps), strB, aac3(IV), hygBr*
V55	Bovine	ApClGmSpStSuTe	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V56	Bovine	ApClGmSpStSuTe	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, strA(Ps), strB, aac3(IV), hygBr*
V57	Bovine	ApClGmNaNeSpStSuTe	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, strA(Ps), strB, aac3(IV), hygBr, SgyrA(83)F*
V59	Bovine	ApClNaSpStSuTeTm	1998	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB, DgyrA(87)N*
V60	Bovine	ApClNaSpStSuTeTm	1998	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
V61	Bovine	ApSpStSu	1998	*aadA2, sulI*
V62	Bovine	ApClKaNaSpStSuTeTm	1999	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V63	Poultry	ApClKaSpStSuTeTm	1999	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V65	Misc.	SpSu	2003	*aadA2, sulI*
V66	Bovine	ApClSpStSuTe	1998	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V67	Feline	ApClSpStSuTeTm	1997	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*

* Table S10 provides the Uniprot identifiers for each of the resistance determinants listed.

Table S3. Human and animal isolates of *S.* Typhimurium DT104 submitted to the Scottish *Salmonella Shigella* and *Clostridium difficile* Reference Laboratory, with antimicrobial resistance (AMR) phenotypic profile and resistance determinants, in the subset of 93 Scottish isolates used to assess the diversity of isolates demonstrating the main phenotypic resistance profile, the 22 Scottish isolates used to investigate the post-epidemic period 2005 – 2011, and the 27 travel-associated isolates. Ap = ampicillin, Cl = chloramphenicol, Sp = spectinomycin, St = streptomycin, Su = sulphonamides, Te = tetracycline, Ka = kanamycin, Cp = ciprofloxacin, Na = nalidixic acid, Gm = gentamicin, Ne = netilmicin, Tm = trimethoprim, Fz = furazolidone. Genes marked as (Ps) are believed to be pseudogenes, either through truncation (Ps) or interruption by another gene (Ps-2f).

Isolate	Isolated from:	Year of isolation	AMR phenotypic profile	Resistance determinants identified
H96	Human	1990	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H97	Human	1991	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H98	Human	1991	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H99	Human	1992	ApClSpStSuTe	*aadA2, sulI*
H100	Human	1992	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H101	Human	1992	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H102	Human	1993	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H103	Human	1993	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H104	Human	1993	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H105	Human	1993	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H106	Human	1993	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H107	Human	1993	ApClSpStSuTe	*aadA2, sulI*
H109	Human	1994	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H110	Human	1994	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H111	Human	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H112	Human	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H113	Human	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H114	Human	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H115	Human	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H116	Human	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H117	Human	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H118	Human	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*

H119	Human	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H120	Human	1996	ApClSpStSuTe	*aadA2, sulI*
H121	Human	1996	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H122	Human	1996	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H123	Human	1996	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H124	Human	1996	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H125	Human	1996	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H126	Human	1996	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H127	Human	1997	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H128	Human	1997	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H129	Human	1997	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H130	Human	1997	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H131	Human	1998	ApClSpStSuTe	*aadA2, sulI*
H132	Human	1998	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H133	Human	1998	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H134	Human	1998	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H135	Human	1998	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H136	Human	1999	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H137	Human	2000	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H138	Human	2000	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H139	Human	2001	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H140	Human	2002	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H141	Human	2003	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H142	Human	2004	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H143	Human	2005	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H144	Human	2005	ApClSpStSuTeTm	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H145	Human	2005	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H147	Human	2007	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H148	Human	2008	ApClNaSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
H149	Human	2008	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H150	Human	2009	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*

H151	Human	2009	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H153	Human	2010	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
H154	Human	2011	pansusceptible	
V68	Bovine	1990	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V69	Bovine	1991	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V70	Bovine	1991	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V71	Bovine	1992	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V72	Bovine	1992	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V73	Bovine	1992	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V74	Bovine	1993	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V75	Bovine	1993	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V76	Porcine	1993	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V77	Bovine	1993	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V78	Canine	1994	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V79	Bovine	1994	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V80	Canine	1994	ApClSpStSuTe	*aadA2, sulI*
V81	Bovine	1994	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V82	Bovine	1994	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V83	Bovine	1994	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V84	Bovine	1994	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V85	Porcine	1994	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V86	Feline	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V87	Bovine	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V88	Bovine	1995	ApClSpStSuTe	*aadA2, sulI*
V89	Bovine	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V90	Bovine	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V91	Ovine	1995	ApClSpStSuTe	*aadA2, sulI*
V92	Bovine	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V93	Bovine	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V94	Bovine	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V95	Bovine	1995	ApClSpStSuTe	*aadA2, sulI*

V96	Ovine	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V97	Ovine	1996	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V98	Bovine	1996	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V99	Bovine	1996	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V100	Bovine	1996	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V101	Bovine	1996	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V102	Bovine	1996	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V103	Bovine	1997	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V104	Bovine	1997	ApClSpStSuTe	*aadA2, sulI*
V105	Bovine	1997	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V106	Bovine	1997	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V107	Poultry	1998	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V108	Bovine	1998	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V109	Bovine	1999	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V110	Bovine	1999	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V111	Porcine	2001	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V112	Equine	2002	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V113	Porcine	2003	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V114	Bovine	2004	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V115	Bovine	2005	ApClNaSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
V116	Bovine	2005	ApClNaSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
V117	Bovine	2005	NaSpStSu	*aadA2, sulI, DgyrA(87)N*
V118	Bovine	2006	ApClNaSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
V119	Bovine	2006	ApClNaSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
V120	Porcine	2007	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V121	Bovine	2008	ApClNaSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
V122	Pigeon	2008	ApClNaSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
V123	Bovine	2008	ApClNaSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
V124	Bovine	2009	ApClNaSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
V125	Porcine	2009	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
V126	Bovine	2010	ApClNaSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*

FAR_EAST	Human	1998	pansusceptible	
THAILAND	Human	1992	pansusceptible	
MOROCCO	Human	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
SPAINe	Human	1997	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
SPAINf	Human	1992	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
SPAINg	Human	1999	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
SPAINa	Human	1998	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
SPAINb	Human	1997	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
SPAINc	Human	1992	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
SPAINh	Human	1994	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
SPAINd	Human	1992	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
FRANCEa	Human	1991	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
GREECE	Human	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
ITALY	Human	1998	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
UNITED_STATES	Human	2002	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
SRI_LANKA	Human	1997	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
MALTAa	Human	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
MALTAb	Human	1995	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
MALTAc	Human	1993	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
MALTAd	Human	1994	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
TURKEYa	Human	1997	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
TURKEYb	Human	2001	ApClSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
SOUTH_AFRICA	Human	1996	ApClSpStSuTeTm	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
FRANCEb	Human	1998	SpStSu	*aadA2, sulI*
CYPRUS	Human	2003	ApClNaSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
ISRAEL	Human	1997	ApClNaSpStSuTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
SPAINi	Human	1996	FzTe	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*

Table S4. Human isolates from Canada, as tested by the Canadian Integrated Program for Antimicrobial Resistance Surveillance, human and animal isolates from Japan, as tested by the National Institute of Infectious Diseases and the National Institute of Animal Health, of *S.* Typhimurium DT104 with antimicrobial resistance (AMR) phenotypic profile and resistance determinants. Ap = ampicillin, Cl = chloramphenicol, St = streptomycin, Su = sulphonamides, Te = tetracycline, Na = nalidixic acid, Tm = trimethoprim. Genes marked as (Ps) are believed to be pseudogenes, either through truncation (Ps) or interruption by another gene (Ps-2f).

Isolate	Isolated from:	AMR phenotypic profile	Year of isolation	Resistance determinants identified
CH1	Human	ApStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH2	Human	pansusceptible	2001	
CH3	Human	StSu	2001	*aadA2, sulI, aph(3')-I*
CH4	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH5	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH6	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH7	Human	ApStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH8	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I*
CH9	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I, dfrA12, sulIII, bla(TEM-1b), mefE*
CH10	Human	StSu	2001	*aadA2, sulI*
CH11	Human	pansusceptible	2001	
CH12	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH13	Human	pansusceptible	2001	
CH14	Human	Te	2001	*aph(3')-I*
CH15	Human	pansusceptible	2001	
CH16	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH17	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I*
CH18	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I*
CH19	Human	SuTe	2001	*tetA, tetR2, sulII, hygBr, aac(3)-IV, aph(3')-I*
CH20	Human	ApClStSuTeTm	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, tetA(A), tetR(A), aph(3')-I, dfrA12*
CH21	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I*
CH22	Human	pansusceptible	2001	

CH23	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I*
CH24	Human	pansusceptible	2001	
CH25	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I*
CH26	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I*
CH27	Human	Te	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH28	Human	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH29	Human	ApClStSuTe	2002	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I*
CH30	Human	Te	2002	*tetA, tetR2, aph(3')-I*
CH31	Human	ApClStSuTe	2002	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH32	Human	pansusceptible	2002	
CH33	Human	ApClStSuTe	2002	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I*
CH34	Human	ApClStSuTe	2002	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH35	Human	Ap	2002	*bla(TEM-1b)*
CH36	Human	ApClStSuTe	2000	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I*
CH37	Human	pansusceptible	2000	*aph(3')-I*
CH38	Human	ApClStSuTe	2000	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH39	Human	pansusceptible	2000	
CH40	Human	ApClStSuTeTm	2000	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, dfrA12*
CH41	Human	ApClStSuTe	2000	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH42	Human	ApClStSuTe	2000	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH43	Human	ApClStSuTe	2000	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I, sulIII, mefE*
CH44	Human	ApClStSuTeTm	2000	*floR, tetA(A), tetR(A), strA, strB, sulII, ampC, sugE, dfrA12, aadA2, bla(TEM-1b), cmlA, aadA1, sulIII, mefE, aac(3)-IV, hygBr, aph(3')-I*
CH45	Human	StSu	2000	*aadA2, sulI*
CH46	Human	ApClStSuTe	2000	*aadA2, sulI, aph(3')-I*
CH47	Human	ApClStSuTe	1999	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH48	Human	ApClStSuTe	1999	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH49	Human	ApClStSuTe	1999	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH50	Human	ApClStSuTe	1999	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
CH51	Human	ApClStSuTe	1999	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
Jp241H	Human	ApClStSuTeNa	1998	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, SgyrA(83)F*

Jp242H	Human	ApClStSuTe	2003	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
Jp243H	Human	ApClStSuTe	2004	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
Jp244H	Human	ApClStSuTe	2008	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
Jp245H	Human	ApClStSuTe	2012	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
Jp246A	Bovine	ApClStSuTe	1994	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
Jp247A	Bovine	ApClStSuTe	1995	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
Jp248A	Bovine	ApClStSuTe	2001	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
Jp249A	Bovine	ApClStSuTe	2003	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
Jp250A	Bovine	ApClStSuTeNa	2007	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, SgyrA(83)F*

Table S5. Human and animal isolates, as tested by Public Health England (formerly the Health Protection Agency) and Animal Health and Veterinary Laboratories Agency respectively (animal isolates processed by the Veterinary Laboratories Agency), from England and Wales of *S.* Typhimurium DT104 with antimicrobial resistance (AMR) phenotypic profile and resistance determinants. Ap = ampicillin, Cl = chloramphenicol, St = streptomycin, Sp = spectinomycin, Su = sulphonamide compounds, Te = tetracycline, Tm = trimethoprim, Fz = furazolidone, Na = nalidixic acid, Cp = ciprofloxacin, Tm = trimethoprim, Sxtm = sulphamethoxazole/trimethoprim. Genes marked as (Ps) are believed to be pseudogenes, either through truncation (Ps) or interruption by another gene (Ps-2f).

Isolate	Isolated from:	AMR phenotypic profile	Year of isolation	Country	Resistance determinants identified
EWH1	Human	pansusceptible	2005	England	
EWH10	Human	ApClStSuSpTeTmNaCp	1999	England	*blaPSE-1, floR, tetG, tetR, sulI, aadA2, SgyrA(83)F*
EWH11	Human	ApClStSuSpTeTm	2000	England	*blaPSE-1, floR, tetG, tetR, sulI, aadA2, strA(Ps-2f), strB, dfrA14, sulII*
EWH12	Human	StSp	2000	England	*aadA2, floR(Ps)*
EWH2	Human	pansusceptible	2004	England	
EWH3	Human	StSuSp	2005	England	*aadA2, sulI*
EWH4	Human	StSuSp	2005	England	*aadA2, sulI*
EWH5	Human	pansusceptible	1991	England	
EWH6	Human	ApClStSuSpTe	1992	England	*blaPSE-1, floR, tetG, tetR, sulI, aadA2*
EWH7	Human	ApClStSuSpTeNaCp	1994	England	*blaPSE-1, floR, tetG, tetR, sulI, aadA2, DgyrA(87)N*
EWH8	Human	ApClStSuSpTeFzCp	1995	England	*blaPSE-1, floR, tetG, tetR, sulI, aadA2, DgyrA(87)N*
EWH9	Human	ApClStSuSpTeTm	1998	England	*blaPSE-1, floR, tetG, tetR, sulI, aadA2*
EWV1	Cattle	ApClStSuTe	2003	England	*blaPSE-1, floR, tetG, tetR, sulI, aadA2*
EWV10	Cattle	ApClStSuTeSxtm	2002	England	*blaPSE-1, floR, tetG, tetR, sulI, aadA2*
EWV11	Sheep	ApClStSuTe	2002	England	*blaPSE-1, floR, tetG, tetR, sulI, aadA2*
EWV2	Chicken	ApClStSuTe	2003	England	*blaPSE-1, floR, tetG, tetR, sulI, aadA2*
EWV3	Horse	ApClStSuTe	2004	Wales	*blaPSE-1, floR, tetG, tetR, sulI, aadA2*
EWV4	Poultry	ApClStSpSuTe	1996	England	*blaPSE-1, floR, tetG, tetR, sulI, aadA2*
EWV5	Pig	ApClStSpSuTe	2003	England	*blaPSE-1, floR, tetG, tetR, sulI, aadA2, strA(Ps-2f), strB, dfrA14, sulII*
EWV6	Dog	ApClStSuTe	2004	Wales	*blaPSE-1, floR, tetG, tetR, sulI, aadA2*
EWV7	Cattle	ApClStSuTe	2003	Wales	*blaPSE-1, floR, tetG, tetR, sulI, aadA2*
EWV8	Cattle	ApClStSuTe	2004	Wales	*blaPSE-1, floR, tetG, tetR, sulI, aadA2*
EWV9	Pig	ApClStSuTe	2002	England	*blaPSE-1, floR, tetG, tetR, sulI, aadA2*

Table S6. Antimicrobial resistance profiles determined by presence and absence of genomic resistance determinants as represented in Figure 1.

Profile number	Genetic resistance determinants
1	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR*
2	*tetA(A), tetR(A), bla(TEM-1b), strA, strB, sulII, aph3'(I)*
3	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
4	*floR, aadA2, sulI, tetG, tetR*
5	*aadA2, sulI*
6	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)N*
7	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB, DgyrA(87)N*
8	None
9	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, tetA(A), tetR(A), strA, strB, aac3(IV), hygBr*
10	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, strA, strB, aac3(IV), hygBr*
11	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aac3(IV), hygBr*
12	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph3'(I), DgyrA(87)N*
13	*bla(PSE-1), sulI, aph3'(I)*
14	*bla(PSE-1), sulI, DgyrA(87)G*
15	*bla(PSE-1), floR, sulI, tetG, tetR, sulII, strA(Ps-2f), dfrA14, strB*
16	*bla(PSE-1), sulI, sulII, strA(Ps-2f), dfrA14, strB*
17	*sulII, strA(Ps-2f), dfrA14, strB*
18	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, dfr1, bla(TEM-1b), sulII, DgyrA(87)N*
19	*bla(PSE-1), sulI*
20	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, SgyrA(83)F*
21	*DgyrA(87)N*
22	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, strA(Ps), strB, aac3(IV), hygBr*
23	*aadA2, sulI, DgyrA(87)N*
24	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, DgyrA(87)G*
25	*floR(Ps), aadA2, sulII, strA(Ps-2f), dfrA14, strB*
26	*aadA2, sulI, SgyrA(83)F*
27	*aadA2, sulI, sulII, aph3'(II), ble, sph, dfrA12, DgyrA(87)N*
28	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, strA(Ps), strB, aac3(IV), hygBr, SgyrA(83)F*
29	*aadA2, sulI, aph(3')-I*
30	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I, dfrA12, sulIII, bla(TEM-1b), mefE*
31	*aph(3')-I*
32	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I*
33	*tetA, tetR2, sulII, hygBr, aac(3)-IV, aph(3')-I*
34	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, tetA(A), tetR(A), aph(3')-I, dfrA12*
35	*tetA, tetR2, aph(3')-I*
36	*bla(TEM-1b)*
37	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, dfrA12*
38	*bla(PSE-1), floR, aadA2, sulI, tetG, tetR, aph(3')-I, sulIII, mefE*
39	*floR, tetA(A), tetR(A), strA, strB, sulII, ampC, sugE, dfrA12, aadA2, bla(TEM-1b), cmlA, aadA1, sulIII, mefE, aac(3)-IV, hygBr, aph(3')-I*
40	*aadA2, floR(Ps)*

Table S7. Concentrations of antimicrobials used in the susceptibility testing of the animal and human *S.* Typhimurium DT104 isolates by the Scottish *Salmonella Shigella* and *Clostridium difficile* Reference Laboratory, 1990 – 2004, and 2005 – 2011.

Antimicrobial	Breakpoint (mg/l) 1990 - 2004	Breakpoint (mg/l) 2005 - 2011
Ampicillin	50	8
Chloramphenicol	20	8
Ciprofloxacin	0.5	0.5
Furazolidone	20	8
Gentamicin	20	4
Kanamycin	20	16
Nalidixic acid	40	16
Netilmicin	20	20
Spectinomycin	100	64
Streptomycin	20	16
Sulphamethoxazole	100	64
Tetracycline	10	8
Trimethoprim	10	2

Table S8. Concentrations used in the disc diffusion susceptibility testing of the animal *S.* Typhimurium DT104 isolates from England and Wales by the Animal Health and Veterinary Laboratories Agency (isolates processed by the Veterinary Laboratories Agency).

Antimicrobial	Concentration (μg)	Zone diameter (mm): resistant if below	Zone diameter (mm): sensitive if above
Amikacin	30	18	19
Amoxycillin/clavulanic acid	30	14	15
Ampicillin	10	13	14
Apramycin	15	13	14
Cefotaxime	30	29	30
Ceftazidime	30	29	30
Chloramphenicol	30	20	21
Ciprofloxacin	1	19	20
Furazolidone	15	13	14
Gentamicin	10	19	20
Nalidixic acid	30	13	14
Neomycin	10	13	14
Streptomycin	10	13	14
Sulphamethoxazole/trimethoprim	25	15	16
Sulphonamide compounds	300	13	14
Tetracycline	10	13	14

Table S9. Concentrations of antimicrobials used in the susceptibility testing of the human *S.* Typhimurium DT104 isolates from England by Public Health England (formerly the Health Protection Agency).

Antimicrobial	Breakpoint (mg/l)
Amikacin	4
Ampicillin	8
Cefotaxime	1
Ceftriaxone	1
Cefuroxime	16
Cephalexin	16
Cephradine	16
Chloramphenicol	8
Ciprofloxacin	0.125
Colomycin	8
Furazolidone	8
Gentamicin	4
Kanamycin	16
Nalidixic acid	16
Neomycin	8
Spectinomycin	64
Streptomycin	16
Sulphonamides	64
Tetracycline	8
Trimethoprim	2

Table S10. Gene, UniProt identifier, and European Nucleotide Archive (ENA) accession number for the antimicrobial resistance genes investigated in the *S.* Typhimurium DT104 isolates.

Gene name	UniProt ID	ENA accession no.	Gene name	UniProt ID	ENA accession no.
bla(PSE-1)	Q7BL37	AAK02055.1	*mph(A)*	Q5QJG2	AAR05762.1
floR	Q7BL41	AAK02049.1	*mefE*	Q5J436	AAS76329.1
sulI	E0D898	AEX00802.1	*dhfrXVI*	O85802	AAC32186.1
aadA2	Q7BL43	AAK02046.1	*dfr1*	Q6J3S3	AAT36680.1
tetR	Q7BL40	AAK02050.1	*dfrA27*	B2ZNP4	ACD56152.1
tetG	Q7BL39	AAK02051.1	*dfrA23*	Q5W314	CAG34233.2
aac(6')-Ib-cr	B9VR93	ACM24779.1	*dfrA21*	Q6Q8S1	AAS66087.1
aac(3)-IV	P08988	X01385	*dfrA19*	Q8VVE6	CAC81324.1
dfrA14	A7WNT6	CAM98046.1	*cmlA*	Q5J429	AAS76336.1
sat2	Q75QQ2	BAD10975.1	*cat*	D0R779	CBA11382.1
aadA1	B0FGV6	ABY50547.1	*catB8*	Q79PD0	AAM92461.1
dfrA15	Q0ZB28	ABG36698.1	*catB3*	O86929	CAA08841.1
dhfrA7	E5G6I0	ADP08975.1	*catB2*	Q8KLQ3	CAD31710.1
B1dhfrVII	Q79K64	AAO89216.1	*cat2*	Q5J470	AAS76295.1
dhfrX	Q79S90	AAL13155.1	*ble*	A8R700	BAF93087.1
dhfrIII	P12833	AAA25550.1	*bla(TEM-1b)*	B5SZN3	ACH85856.1
dfrA17	Q83ZN7	AAP23220.1	*bla(per-2)*	P74842	CAA63714.1
dfrA12	Q8GLV1	ACF21684.1	*bla(OXA-30)*	Q6QLX3	AAS46622.1
hygBr	H9TI80	AFG20898.1	*bla(OXA-53)*	Q7WTW0	AAP43641.1
aph(3')-II	P00552	AAA73390.1	*bla(OXA-2)*	P0A1V8	AAA98357.1
tetR2	Q79VX4	BAB91577.1	*bla(KPC-2)*	Q7B856	AAM10643.1
tetR(A)	B7ZJI1	ACK44536.1	*bla(SHV-2)*	P0AA00	AAA75015.1
tetD	Q9S453	BAB91574.1	*bla(DHA-1)*	O54216	CAB40919.1
tetC	Q93F25	BAB91575.1	*bla(CTX-M-2)*	P74841	CAA63263.1
tetA	Q9K2Y4	BAB91576.1	*aph(3')-I*	Q5QJP8	AAR05693.1
tetA(A)	A7DY41	CAO00285.1	*ampC*	Q5J3Z2	AAS76373.1
sulII	D0R7A7	CBA11366.1	*aac(3)-II*	Q5QJN0	AAR05727.1
sulIII	Q7WZL0	AAP82508.1	*acc-1*	Q49JG6	AAX52125.1
sugE	E7DBI0	ADV39907.1	*aar-3*	Q83ZU8	ACD56151.1
strB	B7ZJI3	ACK44538.1	*aadB*	Q79LX7	AAO46870.1
strA	B7ZJI4	ACK44539.1	*aadA7*	Q6SIX0	AAR21615.1
sph	A8R701	BAF93088.1	*aadA5*	Q75T47	BAD07296.1
qnrS	B7TZ43	ACJ24509.1	*aadA16*	B3V3X6	ACF17980.1
qnr	Q3Y8H2	AAZ78355.1	*aacC*	A4IVL4	ABO41023.1
qnrB19	C6H187	CAZ67058.1	*aacC1*	O86934	CAA08847.1
pef	A5H8A5	ABN13922.1	*aacA4*	Q8KLQ4	CAD31708.1
oqxB	F4MK98	CBL62366.1	*aac(6')-I30*	Q7WTV9	AAP43642.1
oqxA	F4MK97	CBL62365.1	*aac6-II*	Q79PC7	AAM92464.1
mrx	Q5QJG3	AAR05761.1	*aac(3)-Id*	Q6SIX1	AAR21614.1

Table S11. The number of antimicrobial resistance (AMR) determinants, AMR profiles based on presence/absence of AMR determinants in the 133 typical Scottish human and animal isolates *S.* Typhimurium DT104 investigated for AMR diversity. The numbers of determinants or profiles unique to the particular host population (animal or human) are represented in brackets.

Host population	# Determinants (# unique)	# Profiles (# unique)
Human	21 (7)	21 (14)
Animal	20 (6)	14 (7)
Shared	14	7
Total	27	28

Table S12. Log marginal likelihoods of the four assessed models for the Bayesian phylogenetic analysis: bidirectional asymmetric, bidirectional symmetric, unidirectional human-to-animal, unidirectional animal-to-human, and log Bayes factors (logBF) for each model compared to the bidirectional asymmetric model.

Model	Log marginal likelihood	Log(BF)
Bidirectional asymmetric	-207.52	0
Bidirectional symmetric	-208.35	-0.83
Unidirectional: human-to-animal	-241.36	-33.84
Unidirectional: animal-to-human	-267.26	-59.74