Transmission dynamics of Q fever in French Guiana: A population-based cross-sectional study

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Summary

Background Q fever is a zoonosis caused by *Coxiella burnetii* which is among the major agents of community-acquired pneumonia in French Guiana. Despite its relatively high incidence, its epidemiology in French Guiana remains unclear, and all previous studies have considered transmission from livestock unlikely, suggesting that a wild reservoir is responsible for transmission.

Methods A country-wide seroprevalence survey of 2697 participants from French Guiana was conducted. Serum samples were tested for phase II IgG antibodies by ELISA and indirect immunofluorescence assays (IFAs). Factors associated with Q fever were investigated, and a serocatalytic model was used to reconstruct the annual force of infection.

Findings The overall weighted seroprevalence was estimated at 9.6% (95% confidence interval (CI): 8.2%–11.0%). The model revealed constant, low-level circulation across French Guiana, particularly affecting middle-aged males (odds ratio (OR): 3.0, 95% credible interval (CrI): 1.7–5.8) and individuals living close to sheep farms (OR: 4, 95% CrI: 1.5–12). The overall annual number of cases was estimated at 579 (95% CrI: 492–670). In the region around Cayenne, the main urban municipality, the high seroprevalence was explained by an outbreak that may have occurred between 1996 and 2003 and that infected 10% (95% CrI: 6.9%–14%) of the population and males and females alike.

Interpretation This study reveals for the first time Q fever dynamics of transmission and the role of domestic livestock in transmission in French Guiana and highlights the urgent need to reinforce Q fever surveillance in livestocks of the entire Guianese territory.

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Introduction

Q fever is a zoonotic disease caused by the intracellular bacterium *Coxiella burnetii* (*C. burnetii*) that infects a wide range of domesticated and wild animals.[1–3] Infected mammals shed the bacterium in their urine, feces, milk, and birth products. Generally, humans contract Q fever via airborne routes after the organism settles in dust and becomes aerosolized. Most primary infections with *C. burnetii* are asymptomatic and approximately 60% of cases are identified during outbreaks.[1] In humans, clinical

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Research in context

Evidence before this study

We searched PubMed, preprint servers and country-specific public health rapid communications to identify surveillance and epidemiological studies on Q fever and *Coxiella burnetii* in French Guiana. Epidemiological patterns and modes of transmission of *C. burnetii* infection remain unclear and all previous studies have considered transmission from livestock unlikely, suggesting that a wild reservoir is responsible for transmission.

Added value of this study

We conducted a general population survey with individual interviews and a serological study of over 2697 individuals from French Guiana. We identified the risk factors of Q fever transmission and the mode of circulation of the pathogen. In contrast with previous studies, where no classical exposure risks were identified in acute Q fever cases, our survey with precise information on geolocation and sociodemographic conditions showed that living close to a sheep farm increases considerably the risk of being seropositive to Q fever.

Implications of all the available evidence

Using a modeling approach, we showed that there is ongoing transmission in all parts of French Guiana, and not just in the region with the highest seroprevalence. We also identified important risk factors of Q fever transmission in French Guiana and in particular, we highlighted the major role played by livestock.

manifestations of Q fever range from unspecific flu-like symptoms to focal more severe manifestations, such as hepatitis or pneumonia, as well as endocarditis and vascular infections in patients with underlying comorbidities, vascular prosthesis or immunosuppression.[4–7]

In South and Central America, Q fever cases have been reported in some countries, but global epidemiological data are scarce and incomplete.[8–14] In 2005, a serosurvey conducted in Minas Gerais, a Brazilian state, found 3.9% of healthy adults were seropositive.[15] In the Amazon Basin of Ecuador, a longitudinal observational study of 533 patients with acute undifferentiated febrile illness over a three-year period found a seroprevalence for Q fever of 4.9%.[16] In French Guiana, where the disease has been reported more extensively, the epidemiology of Q fever has not been fully elucidated. The geography of this French overseas region located on the northeastern coast of South America consists of a coastal plain that represents 10% of the whole territory and where 90% of the population lives. The rest of the country is covered by the Amazonian rain forest.

After the first identification of *C. burnetii* in 1955 in a slaughterhouse worker living in Cayenne municipality, the main urban municipality,[17] only sporadic cases were reported until 1996 when three patients with acute respiratory distress syndrome were hospitalised in an intensive care unit. A retrospective serosurvey conducted in 1996 in a cohort of febrile patients sent to the arbovirus laboratory for diagnosis of dengue infection between 1992 and 1996 showed an important increase in the prevalence rate of *C. burnetii* infection, from 2% in 1992 to 24% in 1996.[18,19] Q fever incidence in French Guiana was estimated at 17.5 cases/100,000 inhabitants in 2008–2011[19] and at 27.4 cases/100,000 inhabitants in 2007–2017,[20] which seems to be the highest reported incidence rate of the world.[19,20] Additionally, a retrospective case–control study conducted on inpatients admitted in the Department of Infectious Diseases of Cayenne Hospital from 2004 to 2007 showed that *C. burnetii* infection accounts for 24% of community-acquired pneumonia cases, which was also the highest prevalence ever reported.[21] Most cases reported in previous studies were diagnosed in patients from mainland France, located in the urbanised area of Cayenne and its suburbs,[8,20] raising the question of access to diagnostics in vulnerable populations and rural areas. Furthermore, the classical exposure risks were not detected in acute Q fever cases,[22] and no reservoir has been clearly identified to date. All previous studies have considered transmission from livestock unlikely, suggesting that a wild reservoir is responsible for transmission[8,22–24] and factors not usually associated with Q fever were detected, such as living near the forest, seeing wild animals around the house, gardening, and employment in the building trade or public works.[22]

In this study, we report the results of a population-based cross-sectional serosurvey (N = 2697) that was conducted in 2017 in the different communities of French Guiana, alongside individual interviews to improve the understanding of the epidemiology of Q fever in French Guiana and to inform on demographic and socioeconomic characteristics of the participants.[25] We used these data to estimate the seroprevalence of *C. burnetii* infection in the general population in French Guiana and to unravel the drivers and dynamics of Q fever.

Methods

Setting

Ninety-six percent (96%) of French Guiana is covered by the equatorial forest. The majority of the population resides in the coastal area, which is approximately 20 km wide, and the elevation rarely exceeds 30 m. The territory is composed of two main inhabited geographical regions: a central urbanized and coastal strip area along the Atlantic Ocean named “coastal area”, where a

large part of the population lives, and a more remote area located in the Amazonian Forest complex along the Surinamese and Brazilian frontiers called the "interior area" (Fig. 1). In the coastal strip, savannah, swampy areas and dense vegetation alternate with residential areas. The altitude gradually increases toward the interior and in Rémire-Montjoly municipality, which is located on the region surrounding Cayenne municipality. According to the Department of Food, Agriculture and Forestry of French Guiana, there were 843 livestock operations on 574 different farms in the country at the time of the survey, most of them located in coastal municipalities. There were five types of farms including poultry, cattle, sheep, goats and pigs (Supplementary Table S1 and Figure S1).

Ethics statement

Fieldworker teams including investigators and nurses, or medicine residents were trained to visit all households, explain the project objectives, and, when allowed, collect participant's signatures in a free and informed written consent form and carry out the interviews. All members of selected households who were 2–75 years

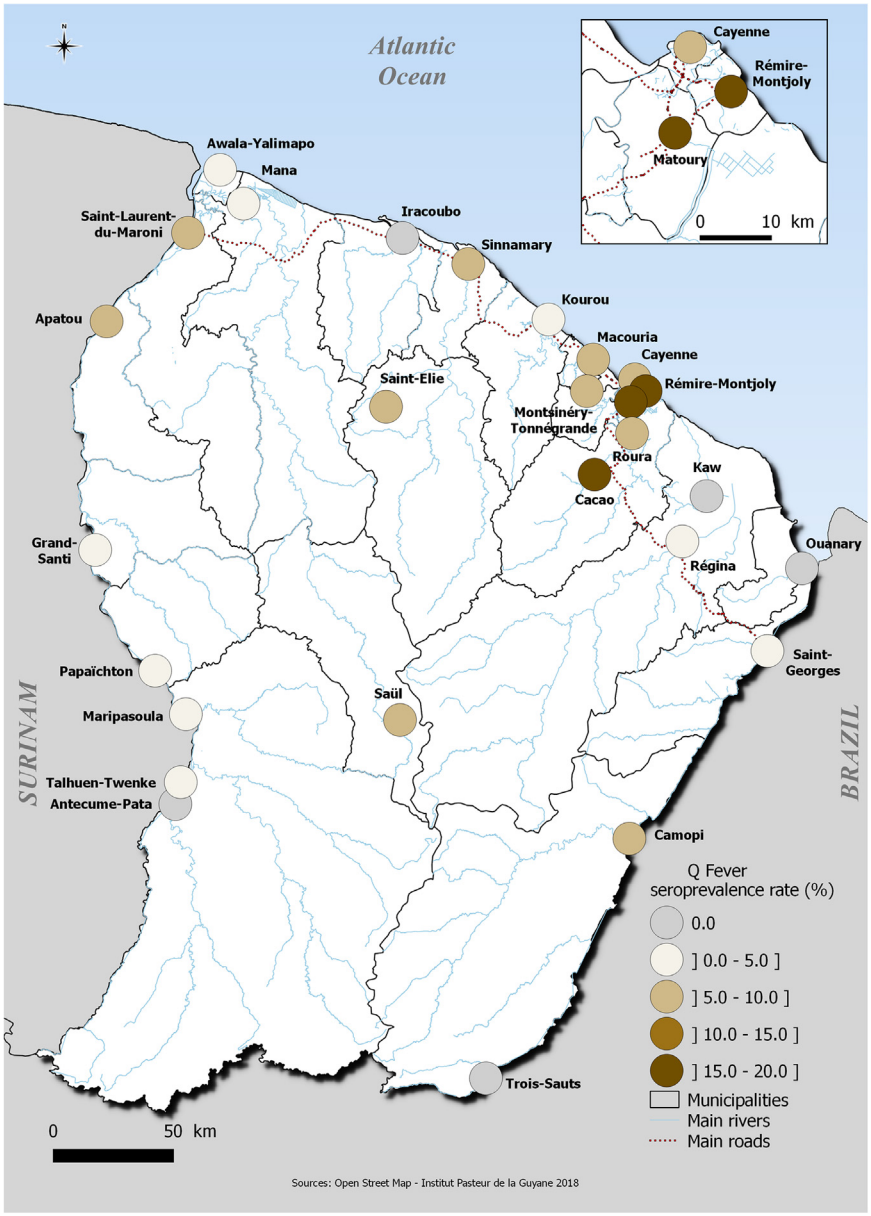

Fig. 1: **Spatial distribution of Q fever seroprevalence, EPIARBO study, French Guiana.**

of age were invited to take part in the study during a preliminary face-to-face interview. For all participants under 18 years of age, one or two responsible adults signed the informed consent. A specific educational-style comic book was designed for children 6–17 years of age to explain, in an understandable way, the nature and objectives of the survey and inform them about the voluntary nature of the participation to the study and their rights to access and rectify their personal information.[25]

The study was recorded on ClinicalTrials.gov (NCT03210363) and approved by the Sud-Ouest & Outre-Mer IV Ethical Research Committee (number CPP17-007a/2017-A00514-49) and by the French Data Protection Authority (number DR-2017–324) responsible for ethical issues and protection of individual data collection.

Study design and participants

A household-based cross-sectional serological survey called EPIARBO was conducted between June and October 2017, involving residents located in the 22 municipalities of French Guiana. We estimated the sample size for this survey at 2500 persons to study the seroprevalence of various pathogens in the different delimited geographical areas, considering a 50% seroprevalence, 95% confidence, 90% power and a cluster effect.[25–27] To reach the desired sample size, 1600 households were randomly selected for possible participation in the study from household databases maintained by the Geographic information and knowledge dissemination unit of the regional environment, planning and housing agency and the National Institute of Economic and Statistical Information (INSEE).[28] A stratified simple random sampling method was adopted to select households from the 22 municipalities (strata), allowing an over-representation of isolated and small municipalities. Villages from 4 municipalities (Roura, Maripasoula, Regina and Camopi) were specifically considered in the sample design to ensure that all existing communities and sub-municipality's areas were adequately represented among the selected households. The distribution of households selected from the 22 strata is presented in Table 1. The global sampling fraction of the households was 1:49 varying from 1:103 to 1:5 according to the municipality.

Data were collected through a standardized questionnaire installed on tablets to register demographics, socioeconomics and household-characteristics. Thereafter, a venous blood sample of 10 mL was collected from each participant, in accordance with current biosafety standards.

Blood sample collection and laboratory analysis

Blood samples were collected into 5 ml gold BD Vacutainer SST II advance tubes with gel for serum separation (Becton–Dickinson, USA). Immediately after puncture, samples were stored at 4 °C–8 °C until centrifugation within 12 h. Sera were then frozen and stored at –20 °C until used at the National Reference Center for respiratory viruses in Institut Pasteur in French Guiana.

All samples were analysed for the presence of IgG antibodies to *C. burnetii* phase II antigen, using a commercial ELISA (Serion ELISA classic, Virion/Serion, Würzburg, Germany) following the manufacturers' instructions.[29] IgG antibodies were measured quantitatively, and the results generated from standard curves were reported in International Units/ml. The manufacturer provided a software (easyANALYSE activity) to establish cut-offs and borderline ranges according to adjustments for interassay deviations and quality control requirements. Samples with values of <20 IU/ml were considered negative, values of 20–30 IU/ml were scored as borderline, and those that had values of >30 IU/ml were considered as positive. ELISA borderline samples were subsequently tested by Indirect Immunofluorescence Assay (IFA) for IgG phase I and phase II specific antibodies using commercial Q fever IFA IgG test kit[30] (IF0200G, Focus Diagnostics, Cypress, CA). A positive IFA sample was defined as a sample with an IFA IgG phase-II specific immunofluorescence at 1:50 dilution. The performance characteristics of the Serion ELISA classic *C. burnetii* Phase II IgG test provided by the manufacturer using 77 sera from blood donors and patients suspected of having Q fever estimated specificity to be 92.5% and sensitivity greater than 99%.[29]

The performance of the IFA test, as evaluated by the manufacturer, estimated a sensitivity of 100% and specificity of 99%, respectively, when compared to a reference laboratory complement fixation test used on 103 sera to test for antibodies to *C. burnetii*.[30]

We internally validated the performance of the serological Serion ELISA test using serum samples previously collected in the framework of diagnosis activities conducted in French Guiana by the laboratory of Institut Pasteur. We randomly selected a panel of 49 sera including 23 positive samples in the dilution ranges 1:50; 1:200; 1:800; 1:>800) and 26 negative samples for which the IFA result was known in order to evaluate the performance of the Serion ELISA test on strains circulating in French Guiana.

In total, 87% (20/23) of the IFA positive samples and 92% (24/26) of the IFA negative samples were concordant with the results of the Serion ELISA test. The results obtained for the three non-matching IFA positive samples (2 samples at dilution range 50-50/1 sample at dilution range 50–200) and for the two non-matching negative samples were all classified as borderline.

Data analysis

We employ the following notation to describe the consideration of study design in data analysis.

Municipality (i) Submunicipality areas	Pop. size	Number of households	Number of selected households	Number of enrolled households	Number of enrolled individuals	Weighted seroprevalence (mean and 95% CI)
Cayenne	57,614	21,659	210	196 (0.9%)	446	9.2% [6.8–12.3]
Matoury	32,427	10,778	180	136 (1.3%)	265	17.1% [13.0–22.3]
Saint Laurent	43,600	9770	180	170 (1.7%)	301	7.5% [4.7–11.7]
Kourou	26,221	8205	180	167 (2.0%)	294	4.5% [2.5–8.0]
Rémire-Montjoly	23,976	8117	120	105 (1.3%)	192	16.9% [11.9–23.4]
Macouria	11,719	4218	80	75 (1.8%)	164	8.3% [4.8–13.9]
Mana	10,241	2297	80	74 (3.2%)	96	3.8% [1.4–9.4]
Maripasoula	11,856	1955	80	74 (3.8%)	145	3.2% [1.3–7.8]
« Maripasoula center area »	.	.	55	50	77	5.0% [1.8–13.1]
"Twenke-Talhuen" village	.	.	15	14	33	2.2% [0.3–14.1]
« Antecume-Pata « village	.	.	10	10	35	0%
Apatou	8431	1839	50	45 (2.5%)	62	5.2% [1.9–13.4]
Grand Santi	6969	1447	30	28 (1.9%)	61	2.6% [0.6–10.9]
Saint Georges	4020	1208	40	32 (2.7%)	86	4.1% [1.0–15.2]
Papaïchton	7266	1150	40	32 (2.8%)	49	3.0% [0.8–11.0]
Sinnamary	2957	1092	30	30 (2.8%)	39	9.3% [3.2–24.4]
Roura	3713	983	50	39 (4.0%)	70	10.6% [5.1–20.7]
"Roura main area"	.	.	30	26	45	5.8% [1.8–17.4]
"Cacao village"	.	.	20	13	25	18.9% [8.4–37.4]
Montsinnery-Tonnegrande	2473	898	30	29 (3.2%)	66	6.4% [2.6–15.0]
Iracoubo	1878	585	30	29 (5.0%)	53	0%
Regina	946	401	50	43(10.7%)	75	3.5% [1.1–10.1]
"Regina main area"	.	.	40	33	64	4.0% [1.3–11.7]
"Kaw village"	.	.	10	10	11	0%
Camopi	1769	346	50	50 (14.5%)	115	4.0% [1.6–10.1]
"Camopi main area"	.	.	34	34	83	5.7% [2.2–13.9]
"Trois-Sauts village"	.	.	16	16	32	0%
Awala	1379	330	30	28 (8.5%)	60	4.2% [0.9–16.6]
Saint Elie	95	143	20	10 (7.0%)	11	8.6% [1.0–15.2]
Ouanary	165	140	20	5 (3.6%)	13	0%
Saül	150	94	20	18 (19.2%)	34	5.8% [1.3–23.1]
Total	259,865	77,655	1600	1415	2697	9.6% [8.3–11.0]

Table 1: **Description of the household selection process and weighted seroprevalence estimated by municipality and submunicipality after post-stratification adjustment, EPIARBO study, French Guiana.**

- i: one of the 22 strata (municipalities);
- M_i: number of primary sampling units (households) in the ith stratum, i=1, ..., 22;
- S_i: number of primary sampling units (households) selected from the ith stratum, i=1, ..., 22;
- mi: number of primary sampling units (households) actually enrolled from the ith stratum, i = 1, ..., 22;
- P_i: number of individuals living within the ith stratum, i=1, ..., 22 (Census data);
- p_i: number of individuals actually enrolled in the ith stratum, i=1, ..., 22;

We considered, that, in each municipality i, the probability of selecting a particular subject was equal to the probability to select his household and was (m_i/M_i), corresponding to a statistical weight equal to $(1/m_i/M_i) = (M_i/m_i)$. This statistical weight indicates the number of people in the population represented by each subject in the sample.

We applied a post-stratification adjustment to each of these weights to arrive at the final statistical weight for each subject. This adjustment helped us to weight the age-sex groups within each municipality to match the distribution in the French Guiana total population. Ten age-groups ([2–5 years], [5–10], [10–15], [15–20], [20–25], [25–35], [35–45], [45–55], [55–65], ≥65 years) were used within males and females groups and for each age-sex subgroups, we applied an adjustment factor $c_{ijk,}$ to have a final statistical weight $w_{ijk} = (M_i/m_i)*c_{ijk}$, where i indexes municipalities, j indexes sex groups and k indexes age groups.

We constructed a socioeconomic index by combining a multiple correspondence analysis and a hierarchical cluster analysis. The type of housing; housing characteristics, such as the presence of a garden, private swimming pool, refrigerator, air conditioning, internet access, mobile phone, car, and boat; type of health insurance; and household income were included to

determine and characterize the natural classification of individuals regarding socioeconomic levels. A vegetation index was constructed in two steps. First, a normalised difference vegetation index (NDVI) was calculated for 2018 from Sentinel-2 images. Only pixels greater than 0.60 were retained (they correspond to dense vegetation) in this NDVI. Finally, the area of pixels greater than 0.60 was calculated in a buffer zone of 1 km around each individual.

Weighted seroprevalence estimates were estimated for the general population, and associated factors were identified by using survey-weighted Poisson regression. Univariate incidence rate ratios (IRRs) were calculated for selected variables possibly relevant for *C. burnetii* exposure including gender, age, type of housing, degree of urbanisation, birthplace, number of years spent in French Guiana and in the same house, socioeconomic index, type of occupation, presence of garden, trees, keeping a pet, distance to sheep farms, goat farms, cattle farms, pig farms, poultry farms and slaughterhouses, distance to mountains, vegetation index, land use and geographical region. We first looked for factors associated with Q fever using the chi^2 test for frequency comparisons. The strength of the association between Q fever seropositivity and selected variables was estimated by crude and adjusted risk ratios (RRs) with their 95% confidence interval (CI), all RR excluding 1.0 being considered as significant. Variables which reached a significance level of $p < 0.25$ in the univariate analysis were included in a multivariate regression model after checking co-linearity between selected explanatory variables. We also tested for potential interaction effects among the explanatory variables selected in the final multivariate model by creating two product terms for these variables and determined the statistical significance using the Wald test.

The potential explanatory variables identified were then included in a multivariate analysis using a Poisson regression model. We used Stata version 15 software,[31] R version 3.6.1[32] and QGIS software[33] for statistical and spatial data analysis.

Serocatalytic model

Seroprevalence stratified by age provides insight about the history of circulation of a pathogen and the risk factors associated with exposure. To assess the characteristics of Q fever infection in French Guiana, we used serocatalytic models which are common tools to reconstructs the force of infection (FOI, the rate of infection of susceptible individuals) through time.[34] These models allow reconstructing the annual probability of infection from the age profile of seroprevalence in the population. Indeed, the age profile of the presence of an antibody response is a signature of the history of infections, and different modes of circulation of a pathogen will result in differences in the increase of seroprevalence with age. We tested in this study different hypotheses concerning the mode of circulation of the pathogen. The first model we considered represents an endemic circulation, characterized by a constant FOI λ. The risk of infection of an individual is proportional to the time of exposure, and therefore the probability $P_s(a)$ that an individual of age a is seropositive is:

$$P_s(a) = 1 - e^{-\lambda . a}.$$

In a second scenario, we assumed an outbreak model characterised by a peak of the FOI at a given year, and no or few infections in the other years. In the case of a peaked infection, the probability that an individual is seropositive is $P_s(a) = 1 - e^{-\lambda}$ if the individual is old enough to have experienced the outbreak, and 0 otherwise (therefore, if $a \geq T$ *or if* $a < T$, respectively, where T is the number of years between the survey and the outbreak). Third, we assume a combination of a constant circulation and an outbreak. The resulting FOI is the sum of the FOI of the two former models. Technical details are given in the Supplementary Information.

Parameter estimation

Parameters were estimated using a Markov Chain Monte Carlo (MCMC) method. For the different models of circulation considered, the mean and 95% credible intervals (CrI) were estimated. Model comparison was done by estimating for each model the deviance information criterion (DIC), which provides a measure of the deviance of the likelihood in a Bayesian setting. Lower DIC indicate a better fit of the model. Additional details are given in the Supplementary Information.

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Results

Statistical analysis of Q fever seroprevalence

A total of 1415 households and 2697 individuals were enrolled from the 27 recruitment areas (Table 1), representing a household participation rate of 88.4% of participation. Reasons for non-participation were refusal of the adult housing contact to participate in the survey and absence during the survey period. The mean participating household size was 1.9 individuals [range:

1–11]. The raw mean age was 34.1 years, ranging from 2 to 75 years old. Comparison of the sociodemographic characteristics of the study sample with the census data demonstrated an overrepresentation of women (58.9% vs 50.0% in the general population of French Guiana) and adults over 25 years (64% vs 53% in French Guiana). These differences were accounted for in the analyses of vaccination coverage and risk factors by allocating a poststratification weight to each participant.

Based on the ELISA IgG-Phase II test only, 170 samples (6.3%) were positive, 2459 were negative (91.2%) and 68 (2.5%) were borderline. The distribution of ELISA titers is shown in Supplementary Figure S2. Of the 68 ELISA borderline samples, 58 were IFA IgG phase-II positive and 27 were IFA IgG phase-I positive. All IFA Phase I positive samples were also IFA Phase II positive. Combining ELISA and IFA tests, the crude proportion seropositive was 8.4% (228/2697). The overall weighted seroprevalence of Q fever antibodies in French Guiana was 9.6% (95% CI: 8.3–11.0) (Table 1). Serological results in the different geographical areas are shown in Fig. 1. The highest seroprevalence was observed in the region surrounding Cayenne, specifically in the municipalities of Matoury (17.2%) and Rémire (16.8%), where it was twice as high as in Cayenne municipality (9.2%) (Table 1).

We defined three larger regions (Cayenne and its surroundings, the coast, and the interior) with distinct geographical characteristics. We ran a multivariate analysis (Table 2) and found a risk ratio (RR) of Q fever seropositivity of 2.3 (95% CI: 1.5–3.6) in the regions of Cayenne compared to the coastal region.

Male overall seroprevalence was higher than female overall seroprevalence, with 11.0% (95% CI: 8.9–13.5) and 8.1% (95% CI: 6.7–9.9) seropositivity, respectively ($p = 0.04$). Seroprevalence increased according to age from 2.6% in children under 18 years to 11.8% and 14.9% in those aged 18–39 years and 40–64 years, respectively, and then decreased to 11.5% ($p < 10^{-4}$) in subjects aged 65 years and older. The RR of exposure to Q fever increased with proximity to a sheep farm; participants living within 2 km and between 2 and 5 km were more exposed than those living beyond 5 km (Table 2). Proximity with other types of farms was not statistically significant in their association with *C. burnetii*. Being born in Haiti also appeared to double the risk of exposure to *C. burnetii* compared to French Guiana natives ($p < 10^{-4}$), and none of the other birthplaces were significantly associated with seroprevalence level. The level of urbanisation, the socioeconomic index and the presence of a garden were not associated with Q fever seropositivity. There were no statistically significant interaction effects in the multivariate model as all the investigated two-way interaction product terms had p-values greater than 0.05.

Serocatalytic modelling to assess the history of Q fever infections

In the secondary analysis, we assessed transmission dynamics in the different regions using serocatalytic models and estimated the annual force of infection (FOI)—the annual risk for a susceptible individual to be infected—considering the age-stratified seroprevalence. If exposure to the bacterium is constant over time, the risk of becoming seropositive is expected to gradually increase with age. We included the sociodemographic factors found to be significant in the multivariate analysis for individual risk of infection in the serocatalytic model. The model of constant circulation provided a good fit to the serological surveys in the coast (Fig. 2A and B) and interior region (Fig. 2C and D). However, it could not explain the sudden increase in seroprevalence observed in Rémire and Matoury (Fig. 2E and F), particularly among females, whose seroprevalence was close to zero in those under 15 years of age and 19% in those above 15 years of age.

Considering that the multivariate analysis showed a large increase in the risk of infection between children and young adults and a small increase between the age groups 18–40 years and 40–65 years, we hypothesized that seroprevalence profile could be explained by a combination of several modes of transmission; and tested these alternative circulation models. We extended the serocatalytic models and assumed a circulation consisting of a constant annual risk of infection and a specific outbreak that affected the regions of Rémire and Matoury only considering the levels of seroprevalence estimated in theses municipalities (Table 1).

Using the DIC for model comparison, we found that this model was more adequate than the simple constant circulation model (Fig. 2, red curves and Table 3). In particular, the sudden increase in seroprevalence in Rémire and Matoury could be explained by an outbreak that may have happened between 1996 and 2003 and infected 10% (95% Credible Interval (CrI): 6.9%–14%) of the population (Fig. 2E and F). This corresponds to 2.4% (95% CrI: 1.6%–3.2%) of the overall population. No association could be found between the degree of vegetation around living locations and infections. Throughout the Guianese territory, the overall annual number of cases (constant part of the model) was estimated at 579 (95% CrI: 492–670), which corresponds to an incidence of 223/100,000 (95% CrI: 189/100,000–258/100,000).

In this serocatalytic model, we found in agreement with the multivariate analysis that the constant, low-level circulation across French Guiana, particularly affected males (3.0, 95% CrI: 1.7–5.8), Haiti natives (OR: 2.5, 95% CrI: 1.4–4.0) and individuals living close to a sheep farm (OR: 4, 95% CrI: 1.5–12) (Supplementary Table S2). No regional difference was found for the constant risk of infection.

Characteristic	Total tested individuals	Weighted prevalence % [95% CI]	Crude IRR [95% CI]	Pearson p-value	Adjusted IRR [95% CI]
Gender					
Female	1589	8.14 [6.69–9.87]	Ref	0.04	Ref
Male	1108	11.00 [8.94–13.46]	1.35 [1.01–1.80]		1.62 [1.21–2.16]
Age, years					
[2–18]	678	2.57 [1.47–4.47]	Ref	$<10^{-4}$	Ref
[18–40]	992	11.84 [9.48–14.69]	4.60 [2.51–8.41]		3.55 [1.80–7.00]
[40–65]	858	14.91 [12.28–17.99]	5.80 [3.25–10.34]		3.88 [1.83–8.20]
≥65	169	11.48 [6.86–18.58]	4.47 [2.11–9.45]		2.25 [0.86–5.84]
Type of housing					
Building/collective	365	7.56 [4.89–11.51]	Ref	0.11	–
Individual	1768	10.85 [9.24–12.7]	1.43 [0.91–2.27]		
« Carbet »/open living	213	4.33 [1.96–9.28]	0.57 [0.23–1.39]		
Makeshift	89	8.84 [3.88–18.93]	1.17 [0.47–2.90]		
Home urbanization					
Rural	776	7.88 [5.53–11.11]	Ref	0.25	Ref
Intermediate	1326	10.73 [8.95–12.81]	1.36 [0.92–2.02]		0.98 [0.37–1.22]
Urban	333	8.66 [5.94–12.46]	1.10 [0.66–1.83]		0.72 [0.38–1.39]
Birthplace					
French Guiana	1482	7.86 [6.22–9.81]	Ref	$<10^{-4}$	Ref
South America	450	8.79 [5.97–12.77]	1.12 [0.71–1.76]		0.96 [0.58–1.59]
Haiti	223	19.00 [13.75–25.64]	2.42 [1.66–3.53]		1.91 [1.09–3.36]
Caribbean Island	136	9.95 [5.64–16.96]	1.27 [0.69–2.31]		0.81 [0.43–1.53]
Europe	349	9.65 [6.89–13.38]	1.23 [0.82–1.84]		0.91 [0.56–1.48]
Others	49	13.1 [3.97–35.45]	1.67 [0.53–5.25]		1.19 [0.41–3.44]
Years in French Guiana					
≥30	818	15.08 [12.18–18.53]	Ref	$<10^{-4}$	Ref
[10–30]	1133	8.91 [7.08–11.15]	0.59 [0.43–0.80]		0.75 [0.52–1.09]
<10	746	6.58 [5.01–9.06]	0.45 [0.31–0.64]		0.58 [0.33–1.00]
Years in the same house					
<4	738	7.02 [5.30–9.26]	Ref	0.02	–
[4–11]	494	10.75 [7.68–14.83]	1.53 [0.99–2.36]		
≥11	561	12.41 [9.50–12.41]	1.77 [1.20–2.60]		
Socioeconomic index					
Low	233	10.01 [5.43–17.74]	Ref	0.21	Ref
Intermediate	908	7.99 [5.86–10.81]	0.80 [0.41–1.56]		0.67 [0.37–1.22]
Elevated	1291	10.81 [9.07–12.84]	1.08 [0.58–2.01]		0.72 [0.38–1.39]
Occupation					
Farmer	44	4.32 [0.85–19.25]	Ref	0.50	–
Craftsman	64	12.61 [5.53–26.23]	2.91 [0.49–17.24]		
Manager	121	10.85 [5.96–18.93]	2.51 [0.46–13.66]		
Intermediate profession	276	11.81 [8.12–16.89]	2.73 [0.53–14.00]		
Employee	283	9.73 [6.23–14.90]	2.25 [0.43–11.72]		
Worker	114	13.72 [7.74–23.16]	3.17 [0.59–17.13]		
Retired	181	17.30 [11.84–24.59]	4.00 [0.78–20.49]		
Unemployed	930	14.23 [11.53–17.44]	3.29 [0.66–16.42]		
Garden					
No	574	7.11 [5.10–9.83]	Ref	0.02	Ref
Yes	1861	10.83 [9.17–12.74]	1.52 [1.05–2.20]		1.32 [0.90–1.95]
Trees					
No	790	7.62 [5.62–10.25]	Ref	0.03	–
Yes	1645	11.19 [9.46–13.18]	1.47 [1.04–2.07]		
Pet					
No	1080	10.17 [8.23–12.52]	Ref	0.66	–
Yes	1355	9.51 [7.23–11.66]	0.93 [0.69–1.26]		

(Table 2 continues on next page)

Characteristic	Total tested individuals	Weighted prevalence % [95% CI]	Crude IRR [95% CI]	Pearson p-value	Adjusted IRR [95% CI]
(Continued from previous page)					
Distance to sheep farms					
>5 km	795	3.62 [2.32–5.62]	Ref	$<10^{-4}$	Ref
[5 km–2 km]	902	9.87 [7.72–12.55]	2.73 [1.64–4.52]		2.57 [1.03–6.38]
<2 km	1001	10.84 [8.97–13.04]	2.99 [1.85–4.84]		2.10 [0.83–5.28]
Distance to goat farms					
>5 km	839	6.35 [4.29–9.32]	Ref	0.09	Ref
[5 km–2 km]	994	9.91 [8.06–12.13]	1.56 [1.00–2.42]		0.66 [0.32–1.37]
<2 km	865	10.65 [8.41–13.39]	1.67 [1.07–2.63]		0.76 [0.37–1.56]
Distance to cattle farms					
>5 km	1086	8.25 [6.39–10.58]	Ref	0.05	Ref
[5 km–2 km]	659	12.54 [9.77–15.94]	1.52 [1.07–2.16]		1.60 [0.96–2.69]
<2 km	953	9.40 [7.49–11.74]	1.14 [0.81–1.60]		1.22 [0.69–2.15]
Distance to pig farms					
>5 km	1047	7.51 [5.59–10.03]	Ref	0.11	Ref
[5 km–2 km]	860	10.34 [8.15–13.03]	1.38 [0.94–2.00]		1.00 [0.59–1.69]
<2 km	791	10.84 [8.66–13.49]	1.44 [0.99–2.08]		0.86 [0.46–1.59]
Distance to poultry farms					
>5 km	926	6.69 [4.83–9.20]	Ref	0.02	Ref
[5 km–2 km]	650	9.69 [7.13–13.04]	1.45 [0.93–2.25]		0.66 [0.34–1.28]
<2 km	1122	11.44 [9.52–13.7]	1.71 [1.18–2.48]		0.85 [0.39–1.85]
Distance to slaughterhouses					
≥100 km	502	3.42 [1.90–6.09]	Ref	$<10^{-4}$	–
[50 km–100 km]	524	4.56 [2.88–7.13]	1.33 [0.63–2.79]		
[10 km–50 km]	879	7.61 [5.84–9.86]	2.22 [1.17–4.22]		
<10 km	792	14.00 [11.58–16.85]	4.09 [2.22–7.57]		
Distance to mountains					
<5 km	1392	11.10 [9.44–13.01]	Ref	$<10^{-4}$	–
[5 km–20 km]	548	6.27 [4.06–9.56]	0.56 [0.36–0.89]		
[20 km–40 km]	244	2.36 [0.80–6.80]	0.21 [0.07–0.63]		
≥40 km	513	7.07 [11.58–16.85]	0.64 [0.41–0.99]		
Vegetation index					
<20%	484	7.55 [5.42–10.44]	Ref	0.03	Ref
[20%–40%]	587	7.33 [4.99–10.65]	0.97 [0.59–1.60]		1.10 [0.60–2.02]
[40%–60%]	803	11.24 [8.81–14.22]	1.49 [0.99–2.23]		1.31 [0.68–2.51]
≥60%	822	11.98 [9.40–15.15]	1.58 [1.06–2.38]		1.66 [0.86–3.20]
Land use					
Artificial area	1881	9.72 [8.29–11.36]	Ref	0.86	–
Total vegetated area	484	8.82 [5.87–13.04]	0.91 [0.59–1.39]		
Degraded vegetation	329	8.74 [4.98–14.89]	0.90 [0.50–1.60]		
Geographical area					
Other coastal	1217	6.61 [5.10–8.53]	Ref	0.00	Ref
Surroundings of Cayenne	905	12.42 [10.39–14.77]	1.88 [1.38–2.57]		2.35 [1.52–3.61]
Interior	576	3.71 [2.23–6.11]	0.56 [0.32–0.99]		0.69 [0.31–1.56]

Table 2: **Factors associated with Q fever using univariate and multivariate regression model, EPIARBO study, French Guiana.**

Discussion

Q fever is a worldwide zoonosis that is considered hyperendemic in French Guiana. Here, we used a countrywide serologic survey of 1415 households and 2697 participants to provide an overview of the transmission of *C. burnetii* in the general population in French Guiana. We estimated the overall weighted seroprevalence at 9.6% (95% confidence interval (CI): 8.2%–11.0%) and highlighted a constant level of circulation across French Guiana, particularly affecting middle-aged males (odds ratio (OR): 3.0, 95% credible interval (CrI): 1.7–5.8)) and individuals living close to sheep

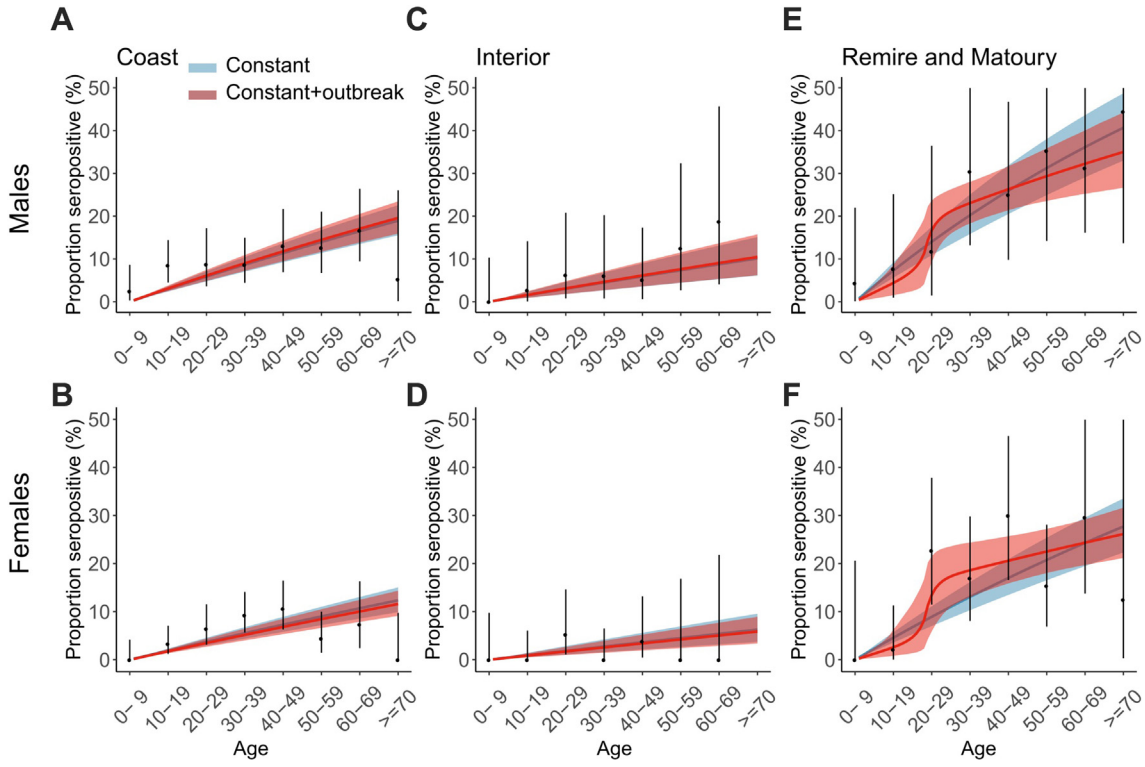

Fig. 2: **Fit of serocatalytic models by age-stratified seroprevalence for males and females in the different regions of French Guiana**. Coast (A, B), Interior (C, D), and Remire and Matoury (E, F). Observations (black) are compared to the fitted seroprevalence (colors) obtained from the model accounting for a risk of constant circulation (blue) and a combination of constant circulation and an outbreak in Rémire (red). Black dots and vertical lines indicate the mean and 95% binomial confidence interval of the seroprevalence. Colored lines and envelopes indicate the means and 95% credible intervals of the fitted seroprevalence.

farms (OR: 4, 95% CrI: 1.5–12). The higher seroprevalence for males could reflect behavioural differences, occupational exposure or a different susceptibility between sex.[35]

Importantly, this is the first time that proximity to livestock was identified as an important risk factor in French Guiana, which is consistent with observations from other parts of the world where most infections have been shown to be transmitted through contaminated aerosols. Previous studies conducted in French Guiana did not indicate a role of livestock in transmission and serological studies conducted among ungulates showed little contamination suggesting that the epidemiology of Q fever was unusual in this territory.[8,18,22] Additionally, we ran sensitivity analysis to assess whether our results were consistent when we varied the threshold distance to a sheep farm for a measure of proximity (Supplementary Table S2) and

Model	DIC	ΔDIC	pD
Baseline model: Constant transmission and outbreak in Rémire. Constant risks: sex, livestock, birthplace	1464	0	7.9
No Outbreak	1472	8	7.1
Age-dependent model	1465	1	6.8
Constant exposure: remove sex	1480	14	6.6
Constant exposure: remove livestock	1471	7	5.9
Constant exposure: remove birthplace	1470	6	6.6
Constant exposure: add environment	1464	0	8.6

The DIC, the difference in DIC with the baseline model and the number of effective parameters (pD) of each model is given.

Table 3: **Comparison of the baseline model with models where one of the predictors is either added or removed from the force of infection.**

found no major difference in the risk of infection for individuals living within 1 km–5 km from a sheep farm.

These results could be related to the fact that the work carried out has always been based on the spatial distribution of confirmed cases which is highly dependent on screening strategies and access to care. In addition, the only studies that have attempted to assess transmission in farms have relied on seroprevalence surveys conducted on a limited number of farms and animals. The use of geo-referenced serological data obtained from a large study allowed us to investigate, with sufficient power, the risk factors associated with the infection by eliminating the biases related to access to diagnosis. Significant regional variations were observed, with the municipalities of Rémire and Matoury having a higher seropositivity than other parts of the country.

The analysis of seroprevalence stratified by age provides insights into the history of the infections by Q fever in French Guiana. By identifying the relevant risk factors, serocatalytic models made it possible to quantify the contribution of different modes of transmission to the observed seroprevalence. We highlighted that the atypical seroprevalence profile in French Guiana was very localised to the municipalities of Rémire and Matoury and could be explained by an outbreak that occurred in the mid to late 1990s. This result is consistent with a previous report that showed an increase in seroprevalence in febrile patients between 1992 and 1996 that was focused on the region surrounding Cayenne.[8,19] This recrudescence was probably favoured by the multiplication of real estate projects in the region of Remire and Matoury that may have led to a significant anthropisation of initially sparsely inhabited areas and consequently an aerosolisation of the bacteria on dust particles. The fast increase in seroprevalence before 20 years old and the plateau in older age groups (Supplementary Figure S3) could also be explained by a model in which younger individuals are more exposed than older individuals (relative annual FOI: 4.2, 95% CrI: 1.5–13.7). However, the occupational hazards frequently reported makes this latter model unlikely.

Moreover, we identified that currently, it was not only this high-seroprevalence region that was at risk, but also that there was an ongoing transmission throughout the French Guiana territory. We evaluated an annual incidence of approximately 223/100,000 inhabitants. This number is extremely high compared to other regions of the world and even to the previously reported incidence based on cases in French Guiana (exact number = 17/100,000). This discrepancy could be due to the large number of asymptomatic *C. burnetii* infections but also to the fact that symptoms are nonspecific. The environment was not found to be a significant risk factor. We cannot exclude that both a wild and domestic cycles coexist in French Guiana since *C. burnetii* was found in wild mammals such as the tree-toed sloth (*Bradypus tridactylus*) or in faecal samples from the capybara (*Hydrochoerus hydrochaeris*)[23,24] but our results indicate for the first time that livestocks play a major role in transmission in French Guiana.[22]

Our study had some limitations inherent to the analysis of the samples, which targeted primarily IgG antibodies against the phase-II antigen of *C. burnetii*, characterizing the antibody response following acute primary infection. The IFA test, considered as the gold standard for diagnosis of *C. burnetii* infections, was used only in case of borderline ELISA results. This approach is often used in seroprevalence surveys[36–39] because of the large resources required to perform IFA tests on a large number of samples and the fact that IgG antibodies to phase II antigens often persist for several years. However, we cannot exclude that some infections, especially those associated with a chronic form, may have escaped detection by the first-line diagnosis and were misclassified as false negatives. Furthermore, the fact that we did not target IgG antibodies against the Phase-I antigen in the first line of testing did not allow us to differentiate between acute and chronic infections on all samples. Due to the high sensitivity and specificity of the test used and the rarity of chronic forms, we believe that this bias, which may have led to an underestimation of seroprevalence rates, was relatively limited. Furthermore, serological cross-reactions have been described between *C. burnetii* and other bacteria such as *Bartonella* spp., *Legionella* spp, and *Chlamydia* spp[40,41] and there may have been an overestimation of seroprevalence estimates in humans due to false positivity. Moreover, as our study was an ancillary study conducted from a survey initially dedicated to arboviruses[25,26,42] (EPIARBO project), the questionnaire did not include information about exposure factors for zoonotic diseases including environmental risk factors related to leisure or work activities, type of animals in the household environment, exposure to animal births and abortions, gardening and/or earth-moving activities favouring dust suspension and inhalation of potentially contaminated aerosols.

Nevertheless, this study improves the understanding of Q fever transmission dynamics in a South American territory, where transmission remains poorly understood until now. Our results highlight the urgent need to implement One Health surveillance activities and serological studies among human and animal populations in the livestocks of French Guiana.

Contributors

NH, SC, SFP and CFl designed and planned the study. CFl and SBi acquired the funding. SBa, NH, AZS, and CFl contributed to the statistical analysis. SBa, CFr and CFl, contributed to data collection. AM, DR, SBi contributed to biological analyses. SBa, NH, AZS, and CFl directly accessed and verified the data. SBa, NH, AZS, SC and CFl wrote the original draft. All authors critically edited the manuscript, had full access to the data reported in the study and had final responsibility to submit for publication.

Data sharing statement

Datasets and analysis code are available from the authors upon request.

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Declaration of interests
The authors declare no competing interest.

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Appendix A. Supplementary data
Supplementary data related to this article can be found at https://doi.org/10.1016/j.lana.2022.100385.

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