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RESEARCH ARTICLE

Dutch Settlers at Voorzorg in Suriname Decimated by 1845 Epidemic: A Multifaceted Approach to Unravel Mystery about Etiologic Microbial Agent

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ABSTRACT

Background. In 1845, an attempt at Dutch farmer colonization of the overseas colony of Suriname failed because within weeks of the arrival of 384 colonists, an outbreak occurred that killed half of them. The outbreak at plantation Voorzorg was identified as 'gastric biliary fever', which was later interpreted as typhoid fever. However, sparse data support this diagnosis. Herein, we took a multifaceted approach to characterize the outbreak and establish the likely microbiological cause.

Methods. Archival research was combined with identification and excavation of a burial site, analysis of aDNA of skeletal remains as well as modelling of the outbreak on epidemiological findings.

Results. A timeline of events constructed from archival records revealed that the 1845 febrile illness affected >95% of the 384 colonists, likely transmitted human-to-human and was characterized by fever, nausea, vomiting, in cases abundant often bloody diarrhea, and progressed into delirium and stupor ('Typhus'). Within 1-2 weeks of symptom onset, half of the affected persons died (189 of 384) with overrepresentation from the young and elderly. A few postmortems had revealed multiple small, purulent colonic ulcerations. We discovered a burial ground and uncovered 17 skeletal remains presumed to be colonists. Subsequently, metagenomic testing did not reveal a pathogenic microorganism fitting the disease description, but typing mitochondrial DNA (possible in 15 of 17) showed that the skeletal remains sampled likely did not originate from Europe. Mathematical modelling of epidemic curves depicting cumulative mortality of those arriving by subsequent ships revealed that transmission characteristics of bacillary dysentery rather than typhoid fever fitted the epidemiological findings the best.

Conclusion. A multifaceted approach revealed that the 1845 outbreak at Voorzorg among Dutch colonists was probably caused by bacillary dysentery and not typhoid fever. Likely, the high mortality was a consequence of dehydration that in tropical conditions particularly affected the young and elderly. This outbreak contributed to the failed colonization attempt.

Introduction

In 1845, three reverends with support of the Dutch government led an attempt at European farmer colonization in the Dutch colony of Suriname in South America[1,2]. Suriname, at the time functioning as a plantation colony, relied on labor-intensive commodity crops for its economy. Anticipating a labor shortage upon abolition of slavery, in the mid-1900s the Dutch government backed initiatives for Dutch farmer colonization in Suriname. Its purpose was to demonstrate that Western people could perform farming work in the tropics and thereby help improve the harsh living conditions in Suriname by way of immigration of a middle class from the motherland[3,4]. The reverends enrolled 50 farmer families, as well as some unmarried young men and women, and set sail to Suriname. The first ships with colonists arrived at the plantation Voorzorg, the established site of colonization along the river Saramacca, in June 1845 and were followed by more ships within 6 weeks. The local government had failed to realize assured necessities like housing and clean water, and Voorzorg offered little more than a badly drained swamp[1,2,5-7]. Crowded living conditions were dreadful and within two weeks of arrival an epidemic broke out[5,6]. In all, 189 of the 384 colonists died within the first months[1-6,8,9]. Government physicians sent from the capital city Paramaribo diagnosed a "gastric biliary fever" characterized by "a nervous fever" with "a rotten character"[7]. The outbreak stopped after several months, but the colonization attempt never overcame this unfortunate start and was set to fail. In 1853, the Dutch government put an end to the enterprise.

The view from those involved in the late nineteenth and early twentieth century is that the 1845 outbreak of "gastric biliary fever" among Dutch colonists concerned typhoid fever. This conclusion was repeated in subsequent writings, although no evidence has been put forward to substantiate this hypothesis[9-13]. Understanding the outbreak provides a more comprehensive historical perspective on the unsuccessful farmer colonization attempt. It can help elucidate the role that sickness, death, and social upheaval played, alongside unfavorable climatic conditions, a lack of leadership, and challenging economic circumstances, in contributing to the failure of the colonization endeavor.

Over 175 years after the outbreak, we employed a comprehensive approach that integrated archival research, mathematical modeling based on epidemiological findings, excavation of presumed colonist remains, and thorough analysis of these remains, including genetic enquiry. This combined effort aimed to better characterize the epidemic among the Dutch farmers and either validate or disprove the potential of *Salmonella (S.) typhi* as the causative agent behind the devastating outbreak.

Methods

Archival research. Information on the European farmer colonization at Voorzorg (map of Suriname in **Supplement 1**) was gathered from primary source documents at the National Archives in The Hague, the Royal National Library in The Hague, the Dutch Population Registry, the National Archive in Paramaribo, the Royal Netherlands Institute of Southeast Asian and Caribbean Studies (KITLV) in Leiden, and historic archives of newspapers (https://www.delpher.nl/nl/). In short, for the period of 1842 – 1853, we studied relevant source documents, official and private correspondence, the complete correspondence collection of Reverend Van den Brandhof at KITLV[14], and articles and book chapters concerning the colonization attempt. Maps of the colonization site Voorzorg and Groningen were studied at the University Library of Leiden to find clues of the location of the burial grounds of those who perished in the epidemic[15]. Two academic theses (written in 1860[6] and 1938[8]) were of particular use for counter-checking archival information. A detailed description of the prelude to and history of the colonization attempt and source data is given in **Supplement 2.**

Permission. For the investigations and in particular the excavation and genetic analysis of physical remains, we obtained permission from the Attorney General at the Court of Justice of Suriname and the District commissioner of the district Saramacca (#1170/11/24.06.2011), the Suriname Office of Public Health BOG (#337/05.03.2011), and from representatives of the descendants of the Dutch colonist survivors (#2010-04/1/26.04.2010 & 15.03.2010; Foundation Sranan Boeroe in Suriname and Foundation Boeroe Kon Makandra in the Netherlands, respectively). The Surinam and Dutch Foundations of descendants were repeatedly updated on the findings.

Excavation. Following identification of the putative burial ground of the deceased farmer colonists in Groningen, Suriname, we defined the area within which we could excavate. The available area for excavation was a square that was limited in the southwest by the present-day graves in the cemetery, in the southeast by multiple graves with gravestones, in the northeast by a row of trees and in the northwest by a ditch (**Supplement 1**, **figure S1.2**). We set up a measuring system that encompassed the entire available area for excavation, based on 4 measuring points of which

the coordinates were determined within the national Suriname measuring system by infrared theodolite. In the available area we dug some small holes layer by layer to get an idea of the buildup of the different layers to know to what depth we had to excavate to find potential graves. Based on this we dug two test trenches of approximately 2 meters wide with an excavator, one along the southwestern limitation, along the present-day cemetery (trench 1), up to the ditch in the northwest, and one parallel to this along the northeastern limitation of the available area (trench 2), also up to the ditch in the northwest (**Supplement 1, figure S1.3**). We removed the soil in layers in the first part of the trenches until grave-like features became visible and then caried on at that level for the rest of the trench. Skeletal remains would be uncovered but were not removed from the grave. The graves were excavated to the level of the skeleton, but due to time constraints not all skeletons were fully excavated. In all cases we at least removed the soil around the skull and shoulder region so that we could investigate the dentition and sample teeth for further analysis, and the stage of epiphyseal fusion of some of the long bones in the upper body could be assessed for a crude age estimation.

Sampling for genetic and metagenomic analysis. At the time of excavation teeth were considered the best parts of an archaeological skeleton for retrieving both human and pathogen ancient(a)DNA[16]. Removing teeth is also relatively little invasive. We therefore decided to collect four teeth per individual where possible. As a background control for the metagenomic analysis we also planned to collect soil samples from several graves inside the coffin next to the cranium, just outside the grave and outside the cemetery at the same level as the graves. To avoid contamination with exogenous DNA, both teeth and soil samples were collected wearing protective gear (forensic suit, hairnet, face mask and gloves) and with instruments that were cleaned with bleach and the sand on the teeth was not removed until sampling and soil samples were collected from unexposed soil.

Anatomical examination. The skeletal remains were only uncovered and cleaned in situ to such an extent that it allowed for a basic investigation of indicators of sex and age at death according to the recommendations of the Workshop of European Anthropologists 1980[17].

Genetic and metagenomic analysis. Sample preparation for genetic and metagenomic analysis was conducted at the department of Human Genetics of the Leiden University Medical Center (LUMC). All steps prior to DNA amplification and massive parallel sequencing (MPS) library preparation were performed in a laboratory specifically equipped for aDNA analysis. Sample preparation and DNA extraction of the human samples was performed as described[18]. DNA extraction of the soil samples was done with the QIAamp DNA Stool Mini Kit (Qiagen) according to the manufacturer's recommendations, with an input of 0.2 gr of soil and eluted in 100 µl of sterile and pyrogen free water. During this process an extraction blank was also created using only the reagents.

General quality, quantity and authentication of the human DNA in the tooth samples was assessed by means of a quantification with the Quantifiler® Duo system, using a 7500 real-time PCR System (Applied Biosystems) and autosomal short tandem repeat (STR) typing with the PowerPlex® ESX 16 system (Promega) as described[18]. Selection of samples for metagenomic analysis by means of shotgun sequencing were based on these results.

Mitochondrial (mt) haplotypes were typed with an in-house developed multiplex assay. We selected 48 mt SNPs to differentiate all major mt-haplogroups and representing the most frequent European sub haplogroups (**Supplement 3 and Table S3.1**). The PCR-primers were designed with primer3 v. 0.4.0 using standard settings, for a total fragment-size between 40 and 70 bp and ensuring that a minimum of three bases remained between both primers in the resulting amplicon [19]. PCR products were sequenced on an MiSeq system (Illumina, San Diego, CA, USA). Data analysis was performed using in-house developed software FDSTools[20]. FASTQ-files, sorted by barcodes, were converted to FASTA-files and used as input-files for analysis by TSSV[21]. For analysis an FDSTools library was constructed (**Table S3.2**). The revised Cambridge Reference Sequence (rCRS)[22] was used as a reference. In addition, the FDSTools visualisation files were manually analysed. Using a spreadsheet the findings were converted to a Haplogrep input file. The Mt haplogroups were defined with Haplogrep 2.0 software[23], based on Phylotree v17 (http://www.phylotree.org/).

Selection of samples for metagenomic analysis by means of shotgun sequencing were based on the results of the quantification test and STR-typing. Libraries for shotgun sequencing were prepared with the KAPA HTP Library Preparation Kit (KR0426 – v3.13). Preparation was done according to the manufacturers protocol, except that DNA was not sheared due to natural fragmentation of ancient DNA. Library fragments were amplified with P5/P7 adapters (Illumina) in 6 PCR cycles and purified two more times

with AMPure beads (1.0x bead volume). Size selection of the library fragments was done using a 6% PAGE gel electrophorese (EC6265box Invitrogen).

Libraries were analysed using Bioanalyzer 2100 DNA high sensitivity chips, to quantify the library size and assess the level of adapter-dimer and primer-dimer contamination.

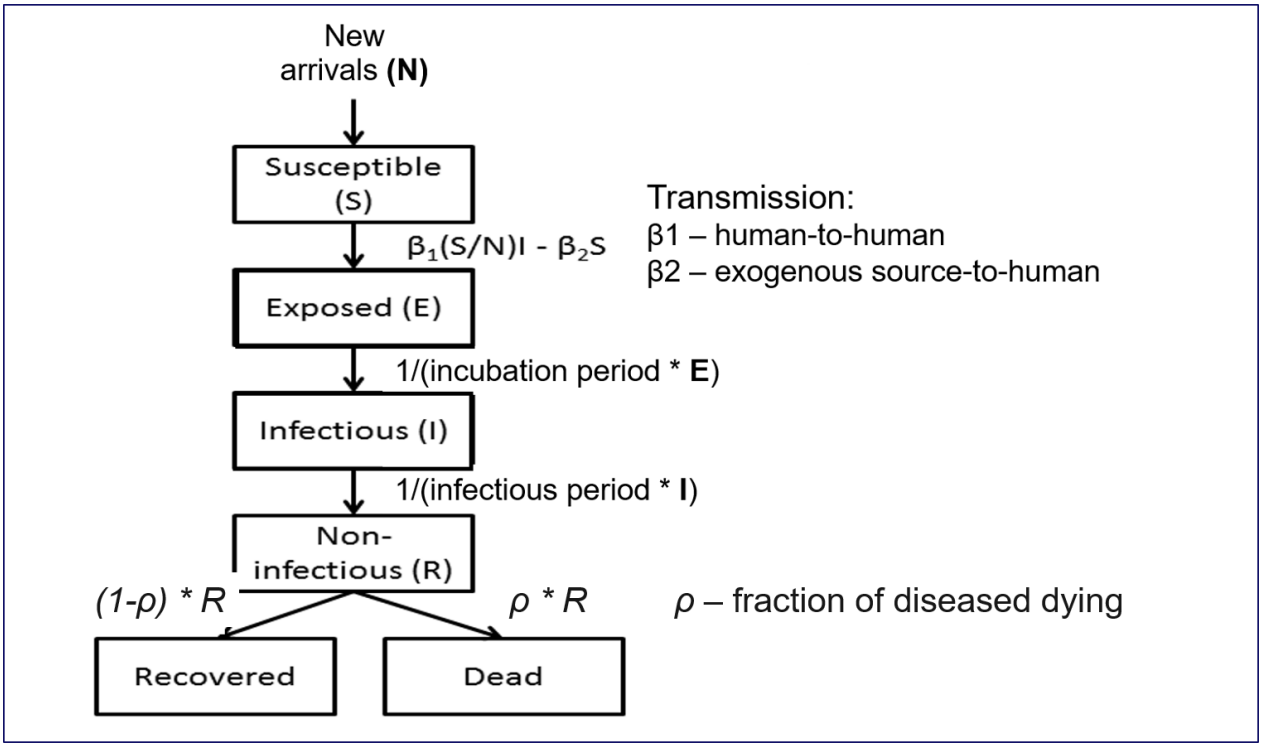
The non-enriched DNA libraries were sequenced on an Illumina MiSeq 2500. Paired-end reads were trimmed and clipped using Flexiprep [https://github.com/biopet/biopet/releases/tag/v0.8.0] (version 0.8.0) with default parameters. Next, using BWA-mem [https://arxiv.org/abs/1303.3997] (version 0.7.10-r789) with default parameters, we proceeded with a targeted analysis to align to a selected number of reference sequences as indicated under results. For every species, we took the number of alignments with high mapping quality (Phred score over 50; SAMtools view -b -q 50 -m 100 -o $@ $^) using SAMtools [http://www.htslib.org/] (version 1.4) and used this number of supporting reads as a proxy for the abundance of the species in the sample. In order to filter out false positive alignments, the alignment files were filtered for skipped regions were filtered by soft clipping, hard clipping and padding with SAMtools. The remaining alignments were visualized with an Integrative Genomics Viewer [https://doi.org/10.1038/nbt.1754] (version 2.3.88). The coverage distribution (negative binomial as expected) is generated by BAMStats (version 1.25) using default parameters. See **Supplement 3** for details on assay design, amplification, sequencing.

Epidemiological findings and mathematical modelling. From the primary source documents, we reconstructed demographics of each of the colonists, including age, sex, family, ship and date of disembarkation, and date of death. Of these demographical variables, the epidemiological curve depicting the observed cumulative mortality was constructed and selected as the modeling endpoint. For typhoid fever and dysentery, we gathered from the literature typical values of incubation period, duration of illness, period of infectiousness (feco-oral transmission, human-to-human) and mortality[24-28] (**Supplement 4** and **Table S4.1**). Along with known disease transmission features, these parameter values were used to construct separate basic infection models for typhoid and dysentery that were used to determine whether known information on (either of) these diseases was able to replicate the observed cumulative mortality curve.

In short, the colonists were divided into two separate (growing) populations based on the location and date of disembarkment (Voorzorg: days 0, 1, and 22 or Mijn Vermaak: day 44), providing one population in which to estimate unknown parameter values ("derivation model") and one population (i.e., Mijn Vermaak) in which to validate these estimated parameter values ("validation model") based on the location of disembarkation. Given the living conditions of the places where the colonists arrived, we assumed that within these two separate populations people were and remained in close contact with each other for the duration of the outbreak. Transmission between the populations occurred through a two nights visits of two farmers from Mijn Vermaak to Voorzorg who became exposed to the disease in Voorzorg and likely brought it back to Mijn Vermaak with them, resulting in an outbreak there. The basic model and assumptions are illustrated in the diagram of the compartmental model (**Figure 1**), with the compartments and rates of movement between compartments reflecting disease transmission features. In short, individuals started as susceptible individuals, and new susceptible individuals arrived when ships disembarked (days 0, 1, and 22, for first three ships at Voorzorg). It was assumed that a first individual was exposed through contact with a (constant) source of infection, becomes infectious after an incubation period specific for the microbial agent, and transmitted infection human-to-human for an infectious period, after which the individual either recovered and became resistant to re-infection, or died. As explained in the **Supplement 4**, for typhoid fever the basic model was modified to accommodate a disease relapse rate of 10%. In the first population (at Voorzorg), we allowed for the possibility that the disease spread through the population both by human-to-human transmission as well as through contact with the exogenous source of infection. Therefore, unknown estimates for human-to-human (β_1) and exogenous source-to-human (β_2) transmission were derived by fitting the expected cumulative mortality curve to the observed cumulative mortality curve of this population. Parameter sets that generated expected cumulative mortality curves that remained (mostly) within the 95% confidence interval of the observed cumulative mortality curve were taken as candidate parameter sets. If none of the parameter sets fit the observed data well, we additionally varied the proportion, ρ, that would have been expected to die. The expected mortality proportion could have been higher in this population than in other populations due to the nature of the climate: mortality due to dehydration could particularly affect the young and elderly in tropical conditions.

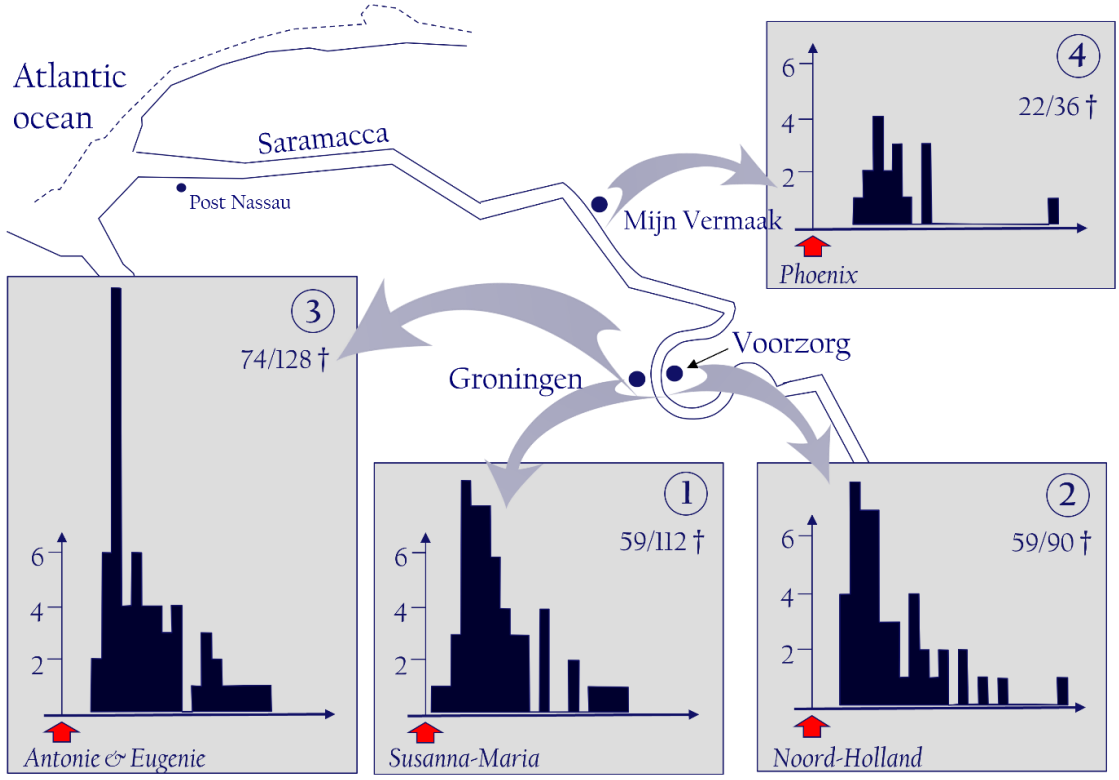
The β_1 parameter for human-to-human transmission can be interpreted as the average number of people infected per day by any one infectious individual given that the rest of the population is still susceptible. β_2 can be interpreted as the average proportion of (still) susceptible people infected from the environmental source per day.

Figure 1: Schematic representation of the compartmental model used to derive parameters for β_1 (human-to-human transmission) and β_2 (exogenous-source-to-person transmission). In short, colonists started out as susceptible persons (S), and new susceptible individuals arrived when ships disembarked (on days 0, 1, and 22, respectively for boats 1-3 arriving at Voorzorg). A first individual was exposed through contact with an exogenous (constant) source of infection, became infectious after an incubation period specific for microbial agent, and was able to transmit human-to-human during an infectious period, after which the individual either recovered and became resistant to re-infection, or died. The extent of the two sources of transmission (i.e., β_1 = human-to-human transmission; β_2 = exogenous source-to= human transmission) is unknown and was modelled taking the observed cumulative mortality rate as the end-point to fit.

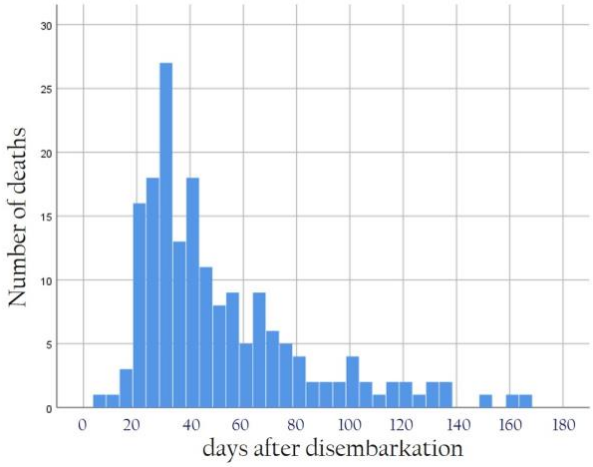


Contour plots were used to illustrate and compare quality of fit to observed cumulative mortality for any two parameter values and reflect sensitivity to the selection of the parameter values. The candidate parameter sets and the same models described above were then used to produce an estimated cumulative mortality curve for the last ship, which was compared to the observed cumulative mortality curve for this population. At Mijn Vermaak, a location quite distinct from Voorzorg and with a water-source and food of its own, the exogenous source-to-human transmission was presumed to be absent and therefore in the validation population the β_2 was set to 0; however, curves where β_2 retained its original fitted value for a given candidate parameter set were also presented for completeness. Any parameter sets that fell (mostly) within the 95% confidence interval of the observed cumulative mortality curve of Mijn Vermaak were considered to be the plausible parameter sets. The presence of such parameter sets suggested that the compartmental model, and the disease that it modelled, appropriately described the disease transmission features in this outbreak in Suriname and pointed to the disease responsible for this outbreak.

Figure 2: A. Daily number of deaths among the colonists arriving with the ships; (1) *Susanna Maria* (June 20th); (2) *Noord-Holland* (June 22nd); (3) *Antonie & Eugenie* (July 12th); and (4) *Phoenix* (Aug 3rd). Numbers depicted in bars by day starting after first debarkation (day 0) for each ship at Voorzorg (first three ships) and at Mijn Vermaak (last ship – *Phoenix*), respectively.



B. Number of deaths every five days for persons of all ships, relative to time of disembarkation of first ship.



Results

Archival research. We studied 549 letters and correspondence of the three reverends and the government secretary and other primary source documents at the archives indicated, and some 136 historic newspapers (at https://www.delpher.nl/nl/). Moreover, we included in the search some 21 articles and book chapters concerning the colonization attempt[1-14, 29-40]. The various source documents differed only slightly on the number of colonists in Voorzorg, Groningen and Mijn Vermaak in Suriname in 1845, and number of deaths during the outbreak (**Supplement 2 Table S2.1**).

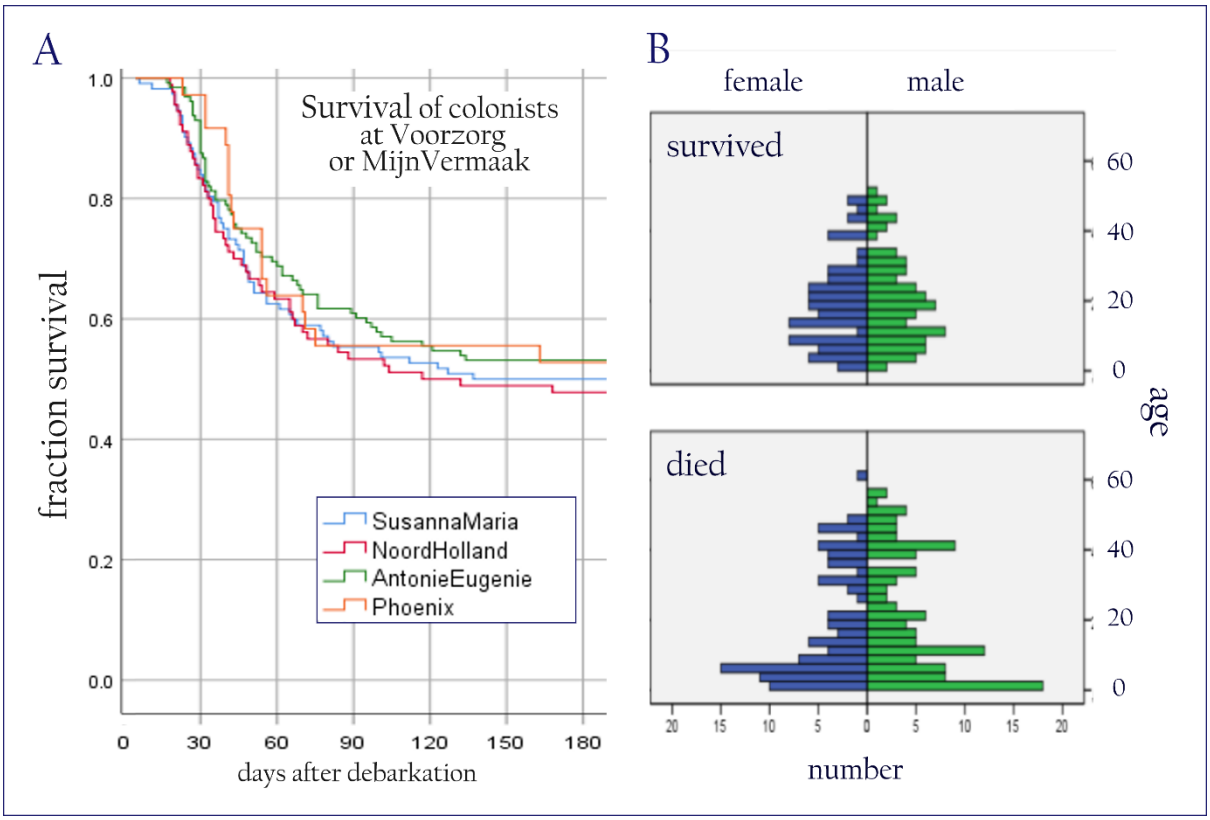
Timeline of events. A timeline of the events leading to the outbreak was constructed (**Supplement 2 Figure S2.1**). The disease started within two weeks after arrival of the first ship, in the family of the farmer Geblij; both parents and children succumbed to their illness[3]. At the end of the outbreak, the disease had affected 360 out of 371 (97%) colonists, and rampaged all but one family. Of 4 families, totaling 18 individuals, all members

died, whereas in 5 families, totaling 15 individuals, none died of the disease. In 12 families, both parents died as well as 32 of their 70 children thus leaving 38 orphans. In all, 189 out of 384 colonists died (**Supplement 2 Table S2.1**).

Demographics and epidemiological data. Cumulative mortality curves for each of the four ships showed that overall mortality plateaued at 47 - 51 % of the passengers (**Figure 2 A** and **B**). Adjusted for their date of arrival/disembarkation in the colony (June 20th/21st: *Susanna-Maria*; June 22nd: *Noord-Holland*; July 12th: *Antonie & Eugenie*; August 3rd: *Phoenix*) and thus the first day of possible exposure to an infectious agent on the Suriname mainland, the survival curve of individuals on each of the four vessels did not differ significantly ($p > 0.60$), despite the 6 weeks interval between their respective arrivals (**Figure 3 A**). There was no difference in percentage deaths among male and female colonists (**Figure 3 B**). Relatively more young children < 15 yr ($p<0.008$) and elderly > 50 yr ($p<0.03$) died as compared to the adolescent and middle age groups (i.e., aged 15 to 50 yr; **Figure 3 B**).

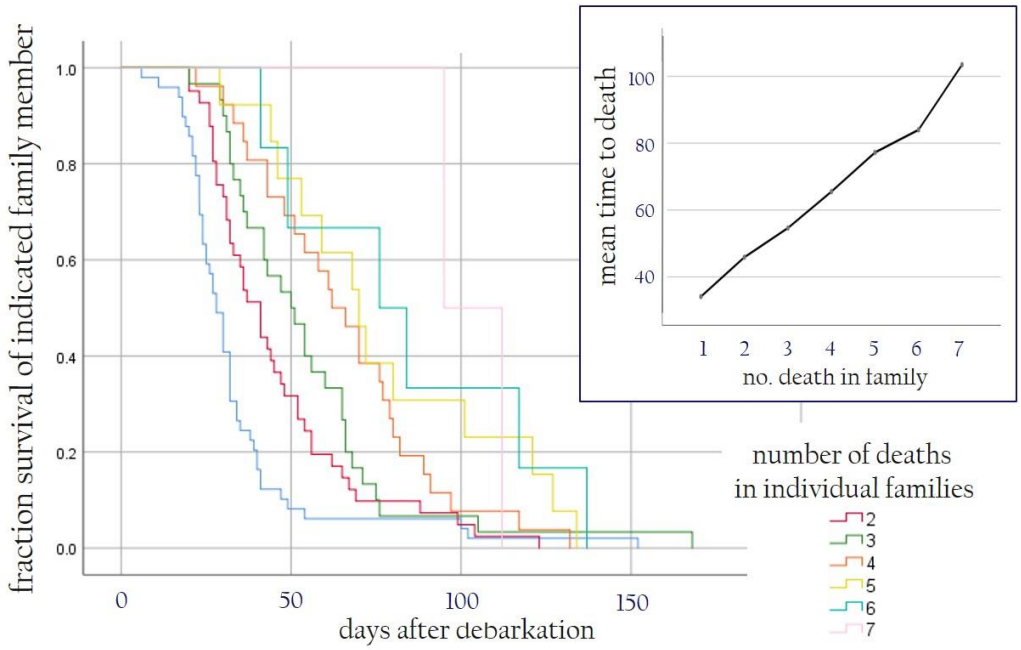
Figure 3.

A. Fraction of survival of the colonists arriving by the four ships, adjusted for date of each ship's debarkation at Voorzorg or Mijn Vermaak, showing no differences in time to death and survival among colonists of the four ships (Kaplan-Meyer curves).
B. The outcome of illness among the various age cohorts of colonists, depicted by sex for those who survived (top) and who died (bottom).



Of note, among 36 colonists who arrived with the fourth ship *Phoenix* and disembarked on the plantation Mijn Vermaak, no disease cases occurred until two colonists transported cattle to Voorzorg and spent two nights there with acquaintances before returning to Mijn Vermaak. Analysis of deaths in families in which multiple members died (**Figure 4**) shows that the intervals of subsequent deaths of family members were, on average, 8 to 10 days.

Figure 4: Time-to-death of members of families in which multiple members died, relative to disembarkation of the first ship. To illustrate the intervals of subsequent deaths, the total number (of first deaths, second deaths and so on) is set to 1. The Figure illustrates that in families with multiple members dying, these deaths tended to occur with, on average, an 8 to 10 day interval. This suggests intrafamily transmission rather than single source exposure.
The inset graph on the right-hand side depicts the mean time to death after first disembarkation, starting with the first death in a family, the second death, and so on until the seventh death that occurred in only few families.



As detailed in the **Supplement 2**, the outbreak also affected crew on board of vessels that had accompanied the colonists ships from the Saramacca river mouth to Voorzorg (the governments' schooner *Henrietta* and military brig *De Brak*). The overlap of the potential exposure of these diverse groups pinpoints the time of initial pathogen exposure to, maximally, the first week after arrival of the first ship *Susanna-Maria* at Voorzorg.

Description of disease. In his 1860 thesis[6], the physician Tijdeman described the outbreak in Voorzorg and Groningen: shortly after disembarkation, an outbreak of a diarrheal disease occurred, without fever or much burden of disease that quickly subsided[3,6]. Soon thereafter, a remittent fever ('gastric biliary disease') developed in an increasing number of settlers, progressing into a soporous condition. Patients complained initially of headache, nausea, and vomiting (symptoms in **Table 1**).

Table 1: Characteristics of the disease outbreak at Voorzorg and Mijn Vermaak, 1845

- highly contagious with >95% attack rate
- human-to-human transmission
- fever, constitutional signs like headache, nausea and weight loss
- vomiting
- abundant diarrhea, often bloody
- progressing into delirium and stupor
- a 50% mortality rate within 1-2 weeks of illness
- mortality preferentially affecting those in extremes of life (<15 yr and >50 yr)
- at postmortem small ulcerations in colon, and much less in small bowel and stomach

As reported by Tijdeman FWL. In: De epidemie van typhus geheerst hebbende op het etablissement voor de Europeesche kolonisatie in Suriname te Groningen aan de Saramacca in 1845. Academic Thesis, Leiden, 1860.

On examination, Tijdeman noted that cases had injected red eyes, and tenderness in the epigastrium and right lower abdominal quadrant. They raved, often had nosebleeds, and became delirious in 4 to 5 days to progress into a soporous condition. A tachycardia of 120 to 130 beats per minute was common. Constipation alternated with a bloody diarrhea that soon became abundant, and this resulted in a stupor. He noted loss of weight due to dehydration. Death followed in about half the cases within 6 to 8 days of disease onset[3,6]. He noted numerous parasitic comorbidities, including ascaris lumbricoides passed 'ore et ano' (from mouth and anus), helminths, as well as furunculosis and scophulosis. Tijdeman describes postmortems in a handful of cases. This revealed a strong vascular injection of the stomach and intestines, with purulent material covering the colon that showed multiple small ulcerations. Of note, in none of the victims the heart and lungs showed abnormalities.

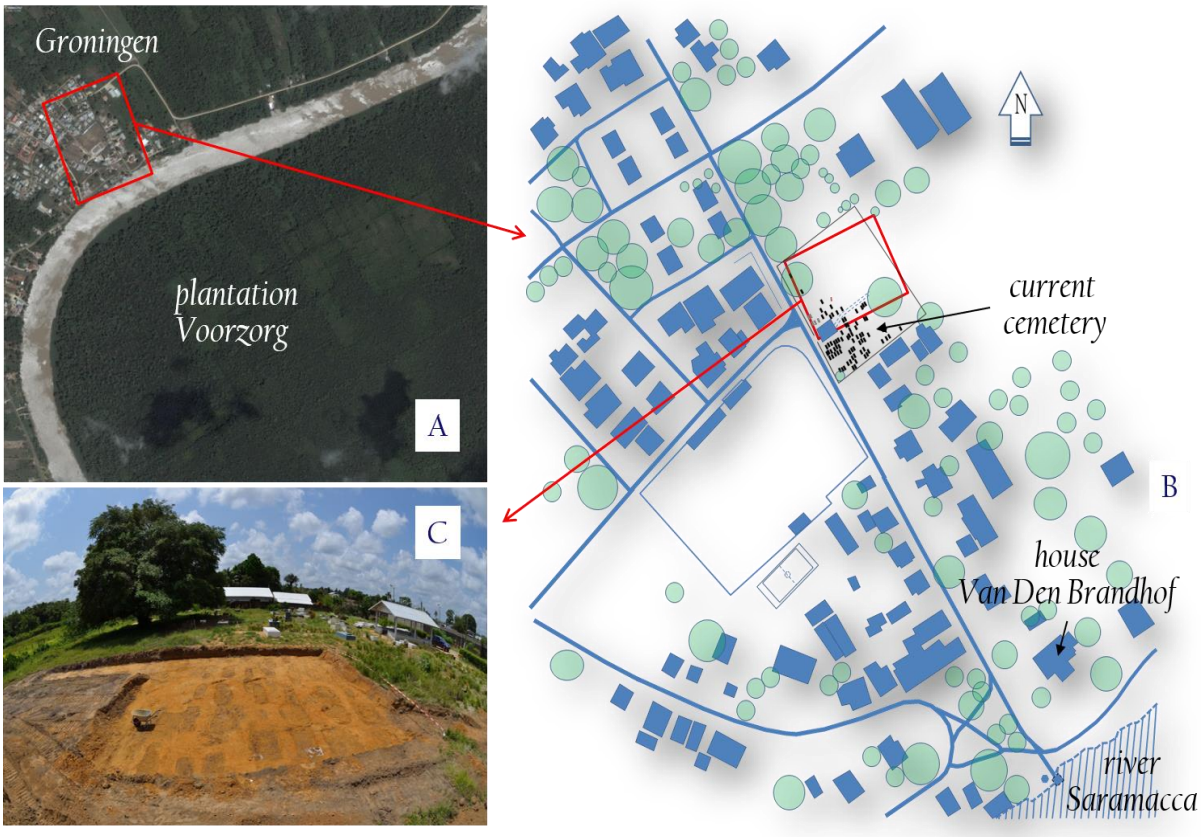
Soon after the start of the outbreak, a committee of physicians from Paramaribo visited Voorzorg and wrote the following in a letter to the governor, dated July 22nd 1845, by name of its chair the physician FM Horstmann: '*… having arrived the 21st at the above-mentioned place (…Voorzorg…), that a considerable number of new colonists, likely more than one hundred, had been affected in a more or less severe manner by a fever with signs of nervous clouding ('Thyphus', i.e., a muttering delirium)…*'[7]. Of note, all but two of the physicians who attended the sick, i.e., Jutting (ship's surgeon of *Noord-Holland*), de Jong (physician of colonization attempt, arrived on *Phoenix*), the officers of health Tydeman, Van der Monde, Wagenaar and Smit, and the Paramaribo city doctors Muller, Horstman and Landré, became ill as well.

Figure 5.

A. Current satellite map situating the plantation Voorzorg opposite the village of Groningen along the river Saramacca.

B. Schematic map of enlarged part of Groningen, showing the remains of the house of Van den Brandhof along the river Saramacca and next to the landing site, and the current cemetery; buildings indicated by blue squares, plantation in green, streets in blue lines. The open square in the middle is the current soccer field.

C. Excavation trench 1 of the burial site of the presumed farmer colonists, indicated by red square in (B), adjacent to the current cemetery of Groningen. In the excavated part, the graves are visible because of their darker colour, as a result of mixing of the yellow undisturbed soil with the darker top soil.



Location of burial site. No records were recovered in the archives that revealed a location of the burial site of the deceased colonists. Some current inhabitants of Groningen suggested that the dead had been buried at Voorzorg, close to the water lock and outlet of the plantation. Most residents of Groningen, however, held the firm belief that the soccer field of Groningen was the likely site of burial (**Figure 5 A/B**). Some indirect clues were found in letters and newspaper accounts: the administrator Van denBrandhof wrote in a letter of Aug 14th 1845 that ' *…8 corpses are carried along the porch of this house, … to be buried in wooden coffins*', and on Dec 8th of that year mentions '*...a graveyard full of crosses*'[14]. At the time, Van denBrandhof probably still resided in the old commander's house of the fortress Groningen situated on the Landingsweg that runs from the stairs of the landing stage in the Saramacca river to the woods behind the fortress (**Figure 5B**). This suggested that the dead were taken from the swampy plantation Voorzorg to the opposite site of the river and buried in higher grounds in Groningen. Consistent herewith was information found in the *Nieuwe Utrechtse Courant* of July 6th and 7th 1849, in which a group of individuals traveling through Suriname described a visit to Groningen. They found the colonists' graveyard located in Groningen (and not Voorzorg) left in an abominable state, repeatedly being burned down rather than mowed to remove the abundant weed and grass. Finally, a location of the graveyard in Groningen is revealed in free-style pencil drawings by Tijdeman, one made at the start of the outbreak and one two years (1847) later, that show a graveyard on the latter that had not yet been present on the former drawing of 1845[15]. This cemetery is located next to a field for cattle (that is consistent with the location of the present soccer field). Finally, the wife of Van denBrandhof, Anna S. Pannekoek, who died in the night of November 11, 1845[14], was buried at this site and left a grave still marked by a machined gravestone. At this putative graveyard, in 2020 a fallow lying field next to the currently used cemetery of Groningen (with gravestones going back to the 1960s), an excavation was undertaken (**Figure 5C, Supplement 1**).

Excavation (maps of excavation site in Supplement 1). In trench 1 we observed one feature with the shape and size of a grave which contained human bone fragments and several similar features that could potentially be graves in the southeastern part of the trench. The northwestern part was empty. Upon this we expanded the southeastern part of the trench in northeastern direction by 9 meters. In trench 1 we observed 53 features in total in 6 rows that could potentially be graves, some of which were intersected (**Supplement 1, figure S1.4**). We selected 22 features that were spatially distributed across the trench and of different sizes for further excavation and all contained human skeletal remains. Eleven graves showed clear signs of a coffin by discoloration of the soil and nails, in three cases it was not possible to determine if a coffin had been present and in the eight remaining graves we did not observe any signs that indicated the presence of a coffin. All graves were oriented in a northeast-southwest position with the heads in the northeast, and all skeletons were in supine extended position. In trench 2 we observed five features that could potentially be graves, but none of them contained skeletal remains.

Sampling for genetic and metagenomic analysis. Of the 22 excavated individuals 17 were suitable for sampling for genetic and metagenomic analysis (two skeletons were below groundwater level, in one case the cranium and jaws were too damaged and disturbed for sampling, one skeleton belonged to a very young child and was severely degraded and in one grave the skeleton was mixed with bones from a secondary deposition) (**Supplement 1, figure S1.4**).

Anatomical examination. Anatomical examination was possible for 16 of the 17 sampled individuals, since one skeleton was mostly below groundwater level. The preservation of the bones was on average moderate, but worse for very young individuals. Six individuals were non-adults (age range of ~1.5-17 years), one individual was non-adult or young adult, and nine individuals were (young) adults. Investigation of the observable sex indicators suggested that of the nine (young) adults two were female and eight were (possibly) male. No gross abnormalities were noted.

Genetic and metagenomic analysis. Of the 17 sampled individuals, only two individuals yielded a measurable concentration of either autosomal DNA (0.002 ng/µl) or Y-chromosomal DNA (0.002 ng/µl) with the Quantifiler system. Nine individuals yielded results for autosomal STRs, but these were minimal with alleles for at most 6/16 markers. These nine individuals were selected for further metagenomic analysis, including one soil sample from outside the burial location, and two soil samples each from both next to the skull and just outside the grave of the selected individuals. The maximum of bacterial aDNA was 6 picograms per µl. Shotgun sequencing of the aDNA libraries produced on average 14,731,992 (range 11,435,665 to 17,505,789) reads of fragments up to 260 (mean read length ~180) base pairs, for

each of the 9 tooth samples. Of these, a median 9.6% (range 5.4 to 15.4%) could be mapped to bacterial genomes and only about 0.03% (range 0.03 to 0.08%) were of human origin. Thus, even in the nine 'best' aDNA samples most reads could not be classified, confirming that overall the aDNA was poorly preserved.

In standard polymerase chain reactions (PCR) in the clinical diagnostic microbiology laboratory the samples tested negative for *S. typhi*. Furthermore, for nine samples, bacterial reads were mapped to a wide variety of bacterial reference genomes including that of *S. typhi* (**Figure 6**) and increased mapping stringency was applied to remove weakly aligned reads (i.e., those based on only a few base pairs within the read). In this metagenomic approach, 0.0% of the bacterial reads mapped to *S. typhi* reference genome. The more stringent mapping reduced nonspecific alignment and reduced overall genomic coverage for all genomes tested to essentially zero. Thus, the alignment against any of the listed pathogens was shown to be insignificant and did not reveal a possible etiologic pathogen. As positive and negative control, we analyzed by identical means aDNA extracted from two skeletons excavated at the cemetery of the former leprosarium Batavia along the river Coppename. This site operated in the mid-19th century as refuge for leprosy patients and was closed in 1897. One of these skeletons showed characteristic facial and tibial periostitis signs of leprosy and these samples were shown to be positive in the RLEP PCR for *M. leprae* DNA; the other that lack such signs tested negative[41]. Only the sample of the positive control, i.e., the leprosy victim excavated at Batavia, convincingly showed preservation of a specific bacterium, in this case *M. leprae* aDNA (further detailed in[41]).

Figure 6: Heatmap of the ratio (reads/all reads), number of reads and normalized reads that mapped to the respective reference bacterial genomes indicated on the left. Samples included soil samples from the excavation at Groningen, samples from two skeletons excavated at the leprosarium Batavia at the Coppename river[41], and human tooth samples from the excavation in Groningen.
With the exception of the alignment signal for *M. leprae* (red arrow) in the remains of an individual of which the skeleton displayed signs of leprosy[41], none of the samples showed alignment similarities to the reference genomes.

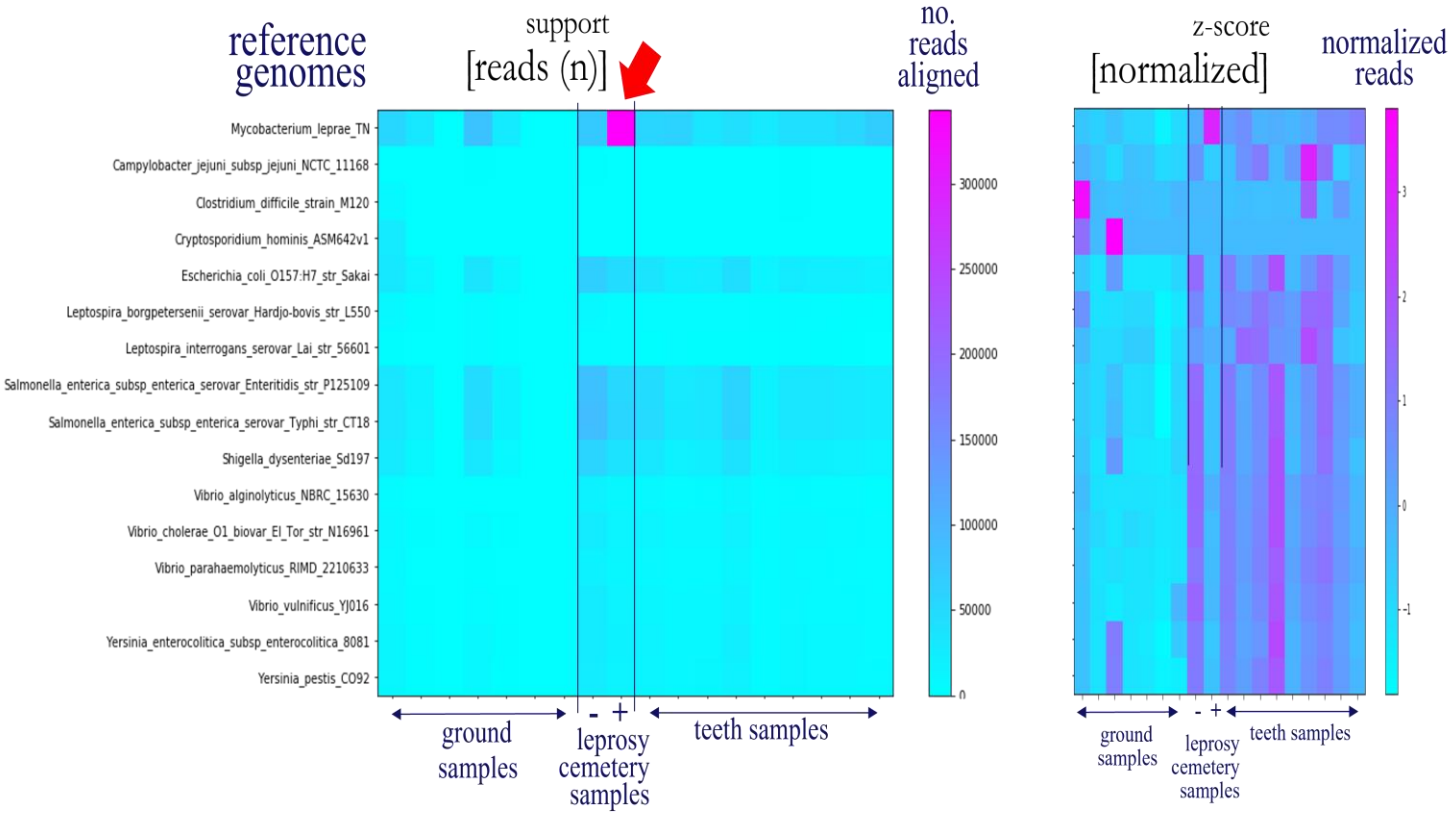
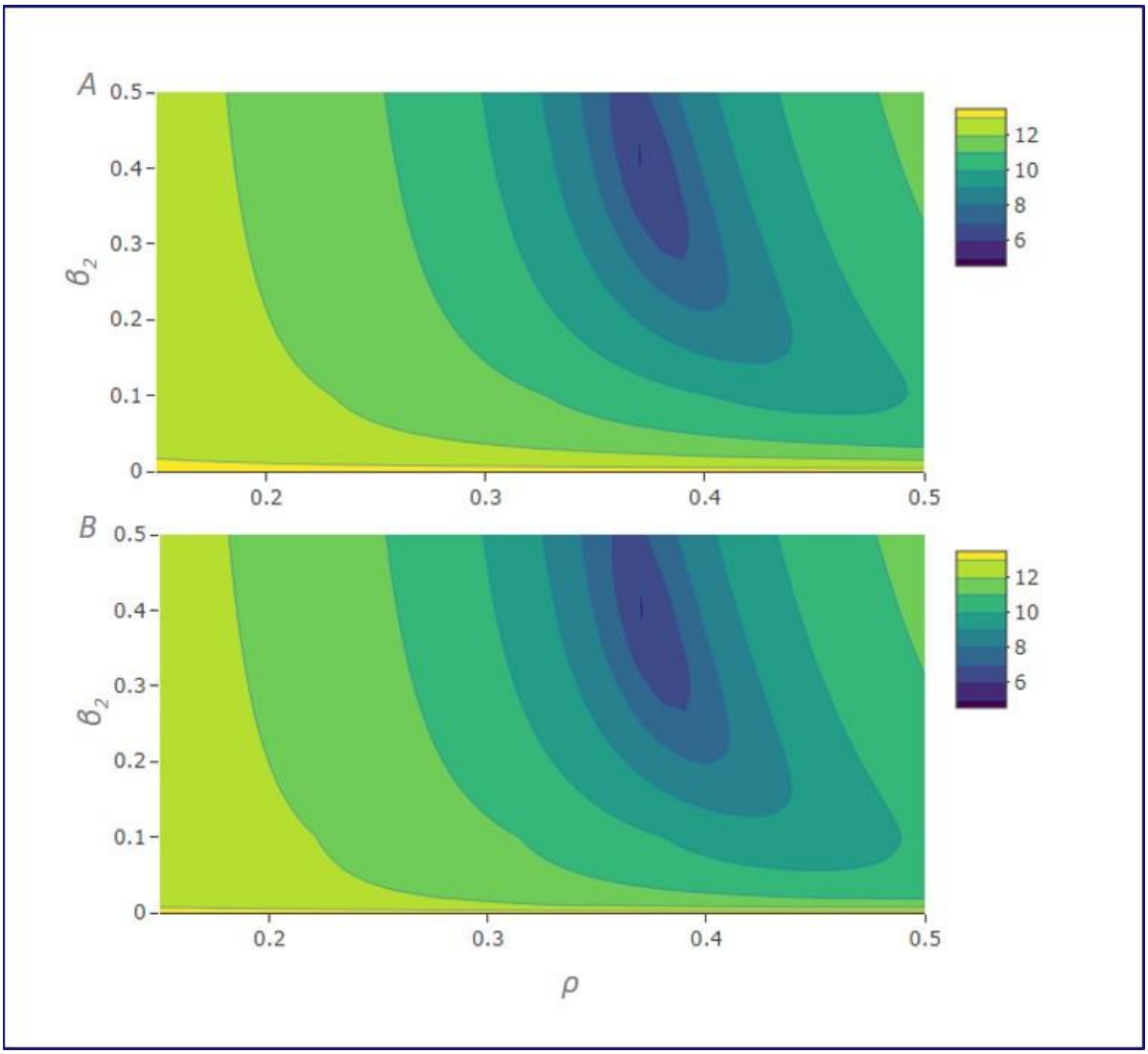


Figure 7: In the mathematical modelling approach to an outbreak due to *Salmonella typhi* infection, over 90,000 parameter sets for β_1, β_2, and ρ were fitted to arrive at the expected cumulative mortality curves for the three ships that disembarked at Voorzorg (*Susanna-Maria*, *Noord-Holland* and *Antonie & Eugenie*); these curves were compared with the observed cumulative mortality curve for individuals from these ships using least squares minimalization. Contour plots depicting the ordinary least squared fit for different parameter sets with β_1 held constant (A: $\beta_1 = 0$; B: $\beta_1 = 0.5$). The different colors represent the log of the least squared; the darker the color, the better the fit (as indicated to the right: log(5) to log(14) of the least squared).



Mitochondrial (Mt-) haplotype typing was done for 16 individuals and we obtained sufficient data to call a haplogroup for 15 of them (**Table 2**). One of them has no clear indication for genetic ancestry (mt haplogroup U), but thirteen of these suggest a genetic ancestry in Asia and one of them among native Americans, rather than Europe according to the EMPOP database (https://empop.online/).

Table 2: Results of mitochondrial haplotyping and reconstructed haplogroups using the rCRS[22] as a reference.

Feature	Missing fragments	Haplotype	Haplogroup
S03	16153-16176	1438G 2706G 11719A 14766T	R
S07	11466-11490;16153-16176	1438G 2706G 11719A 14766T	R
S11	234-247	1438G 2706G 11719A 14766T 16169T 16172C	F1a+16169T
S17	16153-16176	1438G 2706G 11719A 14766T	R
S19		1438G 2706G 11719A 14766T	R
S20	11466-11490;16153-16176	1438G 2706G 11719A 14766T	R
S21		234G 1438G 11467G 11719A 14766T	U2b2
S25	8694-8705;16153-16176	1438G 2706G 11467G 11719A 14766T	U
S26		1438G 2706G 8701G 10873C 11719A 12705T 14766T 14783C 16176T	M4a
S28		1438G 2706G 8701G 10873C 11719A 12705T 14766T 14783C 15262C	M5a2a
S30		1438G 2706G 3010A 8701G 10873C 11719A 12705T 14766T 14783C	C1c2
S32	16153-16176	1438G 2706G 11719A 14766T	R
S33		1438G 2706G 8701G 10873C 11719A 11722C 12705T 14766T 14783C	M7a1a1
S35	234-247	1438G 2706G 11719A 12634G 14766T 16172C	F1a+12634G
S40	234-247	1438G 2706G 11719A 14766T 16162G 16172C	F1a1

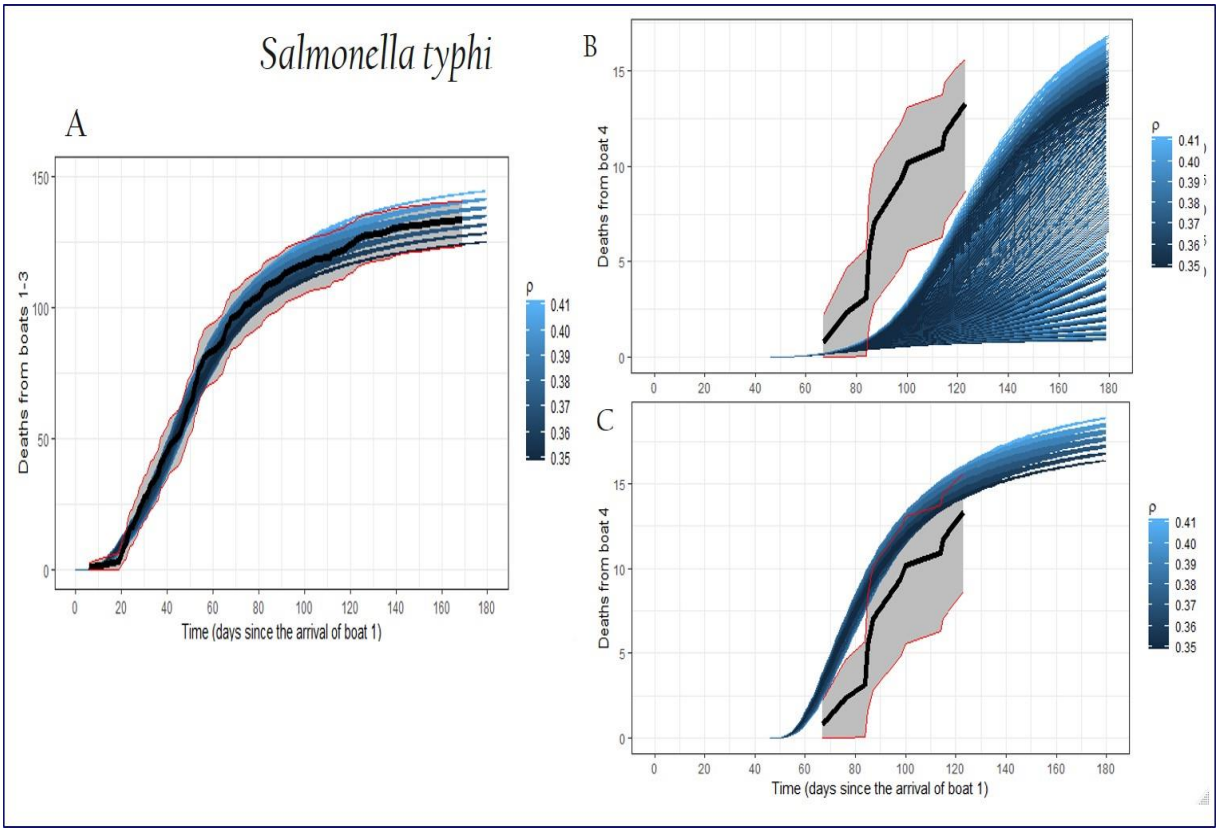
Mathematical modelling on cumulative mortality. Under the assumptions discussed in Methods and using the parameter values described below, 90,000 β_1 and β_2 parameter sets for typhoid and 30,000 for dysentery were fitted to arrive at the expected cumulative mortality curves for the first three ships that disembarked at Voorzorg. For typhoid, β_1 was varied from 0 to 0.5; β_2 from 0 to 0.5. For dysentery, β_1 was varied from 0 to 0.5; β_2 from 0 to 0.2 (**models explained in Figure 1 and Supplement 4 Figure S4.1**). These curves were compared with the observed mortality for boats 1-3 using least squares minimalization.

Typhoid fever. Using the parameter settings obtained from the literature, including the estimate for the mortality rate of about 15%, no combination of values for β_1 and β_2 even came close to a fit within the 95% confidence interval of the observed cumulative mortality at Voorzorg or Mijn Vermaak. For further analysis, we varied the β_1 and β_2 parameters and additionally allowed the proportion of diseased individuals who died, ρ, to vary from 0.15 to 0.5 (i.e., at a much larger rate than expected for typhoid fever[24,25]). Parameter sets that resulted in a least squares of <log(8) (**Figure 7A** and **B**) mostly fell within the 95% confidence interval of the observed cumulative mortality, and amounted to a $\beta_1 \in (0, 0.5)$, $\beta_2 \in (0.2, 0.5)$, and $\rho \in (0.35, 0.41)$. The fit of the derivation model depended heavily on the selection of the parameter for the percentage of individuals who died from disease (ρ), to a lower extent on source-to-human transmission (β_2), and to a negligible degree on human-to-human transmission (β_1) (**Figure 8**). Next, these candidate parameter sets were entered in the validation model. In the setting that the spread of infection depended on human-to-human transmission only, i.e., with $\beta_2 = 0$, none of the estimated cumulative mortality curves came close to the observed mortality, even at the highest mortality rates (**Figure 8B**). Only when the exogenous source of infection was allowed to travel with the two farmers from Voorzorg to Mijn Vermaak and continued to exert its influence there did the estimated cumulative mortality curves touch the upper 95% confidence interval of the observed mortality (**Figure 8C**).

Figure 8.

A. In the mathematical modelling approach to an outbreak due to *Salmonella typhi* infection, using parameter values for the mortality rate ranging from 45-50%, best-fitting parameter sets (by least squares minimalization) generated expected cumulative mortality curves (blue lines) that fell mostly within the 95% confidence interval (grey shaded region, outlined in red) of the observed cumulative mortality (black line). The calculated curves in the derivation model fit only within the observed 95% confidence interval when parameters were entered in the model that lie far out observed values in other epidemics.

B & C. The best-fitting parameter sets from the derivation set was used to generate expected cumulative mortality curves (blue lines) for the forth ship *Phoenix*. The right top figure shows the expected mortality curves when the constant source of infection was not present in population at Mijn Vermaak. The right bottom figure shows the expected cumulative mortality curves when the constant source of infection was present in the population at Mijn Vermaak and continued to infect individuals there.



Dysentery. Taking the same approach as explained above for typhoid fever, we calculated the least squares fits of the different parameter sets for dysentery (**Figure 9**), where β_1 was held constant in each panel (A: $\beta_1 = 0$; B: $\beta_1 = 0.1$; C: $\beta_1 = 0.3$; and D: $\beta_1 = 0.5$) and β_2 and ρ varied over the parameter ranges that we modelled. Parameter sets that resulted in a least squares of <log(8) (**Figure 10**) mostly fell within the 95% confidence interval of the observed cumulative mortality for the first three ships (shown in **Figure 10A**) and were selected as the candidate parameter sets ($\beta_1 \in (0, 0.34)$, $\beta_2 \in (0.01, 0.03)$, and $\rho \in (0.44, 0.50)$) to assess model suitability in the validation model. The derivation model fit depended heavily on the parameter values selected for the percentage of individuals who died from disease (ρ) and the source-to-human transmission parameter β_2. Next, the candidate parameter sets were entered in the validation model. In the setting that the spread of infection depended on human-to-human transmission only, i.e., with $\beta_2 = 0$, the estimated cumulative mortality curves resulted in a good fit to the observed cumulative mortality curve, over a range of plausible mortality rates (**Figure 10B**). One of the resulting plausible parameter sets (shown in green in **Figure 10**) corresponded to a $\beta_1 = 0.25$ (human-to-human transmission) and $\beta_2 = 0.01$ (source-to-human transmission in Voorzorg).

Figure 9: In the mathematical modelling approach to an outbreak due to *Shigella dysenteriae* infection, over 30,000 parameter sets for β_1, β_2, and ρ were fitted to arrive at the expected cumulative mortality curves for the three ships that disembarked at Voorzorg (*Susanna-Maria*, *Noord-Holland* and *Antonie & Eugenie*); these curves were compared with the observed cumulative mortality curve for individuals from these ships using least squares minimalization. Contour plots depicting the ordinary least squared fit for different parameter sets with β_1 held constant (A: $\beta_1 = 0$; B: $\beta_1 = 0.1$; C: $\beta_1 = 0.3$; and D: $\beta_1 = 0.5$). The different colors represent the log of the least squared; the darker the color, the better the fit (as indicated to the right: log(5) to log(14) of the least squared).

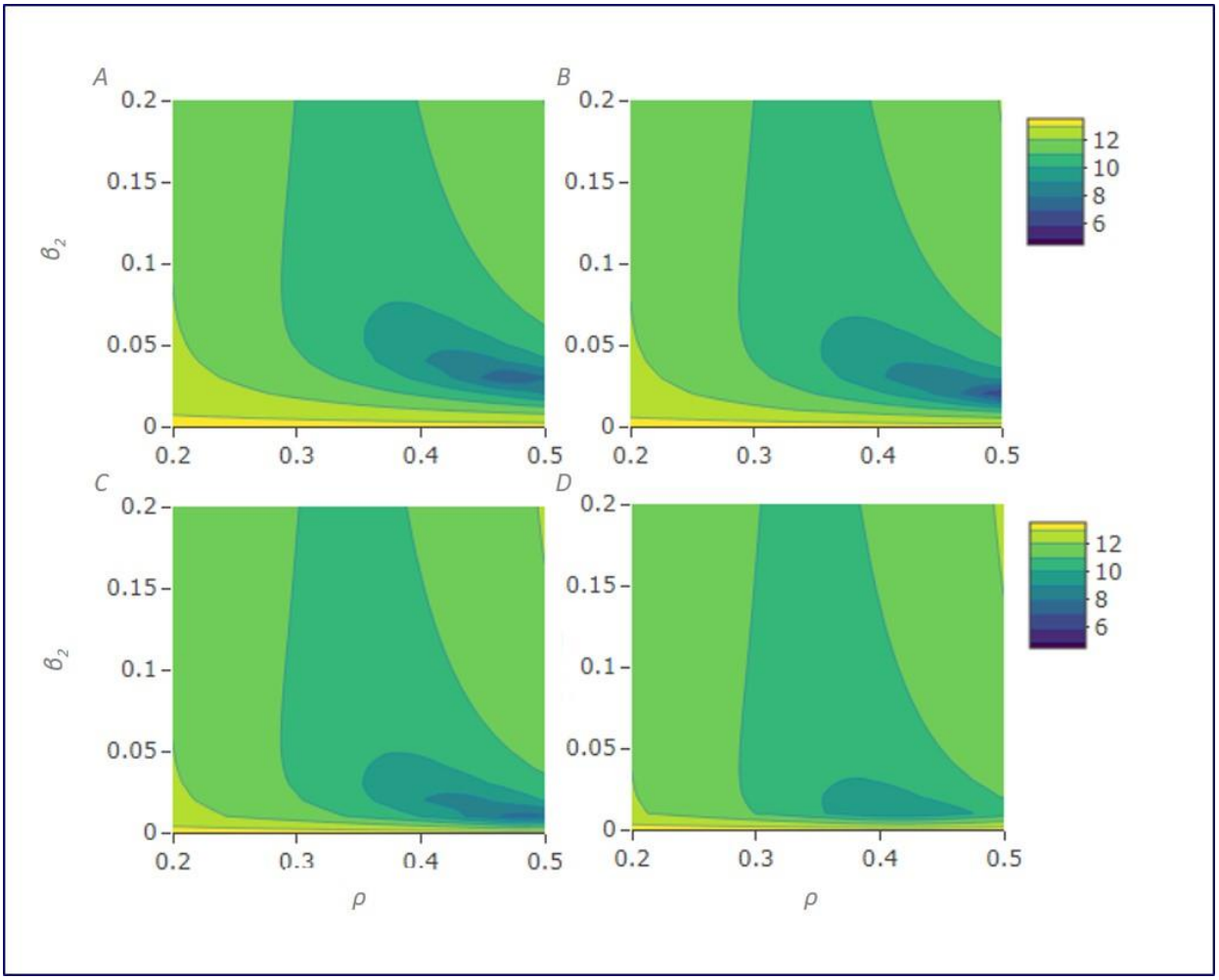
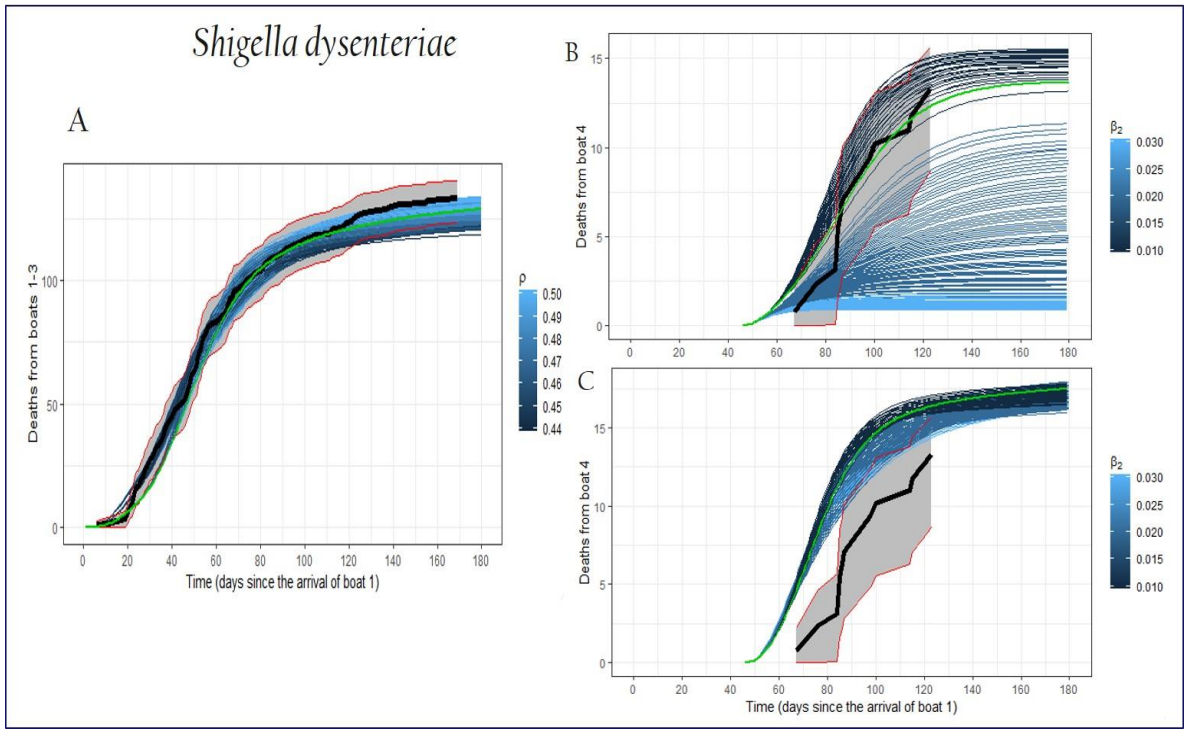


Figure 10.

A. In the mathematical modelling approach to an outbreak due to *Shigella dysenteriae* infection, best-fitting parameter sets (by least squares minimalization) generated expected cumulative mortality curves (blue lines) that fell mostly within the 95% confidence interval (grey shaded region, outlined in red) of the observed cumulative mortality (black line). One of the plausible best- fitting parameter sets, illustrated by the green curve corresponded to a $\beta_1 = 0.25$ (human-to-human transmission) and $\beta_2 = 0.01$ (source-to-human transmission).

B. Extrapolating these derived parameter values to the epidemic curve for deaths of *Phoenix*, the ship disembarking at Mijn Vermaak, showed that observed cumulative mortality (black line) and the 95% confidence interval surrounding this mortality rate (grey shaded region, outlined in red) enclosed the model-calculated expected cumulative mortality (green curve) taking the $\beta_1 = 0.25$ (human-to-human transmission) and $\beta_2 = 0$ (as we postulated that on this spot remote from Voorzorg, the source-to-human transmission was nil). The right bottom figure (C) shows the expected cumulative mortality curves when the constant source of infection was present in population at Mijn Vermaak and continued to infect individuals there.



Discussion

By taking a multifaceted approach, i.e., combining epidemiological findings recovered by archival research and mathematical modelling of the outbreak, we conclude that it is unlikely that the bacterium *Salmonella typhi* caused the outbreak among Dutch colonist farmers at Voorzorg in 1845. Rather than typhoid fever, the combined findings point to dysentery (i.e., *Shigella dysenteriae*) as the prevailing illness during the outbreak. Moreover, we found evidence that the colonist farmers were not the only ones affected by the outbreak. Cases also occurred among the crew on board of the vessels that had escorted them to Voorzorg, offering a helping hand navigating the ships from the Saramacca river mouth to Voorzorg and during disembarkation. Moreover, attending physicians from the capital city of Paramaribo sent to give assistance, became ill and some of them died. This information helps to pinpoint the time of first pathogen exposure to the first week or so after the first ship arrived at the location of Voorzorg. The over-crowded living conditions and complete absence of adequate provisions regarding fundamental hygienic requirements, sanitation, clean drinking water and food supply likely laid the groundwork for the outbreak and allowed the spread of an infectious disease by means of, for instance, contaminated drinking water and next by direct human-to-human contact. Possibly, carriers of infectious pathogens – be it on the ships, the crew of the three assisting vessels or the locally present individuals – played a role in the initialization of the outbreak, and even a zoonotic source cannot be excluded.

Our skepticism about the claim that *S. typhi* (i.e., typhoid fever) caused the outbreak is based on evaluation of historical archives, Tijdemans' thesis[6], and correspondence that provided essential clues as to the epidemiological and clinical characteristics of the illness. FWL Tijdeman was at the time a 3rd-class military physician-in-training at the Government's plantation Catherina Sophia, located opposite Mijn Vermaak and a few hours downstream the Saramacca river from Voorzorg by boat; he assisted during the outbreak and has first-hand information. His thesis and the source documents revealed that the disease (1) was highly contagious and readily transmittable between humans, (2) became manifest after an incubation period of about one week, (3) ran a short course of illness till death, i.e., on average one week with some cases dying within only one to two days of first manifestation, and (4) caused an overall mortality of about 50%, primarily affecting the young and elderly among the farmer colonists. None of these characteristics fit typhoid fever particularly well. The high contagiousness follows from the fact that >95% of the colonists became sick in the course of the outbreak that ran its lethal course over months. Except in rare cases of a single massive exposure, e.g., in food served at a ceremony, typhoid fever has seldom affected >95% of individuals in a population exposed[24]. In such rare instances, the epidemic curve was always much steeper and the length of the outbreak much shorter than that in Voorzorg[24]. Direct human-to-human transmission has been described in typhoid, but mostly from a carrier to other household members but never anywhere to the extent that would explain the ongoing outbreak at Voorzorg and, subsequently, at Mijn Vermaak. Moreover, because of its long incubation period of on average 21 days (*not* matching the one observed at Voorzorg) and an additional week before the feces of the sick would start to contain and potentially spread *S. typhi*, fecal-oral human-to-human transmission would have resulted in a much more spread-out pattern of cases[24,25]. This was confirmed by mathematical disease modelling, which produced an estimated cumulative mortality curve for typhoid that did not fit the documented data. Thus, typhoid cannot explain that four groups of colonists disembarked sequentially and weeks apart and were affected at such identically high rates. Rather, this points to a pathogen that was readily transmitted by direct human-to-human contact, within families, or from the environment (e.g., indirect or vector borne). Finally, unlike the illnesses at Voorzorg, typhoid fever tends to run a protracted course for several weeks before subsiding, relapsing, or progressing to death because of complications such as bowel perforation or massive gastro-intestinal bleeding. Also, typhoid usually does not cause severe lethal disease in the very young whereas the elderly could have been expected to have some immunity from past exposures in The Netherlands where the disease was also prevalent at the time. Even in massive outbreaks, typhoid results in the demise of approximately 15% of those affected[24,25] which is much lower than the 50% observed among the colonists. Finally, the post-mortem description of purulent discharge in a colon covered with small ulcerations[6] does not fit typhoid that characteristically causes large ulcerations to develop in the mucosa overlying Peyer's patches in the terminal ileum[25]. Moreover, post-mortems excluded a pulmonary disease being involved as cause of the outbreak.

Typhoid fever is characterized by bacteremia enduring many days[25], and this would result in the recovery of some *S. typhi* DNA sequences from teeth pulpa in a person who died from this disease. Indeed, the group of Krause showed that salmonella aDNA can be recovered from archeological skeletons[42]. They extracted and sequenced aDNA from the teeth of people buried in the Oaxacan highlands of Mexico and isolated *S. paratyphi* C DNA from some of these, implicating this pathogen as contributor to the 1545-1550 CE epidemic locally known as "cocoliztli"[42]. By similar aDNA techniques, others have incriminated typhoid fever as a probable cause of the Plague of Athens[43]. In contrast, we did not recover *S. typhi* aDNA sequences in the molecular analysis of the pulpa of teeth taken from the skeletal remains in Groningen, either by direct PCR nor by a metagenomics approach. Utilizing identical methodology, we successfully did recover *M. leprae* aDNA from bony remains buried at the leprosarium Batavia in the same period – mid to late nineteenth century – some fifty kilometers away from Voorzorg[41]. Although the absence of *S. typhi* aDNA cannot serve as proof of absence of typhoid fever, our negative molecular findings for typhoid fever are consistent with the evaluation of epidemiological, clinical and post-mortem characteristics of the disease that struck the farmer colonists and that do not fit typhoid fever. Moreover, mitochondrial haplogroups of 15 individuals indicated an ancestry of the demised outside Europe, most likely Asia and America. Given the clear description of the Dutch colonist cemetery on Tydeman's sketches, it is possible that the same burial ground had been used in different time periods, with mixing up of remains and intersecting graves. Be that as it may, the data from the molecular analysis of the teeth must be considered not representative for the deceased Dutch farmers.

If not *Salmonella typhi*, what could be the microbial etiologic agent in this 1845 outbreak characterized by high contagiousness, fever, often bloody diarrheal illness, and purulent ulcerations of the colon? We believe that given the disease characteristics, rapid human-to-human spread and high contagiousness, the outbreak best fits bacillary dysentery. Bacillary dysentery is associated with several species of bacteria, but the term is usually linked to *Shigella* infections, caused by e.g., *Shigella dysenteriae*[26,28]. One characteristic of dysentery is the presence of blood in the stools, which is the result of invasion of the colonic mucosa by the pathogen. Shigellosis is responsible for colonic ulcerations that do not go beyond the lamina propria and by consequence, rarely –unlike typhoid fever – does a patient with shigellosis develop bacteremia and sepsis. The main complication of dysentery is bleeding and dehydration, in particular in cases occurring in the tropics[28]. This primarily complicates the disease in young children and the elderly, putting these at highest risk for death. This was observed for the colonists at Voorzorg and Mijn Vermaak. Moreover, the transmission of *Shigella* is by fecal-oral route and is notable for the very small number of microorganisms that may cause disease (e.g., in human volunteers, 10 ingested organisms cause illness in 10%, and 500 organisms cause disease in 50% of volunteers)[26,28]. Outbreaks of *Shigella* are characterized by easy and rapid human-to-human transmission, and this is consistent with the pattern observed at Voorzorg and Mijn Vermaak. Mathematical modelling showed a remarkably close fit using disease parameters described in the literature for bacillary dysentery. Also, this cause is consistent with the transfer of the Voorzorg outbreak by two visiting colonists to the plantation Mijn Vermaak, where the last group of settlers had disembarked to prevent exposure to sick fellow colonists. In shigellosis, symptoms of disease generally show within days after exposure, and in some cases may result in swift death because of severe dehydration. We did consider other tropical diseases like, e.g., leptospirosis, hantavirus, yellow fever and malaria, but in all, bacillary dysentery fits best the description of disease among the colonists, the epidemiological data and disease transmission, and pathogenesis fitting the post-mortem finding.

Is it possible that we have uncovered the grave field of the Dutch farmer colonists, even though the site apparently was (re-)used for recent burials of other people? Based on the private correspondence from 1845, in particular that of the administrator of the colonization Reverend Van den Brandhof, and information in contemporary articles in Dutch newspapers, we obtained clues that the graves were to be searched for in Groningen rather than Voorzorg or Mijn Vermaak. Sketches of the settlement Groningen by the physician Tijdeman before and after the first year of colonization suggested the exact location, i.e., a fallow lying grass field adjacent to the present cemetery of Groningen[15]. The historical texts stated that deceased colonists were buried in wooden boxes, separate from each other. The excavated remains, however, were not all buried in wooden coffins. The typed mt haplogroups are not a reflection of a 19th century Dutch population, but rather of part of the population that inhabited Groningen since the mid-20th century. Thus, if the burial site of the Dutch colonists, already reported to be left neglected in the late 1850s, was indeed located where we excavated, it apparently has been reused in the mid-1950 to 60s for burials of others. Possibly the graves of the Boeroes were intersected or covered by later internments. In that case we would not have been able to examine these graves during the excavation, because we could not remove skeletal remains.

Remarkably, no reference could be found to reuse of the burial site at the city municipality or local archives, and there were no local records suggesting a reason why these people – in general of young age – were buried there. This is even more striking given that only few people were residing in Groningen between 1855 and 1960. Currently, Groningen counts some 2,800 inhabitants (census 2012). Before 1845, the whole area consisted of thick woods, and the writer and adventurer August Kappler notes in this period about Groningen: "… after the main thing, namely, houses, one searches in vain "[44].

To what extent did the outbreak contribute to the failure of the colonization attempt? In 1892, the Dutch Foreign Secretary declared that attempts at settlement in Suriname of Western people had failed owing to the adverse influence of the climate, sickness and death. These conditions wracked such havoc on the settlement that economic conditions had no chance of exerting an influence. Mid twentieth century, the public health hygienist Swellengrebel investigated the issue[31] and concluded that – after the outbreak stopped – economic conditions such as the congestion of farmers at Groningen, lack of leadership and failure to market their crops, made the colonization attempt collapse. In the end, there was no easy settling for the survivors. Voorzorg and Groningen were simply too far from the main settlement Paramaribo to allow competitive trade in crops. Meanwhile, the colonization was maintained at the expense of the Dutch government, providing

colonists day benefits in exchange for public services such as the construction of streets, parks and terraces. In 1853, the Dutch government put an end to the failed colonization attempt. Most of the descendants of the colonists, Dutch Surinamese, later referred to as 'Boeroes', succeeded in building an existence near Paramaribo.

Of note, the Boeroes' descendants have been the subject of studies in the 1980s, which supported the now generally accepted hypothesis that infectious diseases played an important role in the evolution of HLA polymorphism[45,46]. Among the descendants of the settlers who had survived the epidemic, certain HLA types occurred more frequently than in the general Dutch population whereas another HLA type was absent. This meant that natural selection of certain HLA types can take place due to an infectious disease, although the suggested Darwinian selection by typhoid fever should now likely be changed into Shigellosis, i.e., bacillary dysentery.

Conclusion

In conclusion, by taking a multifaceted approach, combining archival research, mathematical modeling of the outbreak, excavation of physical remains and genetic analysis, we characterized in detail the 1845 outbreak among Dutch colonist farmers at voorzorg in suriname. The study challenges the notion that *Salmonella typhi* caused the outbreak, instead pointing to *Shigella dysenteriae* as the probable etiologic pathogen. Moreover, evidence suggests that the outbreak extended beyond the colonists, affecting crew members of escorting vessels and physicians from Paramaribo. The outbreak, alongside adverse climate and economic factors, and lack of preparations and leadership, contributed to the colonization attempt's failure. Its impact may have indirectly influenced attitudes and deliberations[3,8], around farmer colonization in Suriname and spurred discussions about sustainability of the plantation system.

Conflict of Interests: None.

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Access to Data

Due to the uncertainty about the identity of the excavated and studied human remains the metagenomic data is not made publicly available but can be made available upon request to corresponding author.

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Supplementary Material

Supplement 1. Maps of Suriname and excavation site at Groningen.

Figure S1.1 The map of Suriname displays the plantation Voorzorg, in 1845 a swampy area located in a loop of the river Saramacca, opposite the abandoned military post Groningen. A few hours downstream by boat lies the coffee plantation Mijn Vermaak. The capital city Paramaribo on the Suriname river is shown as well.

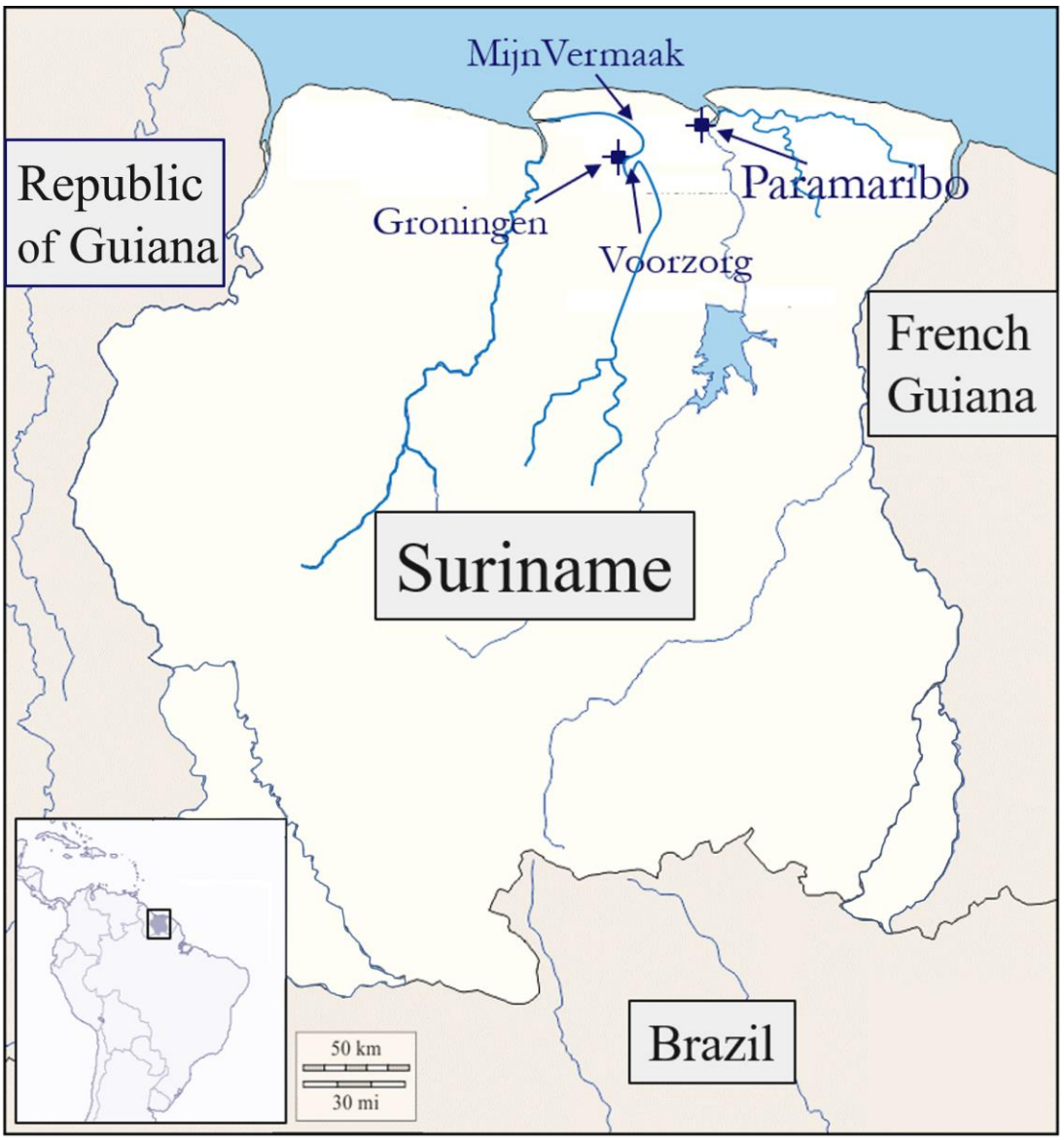


Figure S1.2 The map of the excavation site at the cemetery of Groningen, located close to the river Saramacca, and adjacent to the remains of the abandoned military post Groningen. The excavation site was an empty field to the north of the currently used public cemetery, next to the gravestone of Anna S. Pannekoek, who died in November 1845 and was the spouse of referend Van den Brandhof.

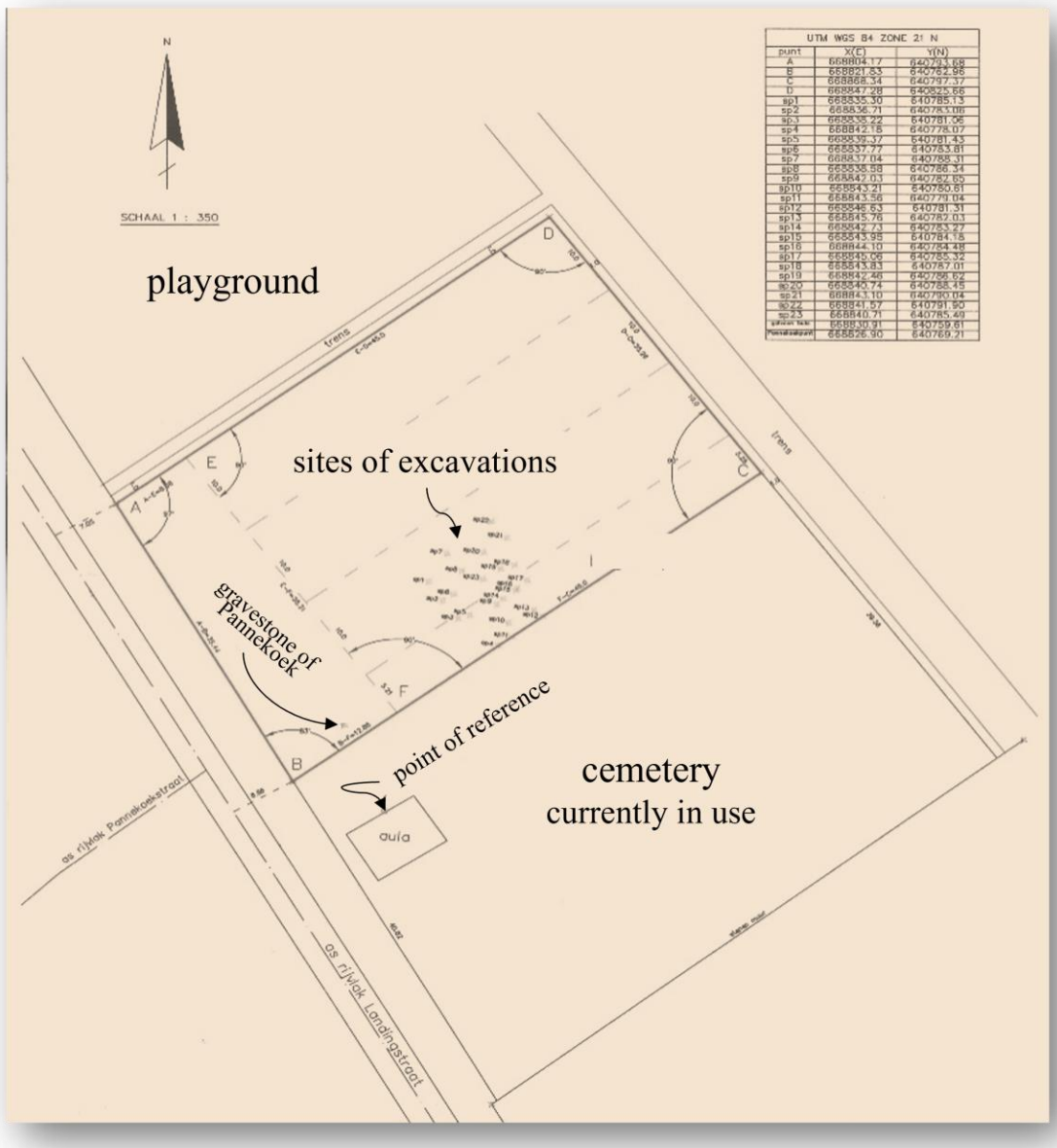


Figure S1.3 Plan of the excavation with trenches 1 and 2, including coordinates in the national Suriname measuring system and the (potential) graves in trench 1 in red.

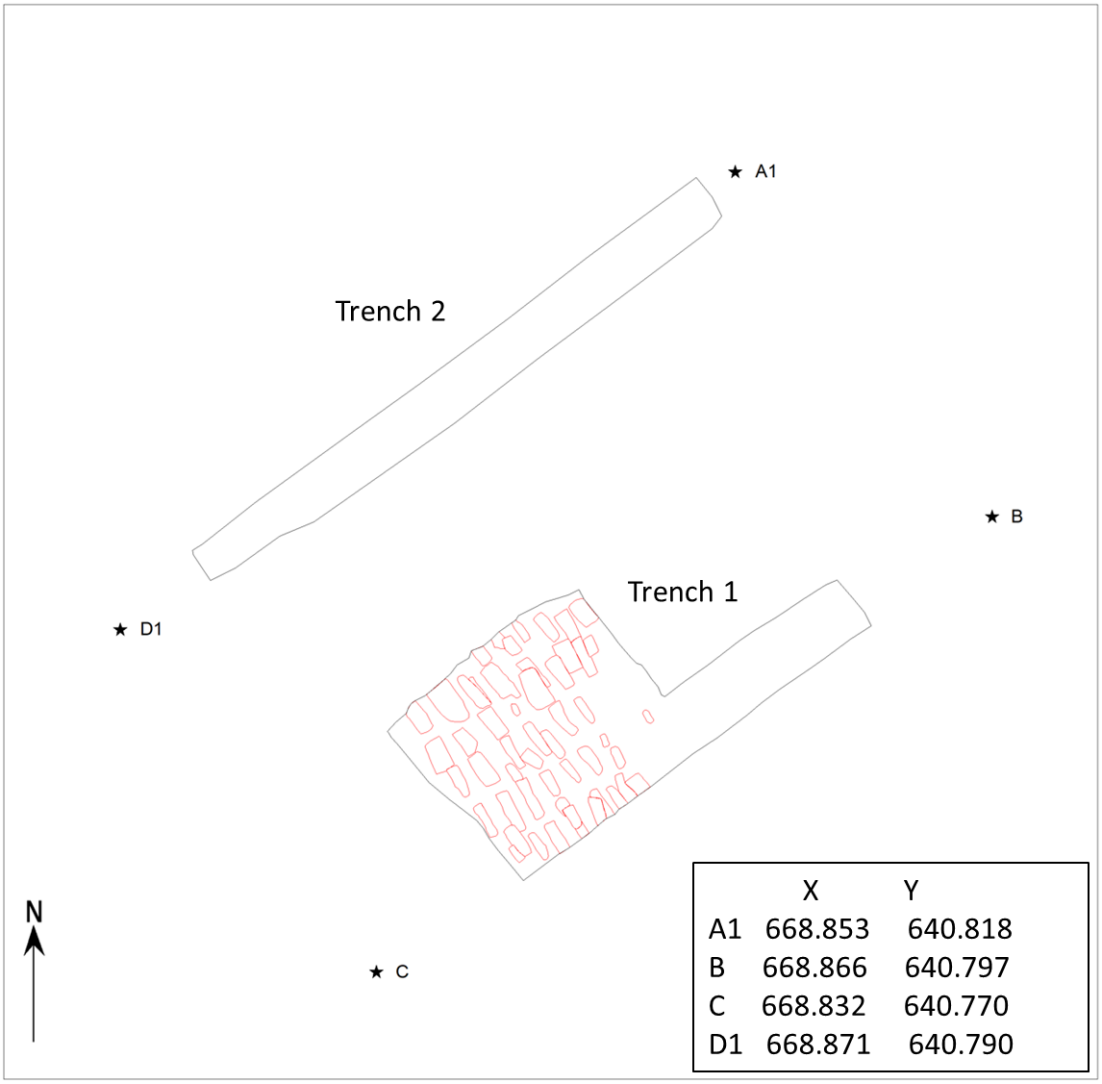
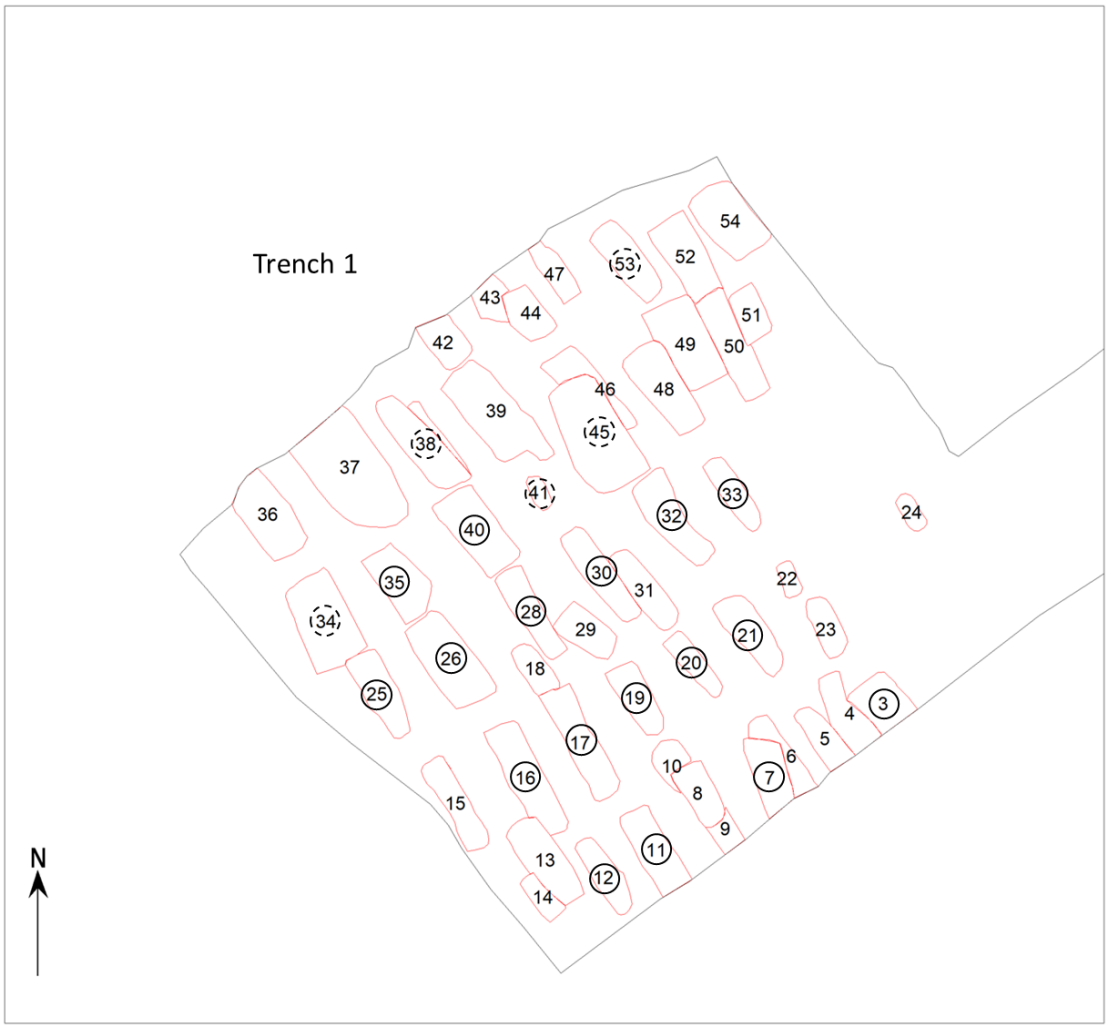
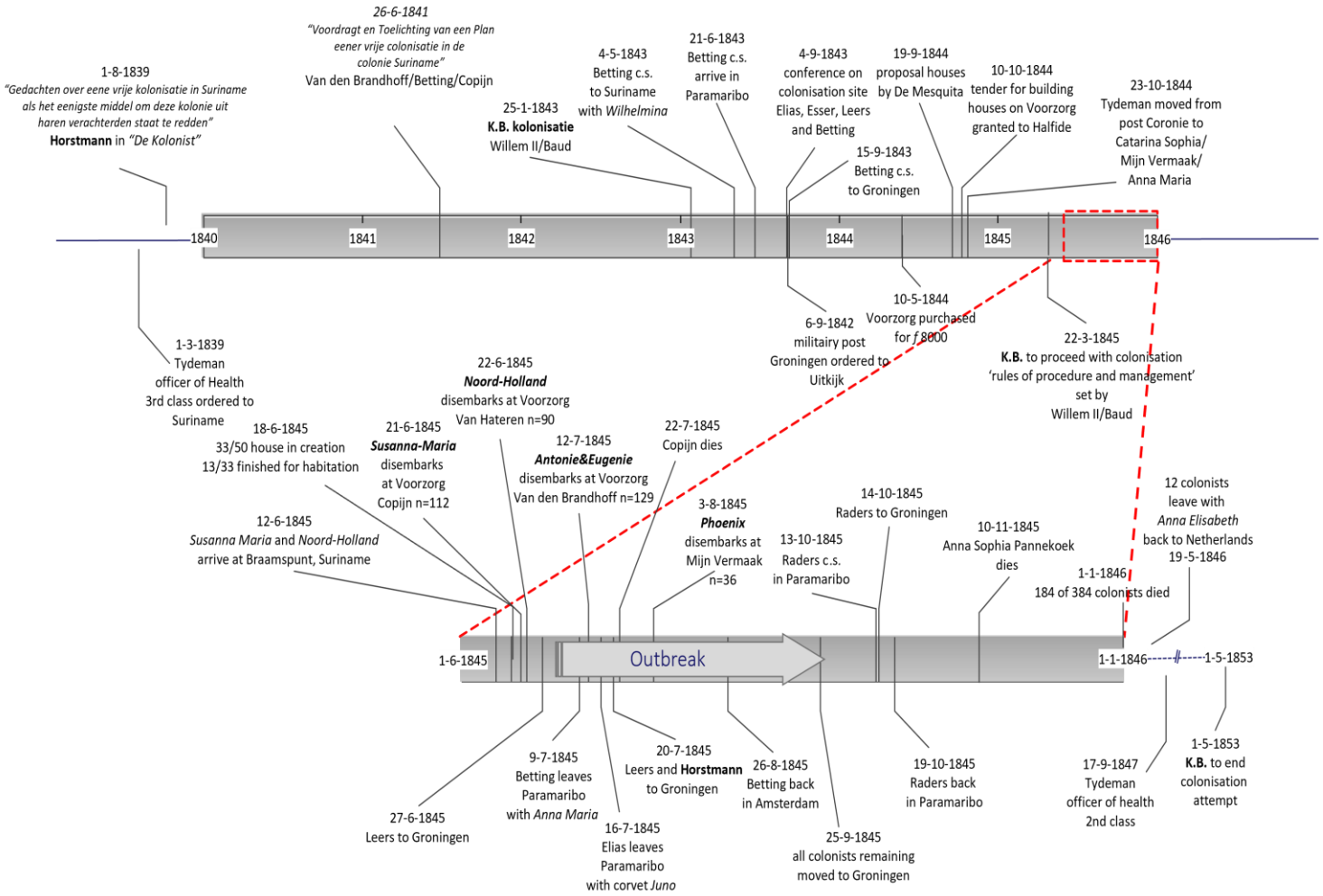


Figure S1.4 Close up of trench 1 with all (potential) graves in red, including grave numbers. Graves with a full circle are excavated and sampled for genetic and metagenomic analysis, graves with a dashed circle are only excavated.



Supplement 2. History of colonization attempt. In 1845, the reverends Betting, Copijn and Van den Brandhof with support of the Dutch government, led an attempt at European farmer colonization in the Dutch colony of Suriname in South America (Timeline events **Figure S2.1**). The attempt followed an 1839 plea in "The Colonist" by the Paramaribo physician FH Horstmann to help improve the harsh living conditions in Suriname by way of immigration of a middle class from the motherland. Although the King Willem II and his minister of colonial affairs Baud rejected this particular plan, they later embraced the 1841 proposal of the three reverends written in the same line.

Figure S2.1 Timeline of events leading up to the 1845 colonization attempt at Voorzorg on the Saramacca river, and subsequent disease outbreak. **K.B.** denote the official decision made by King Willem II and his minister of colonial affairs Baud.



In the 1830-50s, the Dutch government was struggling to overcome widespread poverty in The Netherlands and all emigration attempts were welcomed to reduce the pressure on welfare support. Moreover, the colonization experiment was undertaken at a time when the Netherlands was divided over when and how to put an end to slavery in Suriname, and its purpose was to demonstrate that Europeans could work in the tropics and uphold themselves, something that was renounced by plantation directors in Paramaribo and the owners in The Netherlands. The referend Betting was given the task to oversee in Suriname the necessary preparations for the reception of some 50 farmer families out of a group of some 200 families that were envisioned to constitute the complete colonization force. Betting was accompanied by two farmers and a handyman. Thus, in 1843 and a few months after arrival, a decision was made to proceed during a conference in Paramaribo between governor Elias, Betting, and government officials Leers and Esser: the settlement of Groningen had been chosen as colonization site and the military occupation of the local fortress was ordered to leave and make room for Betting and the farmers. Things soon turned sour as attempts to cultivate the dry and poor soil in Groningen failed and almost a year later, little had come of the preparations. The two farmers, Bovenkamp and De Vries, returned to The Netherlands, whereas Betting and the handyman Rijsdijk were no longer on speaking terms. Betting informed the minister Baud about his doubts

concerning the possibility of colonization. The objections raised by him had the effect that the work started had been stopped for some time and little had been done to receive the settlers when they accepted the trip in May 1845. Soon, Betting advised right on against the colonization attempt, causing alarm in Paramaribo and dismay in The Netherlands. To accommodate at least some of the criticism, the local government bought for *fl.* 8000 the fertile but swampy plantation Voorzorg on the other side of the Saramacca river, opposite Groningen. Tenders were written for built of the necessary houses for the first 50 families. Some 50 enslaved persons were sent to the site to prepare and start cultivating the premises. The proposal of the Paramaribo architect DeMesquita was deemed too expensive (*fl.* 1000 per house including painting and roof webbing), and after exchanging the planks and singles roofs for simple palisades and covering by troeli leaves (straw huts), the tender was granted to the master carpenter Halfhide for *fl.* 700 per house. Others mention *fl.* 520 and *fl.* 250, respectively (e.g., Bijdragen tot de kennis der Nederlandse en vreemde koloniën. Van der Post Jr, Utrecht, 1847, pp 478-479). The work started end 1844 and progressed with much difficulty. Given the negative advice of Betting, the governor Elias hesitated to proceed and spent more money. Early 1845, *fl.* 39.029,17 had already been spent on the preparations at Groningen and Voorzorg. Moreover, he was in a bitter battle with plantation owners over a new reglement of enslaved persons and over methods of payment by *Agio*. He requested for his resignation and prepared to return to the motherland. Meanwhile, the reverends Copijn and Van den Brandhof had enrolled some 50 families of mostly farmers from the middle regions of The Netherlands as well as some unmarried youngsters, for their plan. Most of these had quitted their jobs and until travel were dependent on government welfare for food and shelter. By consequence, the Dutch government put pressure on the project.

The first two ships with colonists arrived at plantation Voorzorg, the designated colonization site on the Saramacca river, on June 20th (*Susanna Maria* with 17 families and 13 free laborers, in total 104 individuals) and June 22nd (*Noord-Holland*, with 12 families and 15 free laborers, in total 86 individuals) 1845, respectively. They were followed by the *Antonie & Eugenie* (with 21 families, in total 124 individuals) on July 12th and the *Phoenix* (with 37 individuals) on August 3th. The local government had failed to realize the promised provisions: Voorzorg offered little more than a badly drained swamp and less than one third (13) of the 50 houses needed, were habitable whereas 20 still had to be built from the ground. The living conditions were abysmal: farmers were overcrowded in small huts infested with rats, on a diet of biscuits with baked bacon and salted meat, having brackish river water as the drinking water source and under an intense tropical sun. Within two weeks of arrival an epidemic broke out among the Dutch settlers. As a measure of precaution, colonists on the last ship disembarked at another plantation Mijn Vermaak, closer to the sea. However, an overnight exposure of two farmers to victims on Voorzorg proved sufficient to transmit the disease to their families on return to Mijn Vermaak. This caused an outbreak of the disease at that plantation as well. In all, some 189 of the 384 settlers passed away within months (**Table S2.1**). Please note that total numbers do not simply add up, because children were born (e.g., 5 during travel on *Antonie & Eugenie*) and some colonists arrived later in 1845.

A committee of government doctors including Horstman from Paramaribo was sent to investigate the outbreak and diagnosed a "gastric biliary fever" characterized by "a nervous fever" with "a rotten character". Unfortunately, they did not provide a systematic description of complaints and physical findings, nor specifics on the natural course of illness. Settlers who survived were transferred from Voorzorg to Groningen, the former military post situated at the other, high and dry side of the Saramacca River. Next, the survivors of the outbreak remained essentially disease free with only a few deaths to regret for several years, until an epidemic of yellow fever swept through the whole country in 1851. Yellow fever killed 27 persons among a population of 122 settlers left, and also affected those stricken by the first epidemic.

In 1853, the Dutch government put an end to the failed colonization attempt.
Van den Brandhof returned to The Netherlands. Most of the descendants of the colonists, later referred to as 'Boeroes', Dutch Surinamese, succeeded in building an existence near Paramaribo.

Table S2.1 Number of colonists arriving in Voorzorg, Groningen and Mijn Vermaak along the river Saramacca in Suriname in 1845, and number dying during the outbreak, according to various primary source documents. Period covers time of arrival of colonists till January 1846, unless indicated otherwise.

No. of colonists who arrived in Suriname		**Born in Suriname**		**Died**		**Remaining on Dec 15st, 1845**		**Primary source**
male	female	male	female	male	female	male	female	
193 *)	178	1	2	89 **)	93	105	87	*Van den Brandhof (1845)*
386				186				*De Castelnau (1847)*
194	176		4	93	91			*Copijn (1855)*
384				189				*Ministerial Report (1857)*
384				189				*Muller and Hoekstra (1895)*
192	174	1	2	88	90			*Cartier-Van Dissel (1937)*

*) excluding the family of Rijsdijk (5 male, 2 female of which died: 3 male and 2 female)

**) including 2 children who died during the boat trip to Suriname (1 male, 1 female)

-Van den Brandhof and Van De Grompel. Bijlage bij rapportage van de bestuurder der kolonisatie, Dec 16th 1845; KITLV archive Van den Brandhof no. 72.

-De Castelnau F. Essai de colonisation européenne à Groningue. In: Revue colonial. Edité par imprimerie Royale, Paris, 1847.

-Copijn A. Schets van de lotgevallen der kolonisten die aan de proeve van Europeesche kolonisatie aan de Saramacca hebben deelgenomen. West-Indie 1855;1: 241-55.

-Verslag ven het beheer en staat der Nederlandse bezittingen en koloniën in oost- en west-Indie en ter kust van Guinea over 1849, ingediend door den minister van koloniën. Section K. kolonisatie; pp 357-63. Utrecht, Kemink en Zoon, 1857.

-Muller JE, Hoekstra C. Het vijftigjarig jubilé der boeren in Suriname. 1845 – 21 juni – 1895. Uitgeverij B Heijde, Suriname, 1895.

-Verkade-Cartier van Dissel EF. De mogelijkheid van landbouw kolonisatie voor blanken in Suriname. Academic PhD thesis, Amsterdam, 1937.

The outbreak affected also crew on board of the vessels that had brought them to Suriname and Voorzorg, and stayed there to help for 14 days (*Susanna-Maria*), 13 days (*Noord-Holland*) and 7 days respectively (*Antonie & Eugenie*), before sailing to Paramaribo. Sick people also included crew of three governmental vessels (*Henrietta*, *De Beschermer*, and *De Brak*) that assisted the ships in their journey on the Saramacca river and stayed some days at Groningen. For instance, Van den Brandhof mentions in a letter to Sloet of sept 14th that captain Hansen of the schooner *Henrietta* had died from the disease in Paramaribo. Many of the crewmen of the brikship *De Brak* anchored at the mouth of the Saramacca river assisted on board of the *Antonie & Eugenie* to navigate the river and disembark, and became ill on return to their Post Nassau (Main text, Figure 2), as evidenced by a request for help from their commanding officer Holl sent on July 19th to the governor.

Supplement 3. Genetic and metagenomic analysis.

Mitochondrial haplotyping. To avoid primer-dimers in the multiplex mt SNP assay, primers with the last four or more 3' bases reverse complementary to the last 3' bases of another primer were redesigned where possible and amplicon-sequences were checked for specificity using BLAST. M13 tails were included in the primers.

PCRs were performed in a 12.5 µl reaction using 1* PCR-buffer (ThermoFisher Scientific), 6.5 mM MgCl2, 200 µM/dNTPs (GE Healthcare lifesciences, Chicago, IL, USA), 0.02 – 0.24 µM primers (Biolegio bv, Nijmegen, the Netherlands) and 2.5 U AmpliTaq Gold DNA Polymerase (ThermoFisher Scientific) in a GeneAmp® PCR System 9700 with a predenaturation of 10 min at 94°C, followed by 35 cycles of 30 s at 94°C, 30 s at 60°C and 30 s at 72°C and a final extension of 5 min at 72°C.

Illumina sequencing libraries were prepared with the KAPA HTP Library Preparation kit (Roche, Bazel, Swiss) without additional amplification, according to the manufacturer's manual, except for some small changes as described below. The end repair step was performed in a 35 µl reaction with 2.5 µl of PCR product without prior purification. Because of the short amplicon length end repair and A-tailing products were purified with the MinElute PCR Purification Kit (Qiagen, Hilden, Duitsland) or ZR-96 DNA Clean & Concentrator-5 D4024 kit (Zymo Research), depending on the number of samples. The purified end repair products were eluted in 13 µl Aqua B. Braun water. The purified A-tailing products were eluted in 17,5 µl of 75-fold diluted barcoded TruSeq adapters (Illumina). A-tailing and ligation steps were performed in 25 µl reactions.

To enable balanced pooling of barcoded samples, sequencing libraries were quantified in duplicate by real time PCR using the KAPA SYBR® FAST qPCR kit (Roche). Quantification reactions were performed on a LightCycler® 480 (Roche) or a 7500 Real Time PCR System (ThermoFisher Scientific) using a dilution series of PhiX control library (Illumina) as standard. After pooling the libraries, the final pool was quantified again using the same method to enable optimal loading of the flow cell. Sequencing was performed on the MiSeq system with the MiSeq Reagent Kit v3 600-cycle (Illumina) paired end according to the manufacturer's protocol with approximately 10% of PhiX control library and 14–19 pM final library concentration.

For data analysis with FDSTools thresholds were set as follows: ≥8 total reads, ≥3 reads per orientation, ≥93% of highest allele to be considered not mixed.

Table S3.1 Primer details of the multiplex Mitochondrial SNP assay. Letters in lowercase display the primertails (M13) and known SNP positions.

Targeted SNPs	Sequenced range (excluding primers)	Forward Primer	Reverse Primer	Fragment Length (bp excluding primertails)	Conc. in PCR (µM)
mt239	234-247	tgtaaaacgacggccagtGTGTTAATTAATTAATGCTTgTrrGACAT	caggaaacagctatgaccGAAAGTGGcTGTGCAGACrTT	64	0.2
mt456+462+477	455-478	tgtaaaacgacggccagtcACCCCcCAACTAACACATTATTT	caggaaacagctatgacccGgGGgTTGTaTTGrTGrGAT	69	0.2
mt930	927-931	tgtaaaacgacggccagtCACACGATTAACCCAAGyCAATA	caggaaacagctatgaccTGATcTAAAACACTCTTTACGCCG	52	0.07
mt1018	1017-1031	tgtaaaacgacggccagtAAAAACTCCAGtTGACACAAAAT	caggaaacagctatgaccGCTATTGTGTgTTCAGAtATGTTAAAG	65	0.03
mt1189	1188-1194	tgtaaaacgacggccagtGACCTGGCGGTGCTTCAT	caggaaacagctatgaccCGATTACAGAACAGGCTCCTCTA	48	0.09
mt1438	1431-1446	tgtaaaacgacggccagtGGTCGAAGGTGGATTTAGCA	caggaaacagctatgaccGGCCcTGTTCAACTAAGCAC	56	0.06
mt1738	1734-1748	tgtaaaacgacggccagtAACCTTAgCcAAACCATTTACC	caggaaacagctatgaccCGCCAGGTTTCAATTTCTATCG	59	0.06
mt2706	2698-2708	tgtaaaacgacggccagtATTGACCTGCCCGTGAAGAG	caggaaacagctatgaccGGGTCTTCTCGTCTTGCTGT	51	0.13
mt3010	3006-3013	tgtaaaacgacggccagtCTCGATGTTGGATCAGGACA	caggaaacagctatgaccACCTTTAATAGCGGCTGCAC	48	0.08
mt3333	3330-3337	tgtaaaacgacggccagtCCATGgCCAACCTCCTACT	caggaaacagctatgaccCCATTGCGATtAGAATGGGTA	48	0.12
mt3423	3421-3441	tgtaaaacgacggccagtCTACGCAAAGGCCCCAAC	caggaaacagctatgaccCGTCAGCGAAgGGyTGTAG	58	0.24
mt3516	3512-3519	tgtaaaacgacggccagtAAACCCgccACATCTrCCATCA	caggaaacagctatgaccAAGGTcGGGGCGGTGAT	47	0.09
mt3796	3796-3801	tgtaaaacgacggccagtAGTGGCTCCTTTAACCTCTCC	caggaaacagctatgaccGAGGTGTTCTTGTGTTGTGAT	48	0.09
mt4793	4792-4795	tgtaaaacgacggccagtCATAaTaGCTATAGCAATAAAACTAGGAA	caggaaacagctatgaccGGGACTCAGAAGTGAAAGGGG	54	0.08
mt5004	4998-5010	tgtaaaacgacggccagtTAAACCAAACCCArCTACGC	caggaaacagctatgacccCCTATgTGGGTAATTGAGGAGT	55	0.08
mt6371	6364-6376	tgtaaaacgacggccagtTCTTCTCCTTACACCTAGCAG	caggaaacagctatgaccTGATGAAaTTGATGGCCCCTAAG	57	0.07
mt6776	6771-6785	tgtaaaacgacggccagtCCTaGGgTTTATCGTGTGAGCA	caggaaacagctatgaccCGTGTGTCTACGTCTATTCCTAC	60	0.06
mt7768	7762-7780	tgtaaaacgacggccagtATACTAACATCTCAGACGCTCA	caggaaacagctatgaccTGATGGCGGGcAGGATAGT	60	0.06
mt8448	8445-8460	tgtaaaacgacggccagtACTATTcCTCATCACCCAACTAA	caggaaacagctatgaccGTGAGGGaGGTAgGTGGTAG	59	0.1
mt8697	8694-8705	tgtaaaacgacggccagtTGACTAATCAAACTAAcCTCAAAACA	caggaaacagctatgaccGGTTCGTCCTTTAGTGTTGTGT	60	0.06
mt9716	9715-9724	tgtaaaacgacggccagtGCACTGCTtATTACAATTTTACTGG	caggaaacagctatgaccTCTGAGGCTTGTAGGAGGGTA	56	0.07
mt10034	10028-10035	tgtaaaacgacggccagtGTATAAATAGTACCGTTAACTTCCAATT	caggaaacagctatgaccGTTTATTACTCTTTTTTGAAtGTTGTCAA	65	0.09
mt10211	10198-10212	tgtaaaacgacggccagtCTTcGACCCTATATyCCCCG	caggaaacagctatgaccGGTaATAGCTACTAAGAAGAATTTTATGG	64	0.06
mt10873	10872-10876	tgtaaaacgacggccagtCCACAGCCTAATTATTAGCATCATCC	caggaaacagctatgaccAGGTTGtTGTtGATTTGGTTAAAAAATAG	60	0.06
mt11176	11164-11186	tgtaaaacgacggccagtACcTTggcTATCATCACCCG	caggaaacagctatgaccGAaGTATGTgCCTGCGTTCA	63	0.06
mt11251	11250-11260	tgtaaaacgacggccagtCCTTCCCCTACTcATCGCAC	caggaaacagctatgaccAGTGAGCCTAGgGTGTTGTG	51	0.08
mt11332	11330-11340	tgtaaaacgacggccagtCCCAAGAaCTATCAAACTCCTGA	caggaaacagctatgaccAAGCTATTGTGTAaGCTAGTCATATT	60	0.08
mt11467+11485	11466-11490	tgtaaaacgacggccagtAGTACTTGCCGCAGTACTCT	caggaaacagctatgaccTGAGAATGAGTGTGAGGCGT	65	0.05
mt11719	11709-11725	tgtaaaacgacggccagtCGGCGCAgTCATtCTCATAA	caggaaacagctatgaccGCTAGGCAGAATAGTArTGAGGA	60	0.07
mt11812	11810-11830	tgtaaaacgacggccagtTCCTCTCTCAAGGaCTTCAAACT	caggaaacagctatgaccAGGCTTGCTAgAAGTCATCA	64	0.07
mt11947	11941-11951	tgtaaaacgacggccagtTCTCCTGATCAAaTATCACTCTCCT	caggaaacagctatgaccAGGGcTGTGAcTAGtATGTTGA	58	0.06
mt12633	12629-12641	tgtaaaacgacggccagtCCCtGTAGCATTgTTCGTTACAT	caggaaacagctatgaccGgTCTGAGTTTATATATCACAGTGAGAAT	65	0.06
mt12705	12693-12705	tgtaaaacgacggccagtGAcCCAAACATTAATCAGTTCTTCAA	caggaaacagctatgaccGTaACTAAGATTAGtATGGTaATTAGGAA	68	0.06
mt13617	13613-13623	tgtaaaacgacggccagtAAGCGCCTATAGCACTCGAA	caggaaacagctatgaccCGAGGTtGaCCTGTTAGGGT	51	0.1
mt13789	13789-13791	tgtaaaacgacggccagtCTTCCAAACAACAaTCCCCCTC	caggaaacagctatgaccGCGAGGGCtGTGAGTTTTAG	45	0.12
mt14470	14461-14471	tgtaaaacgacggccagtTACTCCTCAATAGCCATCGC	caggaaacagctatgaccGGGGaATGaTGGTTGTyTTTG	52	0.085
mt14766	14764-14788	tgtaaaacgacggccagtCCAATGACCCCaATACGCAA	caggaaacagctatgaccAGGTCGATGAaTGAGyGGTT	65	0.2
mt14783+14793+14798	14780-14801	tgtaaaacgacggccagtACGCAAAAcTAaCCCCCTAATA	caggaaacagctatgaccATGGGGTGGGGAGGTCGA	62	0.2
mt15257	15252-15262	tgtaaaacgacggccagtTCAATGaaTCTGAGGaGGCTACT	caggaaacagctatgaccAAGAATCGTGTGAGGGTGGG	54	0.07
mt15775	15774-15776	tgtaaaacgacggccagtCTGAaTCGGAGGaCAACCAG	caggaaacagctatgaccCCAATGATGGTAAAAGGGTAGC	45	0.12
mt15904+15907	15896-15908	tgtaaaacgacggccagtTCAAATGggCCTGTCCTTGT	caggaaacagctatgaccTccGGtTTACAAGACTGGTGT	54	0.068
mt16162	16153-16176	tgtaaaacgacggccagtCgGTACCAtAAAtACTtgrCyACCT	caggaaacagctatgaccATGGGGAGGGGGTkTtGAT	68	0.1

Table S3.2 FDSTools library – in EXEL, made available upon request.

Metagenomic analysis. In metagenomic analysis, paired-end reads were trimmed and clipped using Flexiprep [https://github.com/biopet/biopet/releases/tag/v0.8.0] (version 0.8.0) with default parameters. Next, using BWA-mem [https://arxiv.org/abs/1303.3997] (version 0.7.10-r789) with default parameters, we proceeded with a targeted analysis to align to a selected number of reference sequences as indicated in **Figure 6** of the main text. For every species, we took the number of alignments with high mapping quality (Phred score over 50 and at least 100 matching bases) using SAMtools [http://www.htslib.org/] (version 1.4) and used this number of supporting reads as a proxy for the abundance of the species in the sample. Alignments were filtered for soft clipping, hard clipping and padding using SAMtools to reduce the number of false positive alignments.

Supplement 4. Parameter settings used for modelling an outbreak of typhoid fever and bacillary dysentery, respectively and **Model of Typhoid Fever.**

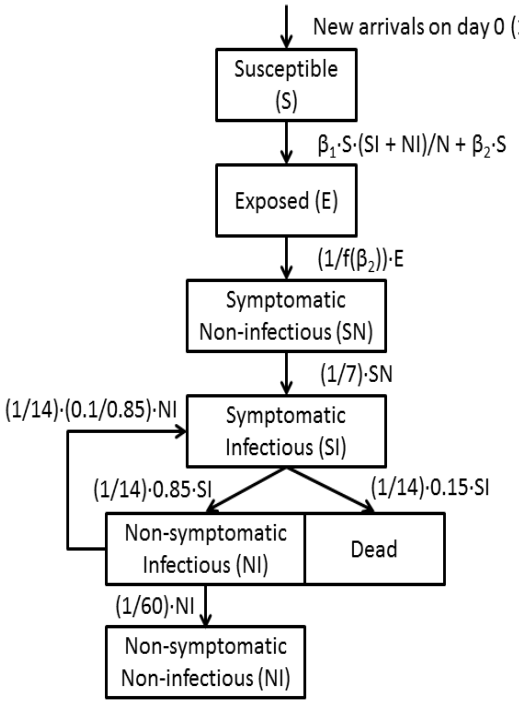
Table S4.1 The parameter settings used for modelling an outbreak of typhoid fever and bacillary dysentery, respectively. Average values derived from literature (summarized in[26-30]).

Disease	Incubation Period	Duration of illness to recovery or death	Start being infectious after exposure	Duration of being infectious after exposure	Relapse rate	Mortality rate
	(days)	(days)	(days)	(days)	(%)	(%)
Typhoid Fever	18-22	21	28	60	10	15%[1)]
Dysentery	3-5	7	3-5	7-12	0	25-40%[2)]

Incubation period: number of days between exposure and first disease symptoms.
Duration of illness to recovery of death: number of days between start of illness and recovery or death.
Start infectiousness: number of days between exposure and start of being infectious to susceptible individuals.
Duration infectiousness: days a diseased individual remains infectious to susceptible individuals.
Relapse rate: percentage of diseased individuals that experience relapse of disease, within two weeks of recovery.
Mortality rate: average percentage of diseased individuals that die from the disease, in pre-treatment era.
[1)] rate in outbreaks independent of percentage of exposed individuals becoming ill;
[2)] as reported for *Shigella dysenteriae* in 1900s outbreaks occurring in Tropics.

Model of Typhoid Fever. Schematic representation of the compartmental model used to derive parameters for β_1 (human-to-human transmission) and β_2 (exogenous-source-to-human transmission) for typhoid fever. Just like the Shigella model, individuals start out as susceptible persons (S), and new susceptible individuals arrive when ships disembark (on days 0, 1, and 22, respectively for boats 1-3). A first individual is exposed through contact with an exogenous (constant) source of infection, becomes infectious after an incubation period specific for microbial agent, and is able to transmit person-to-person during an infectious period, after which the person either recovers and becomes resistant to re-infection, or dies. For typhoid fever, we also allowed for relapses to occur in 10% of the cases with disease[26,27]. The extent of the two sources of transmission (i.e., β_1 = human-to-human transmission; β_2 = exogenous source-to-human transmission) is unknown and was modelled taking the observed cumulative mortality rate as the end-point to fit.

Figure S4.1 Model of Typhoid Fever.



Assumption 1: transmission via human-to-human contact and a constant source-to-human
Assumption 2: transmission via contact with symptomatic infectious and non-symptomatic infectious individuals is equal

Assumption 3: incubation period depends on source transmission rate

$$f(\beta_2) = \begin{cases} 21, & \beta_2 < 0.1 \\ \dfrac{16 \log(\beta_2)}{\log(0.1)} + 5, & \beta_2 \geq 0.1 \end{cases}$$

Assumption 4: symptomatic non-infectious period is 7 days

Assumption 5: symptomatic infectious period is 14 days
Assumption 6: 15% of the symptomatic infectious individuals die
Assumption 7: 10% of the people who became infected relapse after a non-symptomatic period of 14 days

Assumption 8: non-symptomatic infectious period is 60 days