Systematic review and modelling of *Toxoplasma gondii* seroprevalence in humans, Europe, 2000 to 2021

Ingrid HM Friesema[1,*], Helga Waap[1,18,*], Arno Swart[1], Adriana Györke[2], Delphine Le Roux[3], Francisco MD Evangelista[4,17], Furio Spano[5], Gereon Schares[6], Gunita Deksne[7], Maria João Gargaté[8], Rafael Calero-Bernal[9], Pikka Jokelainen[10], Frank Seeber[11], Jacek Sroka[12], Anna Lundén[13], Oda van den Berg[1], Solveig Jore[14], Henk J Wisselink[15], Filip Dámek[3], Lasse S Vestergaard[16], Marieke Opsteegh[1]

1. Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, The Netherlands
2. Department of Parasitology and Parasitic Diseases, Faculty of Veterinary Medicine, University of Agricultural Sciences and Veterinary Medicine Cluj-Napoca, Cluj-Napoca, Romania
3. Anses, INRAE, Ecole Nationale Vétérinaire d'Alfort, Laboratoire de Santé Animale, BIPAR, Maisons-Alfort, France
4. Department of Comparative Biomedical Sciences, School of Veterinary Medicine, Faculty of Health and Medical Sciences, University of Surrey, Guildford, United Kingdom
5. Unit of Foodborne and Neglected Parasitic Diseases, Department of Infectious Diseases, Istituto Superiore di Sanità, Rome, Italy
6. Institute of Epidemiology, Friedrich-Loeffler-Institut, Federal Research Institute for Animal Health, Greifswald, Germany
7. Institute of Food Safety, Animal Health and Environment "BIOR", Riga, Latvia; Faculty of Medicine and Life Sciences, University of Latvia, Riga, Latvia
8. Department of Infectious Diseases, National Institute of Health Dr. Ricardo Jorge (INSA), Lisbon, Portugal
9. SALUVET, Animal Health Department, Faculty of Veterinary Sciences, Complutense University of Madrid, Madrid, Spain
10. Infectious Disease Preparedness and One Health, Statens Serum Institut, Copenhagen, Denmark
11. FG 16: Mycotic and parasitic agents and mycobacteria, Robert Koch-Institute, Berlin, Germany
12. Department of Parasitology and Invasive Diseases, Bee Diseases and Aquatic Animal Diseases, National Veterinary Research Institute, Pulawy, Poland
13. Department of Microbiology, Swedish Veterinary Agency, Uppsala, Sweden
14. Zoonotic and Waterborne infections, Norwegian Institute for Public Health (NIPH), Oslo, Norway
15. Wageningen Bioveterinary Research, Wageningen University and Research, Lelystad, the Netherlands
16. Department of Infectious Disease Epidemiology and Prevention, and Department of Bacteriology, Parasitology and Mycology, Statens Serum Institut, Copenhagen, Denmark
17. Egas Moniz Center for Interdisciplinary Research (CiiEM), Egas Moniz School of Health & Science, Caparica, Portugal
18. Laboratório de Parasitologia, Instituto Nacional de Investigação Agrária e Veterinária, Oeiras, Portugal
* These authors contributed equally to the work and share first authorship.

Correspondence: Ingrid Friesema (ingrid.friesema@rivm.nl)

Background: *Toxoplasma gondii* is a zoonotic protozoan capable of infecting warm-blooded animal species and humans. Although toxoplasmosis presents mostly as mild or asymptomatic infection in immunocompetent individuals, in unborn children and people with weakened immune systems, the disease can be severe with ocular, neurological or multi-systemic manifestations and even death. **Aim:** We aimed to collate and analyse data on *T. gondii* seroprevalence in humans to model and compare age-dependent prevalence in geographic regions in Europe. **Methods:** A systematic review identified 1,822 scientific publications, from which seroprevalence data were extracted from 69 studies. Data were analysed using a Bayesian hierarchical model. **Results:** The modelling of the seroprevalence indicated the highest incidence rates in eastern (50%) and western (48%) Europe, with the lowest estimates in northern Europe (18%) and the United Kingdom (UK) (18%). Eastern and western Europe were regions where *T. gondii* infections occurred earliest in life, with half of the population expected to be seropositive by the age of 44 and 47 years, respectively. In contrast, in northern Europe and the UK the modelled median time to infection exceeded 170 years. **Conclusion:** Results of the study provide a robust baseline for future epidemiological research on human *T. gondii* infections in Europe and may be useful to validate subsequent research, such as risk assessment studies.

Introduction

Toxoplasma gondii, a protozoan parasite with a worldwide distribution, is capable of infecting humans and potentially all warm-blooded vertebrates [1]. Felids serve as the definitive hosts for *T. gondii* [2]. When ingested, the parasite replicates in the felid's intestine, followed by shedding of the oocysts via faeces into the environment. The oocysts can sporulate and survive for long periods in the environment [3]. Ingestion of sporulated *T. gondii* oocysts present in contaminated water, soil or fresh produce can lead to formation of tissue cysts in all susceptible hosts, including humans

[4]. The bradyzoites in these tissue cysts are infective, allowing transmission through the consumption of undercooked or raw meat from infected hosts [5,6]. Humans can become infected both via the environmental route and via consumption of undercooked or raw meat of infected animals. Another route is transplacental transmission to a fetus, causing congenital infection potentially resulting in abortion or stillbirth [7]. Moreover, *T. gondii* can be transmitted via blood transfusions or organ transplants [5,8].

Acquired *T. gondii* infections in humans are generally asymptomatic or cause non-specific and self-limiting symptoms, but they can also present as ocular toxoplasmosis. Severe acute toxoplasmosis, although rare, may manifest as myocarditis, polymyositis, pneumonitis, retinitis, hepatitis or encephalitis, and mainly occurs in people with severely weakened immune systems [5]. Prevalence of *T. gondii* infection is influenced by factors such as climate, cultural habits such as consumption of raw meat, hygiene practices and socioeconomic conditions [9].

Serological testing for *T. gondii* infection in humans is performed for several reasons. In some countries, screening is conducted during pregnancy to monitor seroconversion and guide treatment. Testing also helps to assess population seroprevalence and aids in diagnosing clinical toxoplasmosis. Both, infection with *T. gondii* and the presence of detectable antibodies, are assumed to persist lifelong, with the prevalence of anti-*T. gondii* IgG in humans increasing with age [9].

The aim of this work was to collate available published data on human *T. gondii* seroprevalence to model and compare the age-dependent prevalence of the infection in Europe.

Methods

Literature screening and study selection
A structured literature search was carried out according to the PRISMA guidelines [10], using Emtree terms within the Embase literature database. The search string can be found in Supplementary Table S1. The search terms were chosen to cover human seroprevalence and risk factors of infections with *T. gondii* in Europe. For the study area, 41 countries in Europe were considered, including the 27 European Union (EU) countries. The list of the countries included is presented in Supplementary Table S2. The publication period of interest was set from January 2000 to May 2021. The search strategy had no limitations on publication language. The search was conducted in May 2021.

A group of 17 scientists with expertise in *T. gondii* and toxoplasmosis from 12 countries across Europe assessed the eligibility of the publications identified. The screening of the publications was performed within Cadima [11], an open-access online software tool for conducting systematic reviews. The systematic review

was done in two stages based on a set of predefined criteria: an article was eligible if (i) it reported a study based on original data; (ii) the study was on human seroprevalence and/or risk factors for *T. gondii* infection in the included European countries, with at least part of the data collected from the year 2000 onwards; and (iii) had been published in a peer-reviewed journal. Reviews, meta-analyses and other articles not reporting original data were excluded, as were studies investigating the prevalence of *T. gondii* in particular risk groups and studies investigating *T. gondii* infection as a risk factor for another condition. First, the title and abstract were screened by two randomly chosen scientists from the group, after which consensus on inclusion had to be reached in case of initial disagreement. All inconsistencies were solved between the two scientists without the need of a third person. Second, full text of the remaining publication was screened and again consensus on inclusion was reached. The same criteria were used in both screening steps.

The next step involved extracting relevant data from the selected articles. Per article, data were extracted by one scientist and then checked by another. Thirteen scientists from the previous group were involved in this process, and four additional scientists helped extracting data from articles in different languages. The data were gathered in a template file created in Microsoft Excel. For each study, data on study design, period, population, serological tests used, and results were registered. Extracted data on seroprevalence were harmonised and categorised for modelling. For this, countries were assigned to one of five European regions (western, northern, eastern, southeastern, southwestern), as described previously [12,13].

Data analysis
Some publications presented more than one set of results on seroprevalence for the same population (e.g. results for the total study population, as well as for various subcategories based on, for example, age, sex and/or region), resulting in several rows of data for those populations. In those cases, the subpopulations were weighted by their probability to ensure that they contributed proportionally to the actual number of participants in the study. The meta-analysis was done using the data with specification on age, as reported in the publications. Since the exact ages of individual participants at the time of sampling were not provided, we defined an uncertainty distribution based on the estimates of the minimum, maximum and most probable age at sampling. If a median or mean age was given per age range, this was used as most probable age; otherwise, the median age was calculated from the minimum and maximum age of the age range. Data from studies that did not specify age of the participants or only reported data for all ages combined were excluded from data analysis.

A Bayesian hierarchical model built for estimating the age-dependent seroprevalence of *T. gondii* in animal

species [13] was adapted to the human data collected in the present review. This model consists of an age-dependent Susceptible-Infected-Susceptible (SIS) framework, where individuals move from susceptible (i.e. seronegative) to infected (i.e. seropositive), with the possibility of reversion to susceptible (i.e. loss of detectable antibody response). Individuals were considered born susceptible, and hence able to move into the infected compartment based on a constant force of infection (λ, incidence rate, i.e. the rate at which individuals acquire infection measured in new infections per year) and with the reversion to seronegative at rate γ.

The Bayesian hierarchical model was built to be able to estimate the parameters through partial pooling, granting the possibility to overcome data gaps. Variables used in the model are shown in Table 1.

In the process of model fitting by means of Bayesian inference, the age distribution for each population was updated, i.e. a posterior age distribution was obtained. Differences between regions were considered using a hierarchical model and modelled as linear contributions to the logarithmic baseline force of infection (λ). No regional differences were considered for the reversion rate (γ). Model fitting was performed using Stan (https://mc-stan.org) (interfaced with R version 4.1.3 (https://www.r-project.org/). Trace plots of the Markov chains were visually assessed to confirm the convergence of the model.

Results

Data collection

A total of 1,822 publications were identified, of which 12 were removed as duplicates. After screening titles and abstracts, 367 articles were selected for full-text screening, of which 142 articles met the inclusion criteria. During data extraction, a further 67 articles were excluded because of missing or incomplete information. Of the remaining 75 publications, 69 provided seroprevalence data [14-83] and 22 contained data
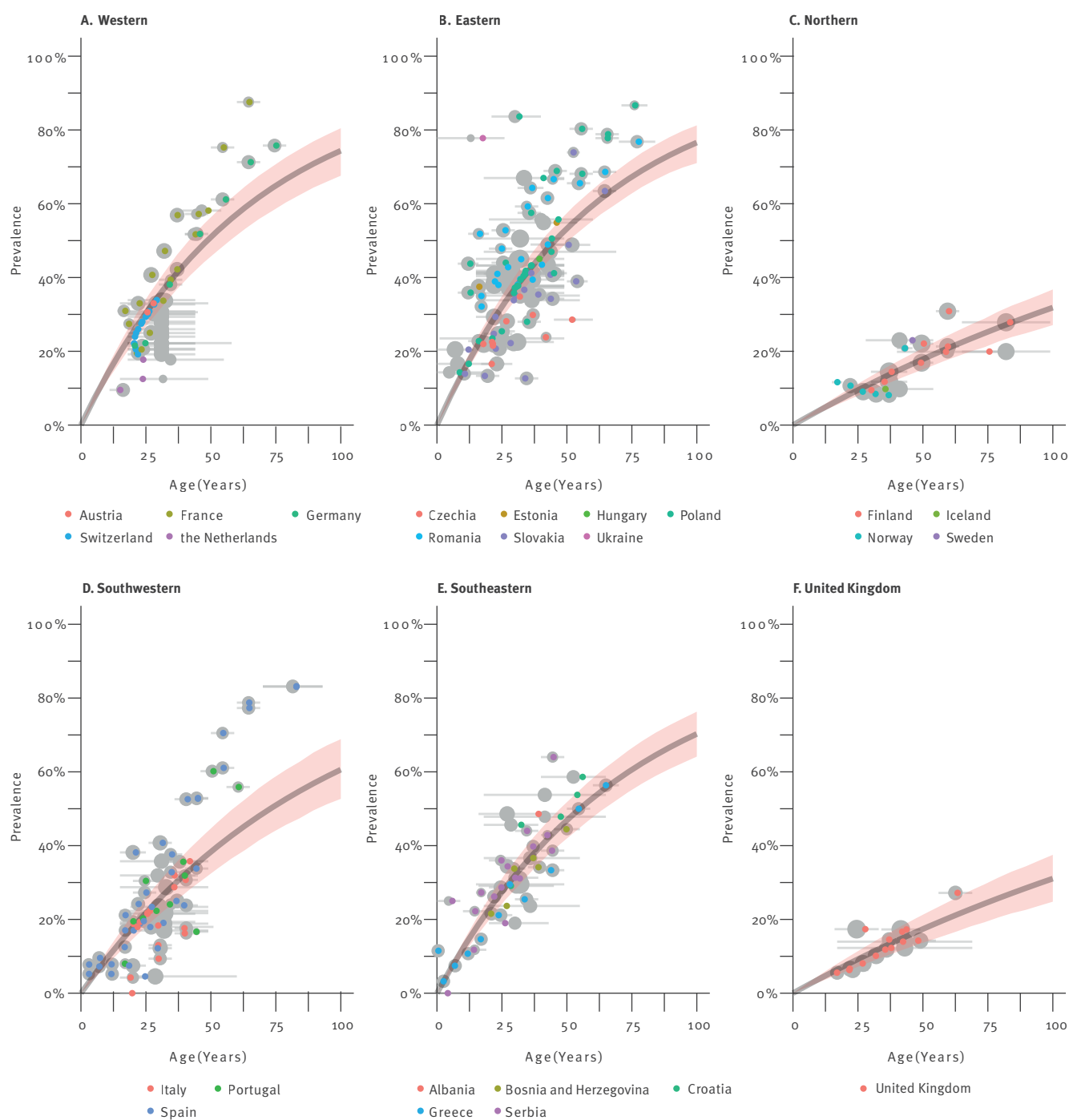
TABLE 1

Data used in the Bayesian hierarchical model of *Toxoplasma gondii* seroprevalence in humans, Europe, 2000–2021

Variable[a]	Values
region[i]	Eastern, Northern, Southeastern, Southwestern, Western Europe
pop[i]	A unique identifier for a population
ntot[i]	Total number of participants tested
npos[i]	Total number of participants test positive
agemin[i]	Lower bound of the age range
agemax[i]	Upper bound of the age range
agemean[i]	The most probable age at sampling

[a] Variables as included in the model with corresponding values and the index [i] corresponding to the i-th data point.

on risk factors. A PRISMA flow diagram is presented in Supplementary Figure S1, and a list of the 22 references is also included in the Supplementary Material. The further analyses focused solely on seroprevalence. Relevant seroprevalence data could be recovered from 25 of the 41 countries considered in the search strategy.

Regional seroprevalence of *Toxoplasma gondii* in Europe

The average *T. gondii* seroprevalence per region and by age derived from the model is presented in Figure 1 and Table 2. The United Kingdom (UK) was initially a country included in the western region. However, the analysis per region and age showed a deviant seroprevalence for the UK compared with the other countries included in our categorisation of western Europe. Therefore, the UK was analysed separately. The highest prevalence estimates were seen in eastern (50%), western (48%), southeastern (45%) and southwestern (38%) Europe. The seroprevalence was markedly lower in northern Europe (18%) and the UK (18%). Thus, while the seroprevalence increased with age from 13% to 16% in those aged ≤ 25 years to above 50% in those aged › 50 years in most regions, it increased from 4% to 26–27% in northern Europe and the UK.

In addition to regional seroprevalence estimates, the model also provides estimates for the force of infection and the rate of reversion to seronegative status (Figure 2). For the force of infection, the inverse of the posterior coefficient represents the average waiting time in years until the event. For *T. gondii* infection, this results in an average waiting time of 1/0.009 ca 137 years (Figure 2), with a median waiting time of 95 years (Table 2). The lowest force of infection in Europe was observed in the UK ($\exp(\lambda_{region}) = 0.445$) and the northern region ($\exp(\lambda_{region}) = 0.459$), followed by the southwestern ($\exp(\lambda_{region}) = 1.13$) and the southeastern region ($\exp(\lambda_{region}) = 1.48$). Highest forces of infection were seen for the western ($\exp(\lambda_{region}) = 1.67$) and the eastern region ($\exp(\lambda_{region}) = 1.79$).

To reconstruct the total force of infection per year for each region, the baseline force of infection was multiplied by the region-specific exponentiated contributions. For example, in the eastern region, the average time until infection was estimated to be ca 64 years (1/(0.009 × 1.79)), with 50% of the population becoming infected by age 44 years (the 50% quantile of the exponential distribution with parameter 0.009 × 1.79). In contrast, the average time until infection in the northern region and the UK exceeded 250 years, and the time 50% of the population becoming infected exceeding 170 years (Table 2). Despite this long average, 10% of the population would be infected at the age of 26 years, reflecting the skewed distribution of the infection age distribution.

The reversion rate was estimated at $\gamma = 9.0 \times 10^{-4}$ (3.0×10^{-4}, 3.5×10^{-3}), which sets an average waiting time of › 1,000 years. However, at the upper end

FIGURE 1

Susceptible-Infected-Susceptible (SIS) model fit for age-dependent seroprevalence of *Toxoplasma gondii* in humans, Europe, 2000–2021

In total, 69 studies with data from 25 countries were included in the model. The line indicates the fitted seroprevalence by age, with the orange area being the 95% confidence interval. The grey dots represent seroprevalence data points at the best estimate of age in the data for the studied populations. The size of the dots reflects the number of persons tested. The dots are shifted horizontally along the grey lines extending from the minimum to the maximum possible age, to the best fitting age (coloured dots).

TABLE 2

Modelled average seroprevalence estimates of *Toxoplasma gondii* in humans, by age group and age at infection, Europe, 2000–2021

| Regionª	Seroprevalence (%), by age group			Age at infection (years)			
	0–25 years	26–50 years	› 50 years	Mean	10% quantile	Median	90% quantile
Eastern	16	43	68	63.96	6.74	44.34	147.28
Northern	4	14	27	249.95	26.33	173.25	575.53
Southeastern	13	38	62	77.19	8.13	53.51	177.75
Southwestern	10	30	52	101.66	10.71	70.46	234.08
UK	4	13	26	259.07	27.30	179.58	596.54
Western	15	41	66	68.46	7.21	47.45	157.63
Overall	NA			136.72	14.40	94.76	314.80

NA: not applicable; UK: United Kingdom.

ª Eastern: Belarus, Czechia, Estonia, Hungary, Latvia, Lithuania, Poland, Romania, Slovakia, Ukraine; Northern: Denmark, Finland, Iceland, Norway, Sweden; Western: Austria, France, Germany, Ireland, Liechtenstein, Luxembourg, the Netherlands, Switzerland; Southeastern: Albania, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Greece, Kosovo, Moldova, North Macedonia, Serbia, Slovenia; Southwestern: Andorra, Italy, Malta, Portugal, San Marino, Spain.

A total of 69 studies were included in the analysis (two studies with results for more than one region): eastern (26 studies, 7 countries), northern (4 studies, 4 countries), southeastern (9 studies, 5 countries), southwestern (18 studies, 3 countries), western (11 studies, 5 countries), UK (3 studies).

FIGURE 2

Bayesian hierarchical model outcomes (i.e. posterior probabilities) for the force of infection (λ) and reversion rate (γ) to seronegative status of *Toxoplasma gondii* in humans, Europe, 2000–2021
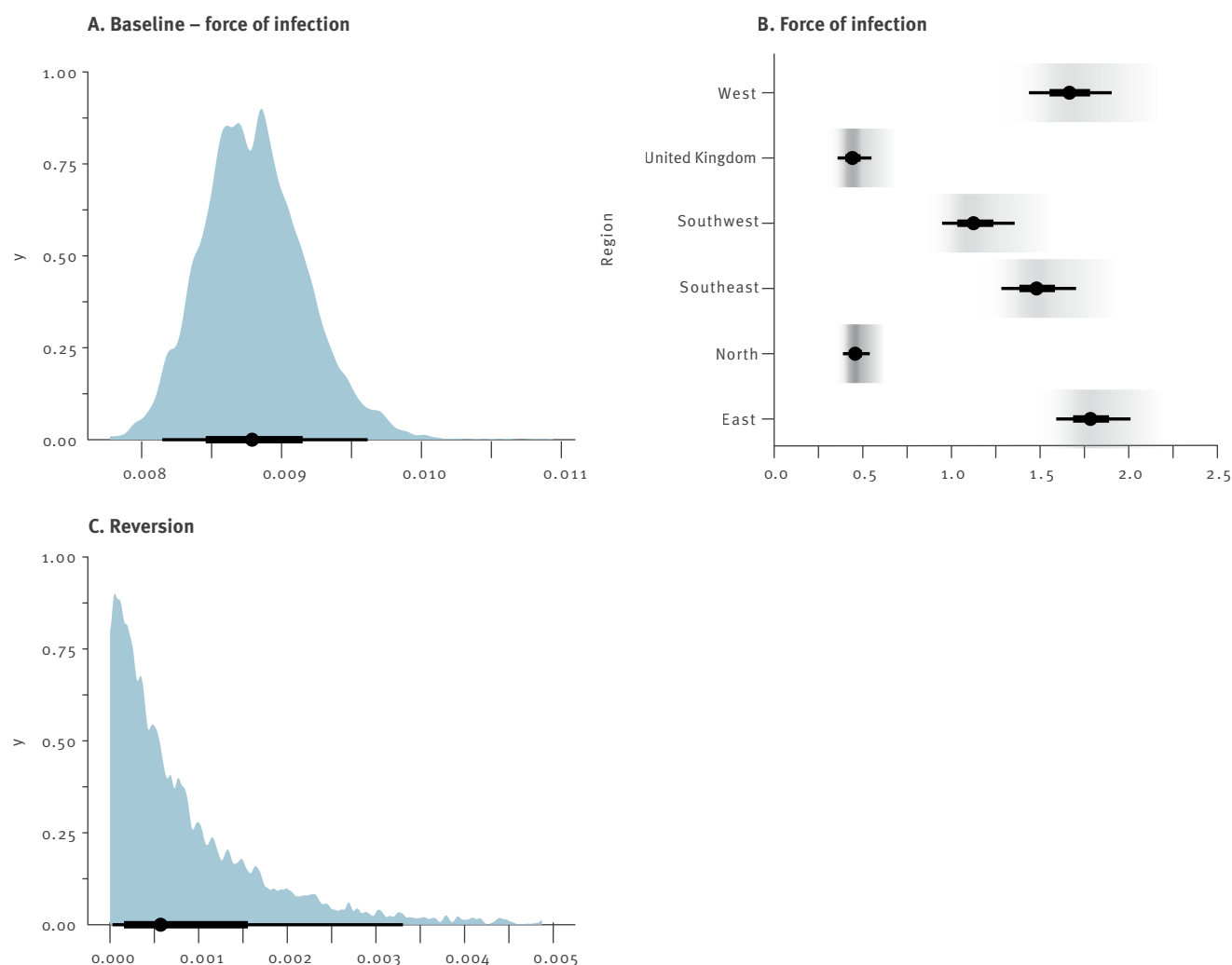
Values for the force of infection in the regions are all exponentiated, which means that a value of 1 indicates the absence of an effect on the baseline probability. Grey area represents the uncertainty distribution, the thin and thick black lines indicate the 95% and 50% Bayesian credible intervals, respectively, with dots indicating the mean of exponentiated forces of infection per region. In total, 69 studies with data from 25 countries were included in the model.

of the credible interval this average waiting time was 275 years, with 10% of the population reverted at 29 years and 20% at 60 years. Hence, considerable reversion is realistic within the credible interval.

Discussion

The aim of this study was to model the age-dependent prevalence of *T. gondii* in the human population in Europe. To achieve this, a systematic review of seroprevalence studies in humans published in 2000–2021 was conducted. Data were extracted from 69 papers selected from 1,822 publications identified by the search strategy and, where possible, analysed using a Bayesian hierarchical model. Compared with conventional analytical techniques, Bayesian methods may perform better in meta-analyses, particularly by dealing better with uncertainty [84]. This is especially important when analysing population-based studies, where heterogeneity may arise from factors such as study design, geographic region, serological test used or missing data.

Human *T. gondii* seroprevalence data were obtained for 25 of the 41 countries included in the search. A similar geographic coverage of European *T. gondii* seroprevalence studies was achieved in a previous systematic review [85], indicating geographic gaps in available data. Meta-analysis was performed on a regional scale, by aggregating countries into five geographic areas. Albeit at the cost of loss of detail, grouping the data allowed for a broader geographic coverage, making it easier to identify regional differences and establish regional correlations. By using partial pooling of prevalence distributions from regions with a larger amount of data, the Bayesian hierarchical model allowed to provide seroprevalence estimates for regions lacking data, though with a larger uncertainty. Furthermore, age information given in the studies was notoriously incomplete, with differing age ranges used to categorise data, missing age data or use of categories that only gave an indication of age (e.g. children or pregnant women). The Bayesian hierarchical model helped to address these gaps by incorporating uncertainty on this variable, which made it possible to derive posterior predictive distributions for the age-dependent seroprevalence in each region in Europe. Modelling the prevalence of *T. gondii* by age provides a better understanding of infection dynamics, from birth to any given age, and holds the potential for developing age-specific prevention strategies. Thus far, most systematic review and meta-analysis studies have focused primarily on identifying sources of infection in outbreaks [86] and sporadic toxoplasmosis [3] or assessing prevalence in specific risk groups [87,88]. To our knowledge, one other study has reviewed seroprevalence data for the European general population [85], but age was not considered in the subgroup analysis in that study.

When estimating the age-dependent seroprevalence of *T. gondii*, we used the SIS model which includes the possibility that individuals can return to the susceptible state (some time) after infection. This approach was used before to model the age-dependent prevalence of *T. gondii* in animals [13]. In that study, the plateau in seroprevalence observed in animals at higher age was better explained by the SIS model, than the SI (Susceptible-Infected) model (where 100% of susceptible individuals would become infected if living long enough). Although hardly reported in literature, evidence of seroreversion in humans was, for example, reported in a cohort of blood donors followed over 4 years [23]. Nevertheless, the reversion rate estimated in the present study was negligible, supporting the hypothesis of lifelong persistence of anti-*T. gondii* antibodies in humans [89].

Results from this study revealed considerable differences in seroprevalence between geographic regions across Europe. The estimates for *T. gondii* seroprevalence were highest in eastern, western, and southeastern Europe, with a mean seroprevalence of 45–50%, followed by the southwestern region (38%), and were lowest in the UK and northern Europe where the model predicted a mean infection rate of 18%. Based on our results, seroprevalence in the age group 25–50 years varied between 13% and 43% in Europe. Worldwide, highest seroprevalence in pregnant women has been observed in South America (53–56%), mostly based on Brazil, and Africa (47–49%); the seroprevalence in Europe in this group was 25–31%, whereas the seroprevalence in North America was 20–28% [87,90,91]. Importantly, measured seroprevalences between countries within a continent can vary largely, as they can even within countries [92]. In line with the assumption of lifelong infection, the seroprevalence increased between the three age groups, with as few as 4% of individuals seropositive in the youngest age group in the UK and northern Europe and a several-fold increase up to 68% by the age of › 50 years in eastern Europe. Measuring the force of infection, i.e. the rate at which individuals acquire infection, is a key to understanding the epidemiology of infectious diseases and estimating disease burden. Estimates for this parameter clearly showed that individuals in eastern and western Europe became infected at a younger age, compared with the other regions. Translated into time until infection, this means that on average half of the population in eastern and western Europe was expected to be infected by the age of 47 years, while in northern Europe and the UK this was expected at an unreachable age of 173 and 179 years, respectively. Noteworthily, the strong force of infection estimated for western Europe is in agreement with the results from a recent large-scale *T. gondii* serosurvey in female children and adolescents in Germany, showing that with each year of life the chance of becoming seropositive increased by 1.2 [93].

Comparing *T. gondii* prevalence and force of infection in humans and animals in the same geographic area may provide One Health insights into potential sources. Interestingly, results obtained for humans in the present study parallel the force of infection trends among

geographic regions disclosed in the previous review of the animal prevalence in Europe [13], except for western Europe, where the force of infection ranked second highest in humans but was lowest in animals. Although results from the two studies do not provide direct evidence of specific sources of human infection, a high prevalence in herbivorous animals that have outdoor access or are raised as free-range (e.g. sheep, wild ruminants) suggests that environmental contamination of T. gondii is a contributing factor [94,95]. While there is a possible association between high prevalence in animals with outdoor access and increased risk of human exposure from the environment, this does not necessarily translate into a higher seroprevalence in humans, as direct environmental exposure is not the only possible route of infection to humans.

To understand seroprevalence differences between countries or regions, more data are needed on the cultural differences in behaviours that can influence the risk of T. gondii infection. Seroprevalence in humans is likely influenced by consumption habits and consumed products, including imported products from other countries. For example, the frequency, amount, preparation and types of meat or meat products consumed, and especially local preferences for specific products made of raw or undercooked meat are important. Previously, two quantitative microbiological risk assessment (QMRA) models suggested that filet américain, a typical Dutch raw beef spread, was the most important source of T. gondii infection in the Netherlands [96,97]. Similarly, Hackepeter or Mett, a German dish made of raw minced pork meat, is more popular and consumed more frequently in eastern Germany compared with western Germany. This dietary preference was linked to a higher T. gondii seroprevalence in the human adult population in eastern Germany [81]. Moreover, exposure to oocysts can vary locally due to differences in soil exposure, frequency of consumption of raw vegetables, fruits and shellfish, or drinking water treatment [89].

Yet, studies assessing the relative contribution of the various sources of infection in Europe are scarce. Underlining the varying importance of animals raised for human consumption in the transmission of T. gondii, a previous multicentre case-control study attributed 30–63% of infections to the consumption of undercooked or cured meat products and 6–17% to soil contact [98]. Also, several studies identifying significant foodborne risk factors have found a link between the consumption of livestock-derived foods, such as raw or undercooked meat [17,21,34,37,40,50,77,99], types of processed meat [43,77], unpasteurised milk and raw milk cheese [17,34], and T. gondii infection. With regards to oocyst-driven infections, eating raw or unwashed vegetables or fruits [17,43], contact with cats [17,37,40,50,55,77,81] and contact with soil [21,43,66,74,77] were reported as risk factors. However, for a risk factor to be an important source of infection at a population level, exposure to the factor

also needs to be common. Exposure behaviour can vary between and within populations, and these data are often lacking. The recent implementation of a harmonised European survey tailored to capture variation in the frequency and amount of meat and vegetable products of known risk consumed, as well as consumers' behaviour associated with an increased risk of infection (e.g. preference for raw or undercooked meat, washing of vegetables) will bring new data for T. gondii food-borne risk assessment (https://onehealthejp.eu/projects/foodborne-zoonoses/jrp-toxosources).

In this study, only region and age were included in the model. Any differences related to sex will therefore be missed. Nevertheless, in most studies reporting results on sex, differences between sexes were not observed [15,17,70,100], except for one study where males were more often seropositive [81]. Other study limitations were mainly related to the absence of seroprevalence data for some European countries, the small scale of some studies and incomplete or inconsistent data reporting. Also, policies towards screening for T. gondii infections differ between countries. Although the Bayesian model could address uncertainty in both prevalence and age data, the lack of diagnostic performance characteristics of in-house serological tests and commercial kits used in the selected studies made it impossible to estimate 'true prevalence' [101]. To fill this gap, data on test sensitivity and specificity could potentially be sourced from validation studies by the manufacturer or diagnostic accuracy studies. However, previous attempts to retrieve this information from the literature have shown inconsistent results due to a variety of factors, including the characteristics of the sample population (e.g. immune status, time since infection, potentially cross-reacting pathogens or rheumatic factors), study design, quality of the reference standard used, or different cutoffs employed [102,103]. Thus, even when data on test characteristics are available, it is important to keep in mind that such data may not be constant over populations and that the reproducibility of serological test results is not warranted [102,104,105].

For future work to overcome the hurdles associated with data heterogeneity in serological studies, we emphasise the importance of the primary data source when publishing original research. A main challenge is assuring that raw data are reported in a way that allows their accessibility and their further reuse in reviews and meta-analyses [106]. A solution to this challenge is the development and adoption of standardised templates that enable harmonised reporting of data. Ideally, results from serological surveys should be provided on an individual basis, when possible, and include demographic information on age and sex, together with test performance characteristics, cutoffs, as well as titres or OD values. Additional details are desirable, e.g. the ELISA plate identification or analysis date, which allows for plate-to-plate correction when using binary mixture models [107]. A spreadsheet for

epidemiological data reporting that could function as such a template was previously proposed [13]. These data templates could be used, for example, in the online supplementary files of research papers or made available in public repositories.

Conclusion

Knowing the prevalence of infection is key information in assessing disease burden and estimating costs of illness and prevention efforts in a population. The results of this review revealed a considerably higher seroprevalence in eastern and western Europe, compared with northern Europe and the UK, and that *T. gondii* infection is occurring at an earlier age in these regions. The commonly held belief that the infection is lifelong is corroborated by our results, as the current best estimate of the reversion rate equates to infection durations that far exceed a human lifespan. However, the uncertainty in the estimate is large, and reversion rates that correspond to infection durations of decades are within the 95% credible interval. Prevalence distributions derived by the model contribute to a better understanding of disease burden caused by *T. gondii* and provide a baseline for future epidemiological research in the different European regions.

Authors' contributions

Ingrid HM Friesema: Conceptualisation, Data curation, Formal analysis, Methodology, Validation, Supervision, Writing – original draft, Writing – review & editing. Helga Waap: Writing – original draft, Writing – review & editing. Arno Swart: Formal analysis, Methodology, Validation, Writing – original draft, Writing – review & editing. Adriana Györke: Data curation, Formal analysis, Methodology, Writing – review & editing. Delphine Le Roux: Data curation, Formal analysis, Methodology, Writing – review & editing. Francisco Evangelista: Data curation, Formal analysis, Methodology, Writing – review & editing. Furio Spano: Data curation, Formal analysis, Methodology, Writing – review & editing. Gereon Schares: Data curation, Formal analysis, Methodology, Writing – review & editing. Gunita Deksne: Data curation, Formal analysis, Methodology, Writing – review & editing. Maria João Gargaté: Data curation, Formal analysis, Methodology, Writing – review & editing. Rafael Calero-Bernal: Data curation, Formal analysis, Methodology, Writing – review & editing. Pikka Jokelainen: Data curation, Formal analysis, Methodology, Supervision, Writing – review & editing. Frank Seeber: Data curation, Formal analysis, Methodology, Writing – review & editing. Jacek Sroka: Data curation, Formal analysis, Methodology, Writing – review & editing. Anna Lundén: Data curation, Formal analysis, Methodology, Writing – review & editing. Oda van den Berg: Data curation, Formal analysis, Methodology, Writing – review & editing. Solveig Jore: Data curation, Formal analysis, Methodology, Writing – review & editing. Henk J Wisselink: Data curation, Formal analysis, Methodology, Writing – review & editing. Filip Dámek: Data curation, Formal analysis, Methodology, Writing – review & editing. Lasse S Vestergaard: Data curation, Formal analysis, Methodology, Writing – review & editing. Marieke Opsteegh: Conceptualisation, Data curation, Formal analysis, Methodology, Validation, Supervision, Writing – original draft, Writing – review & editing.

References

1. Dubey JP. The history of Toxoplasma gondii--the first 100 years. J Eukaryot Microbiol. 2008;55(6):467-75. https://doi.org/10.1111/j.1550-7408.2008.00345.x PMID: 19120791

2. Dubey JP. History of the discovery of the life cycle of Toxoplasma gondii. Int J Parasitol. 2009;39(8):877-82. https://doi.org/10.1016/j.ijpara.2009.01.005 PMID: 19630138

3. Thebault A, Kooh P, Cadavez V, Gonzales-Barron U, Villena I. Risk factors for sporadic toxoplasmosis: a systematic review and meta-analysis. Microb Risk Anal. 2021;17:100133. https://doi.org/10.1016/j.mran.2020.100133

4. López Ureña NM, Chaudhry U, Calero Bernal R, Cano Alsua S, Messina D, Evangelista F, et al. Contamination of soil, water, fresh produce, and bivalve mollusks with Toxoplasma gondii oocysts: a systematic review. Microorganisms. 2022;10(3):517. https://doi.org/10.3390/microorganisms10030517 PMID: 35336093

5. Montoya JG, Liesenfeld O. Toxoplasmosis. Lancet. 2004;363(9425):1965-76. https://doi.org/10.1016/S0140-6736(04)16412-X PMID: 15194258

6. Sullivan WJ Jr, Jeffers V. Mechanisms of Toxoplasma gondii persistence and latency. FEMS Microbiol Rev. 2012;36(3):717-33. https://doi.org/10.1111/j.1574-6976.2011.00305.x PMID: 22091606

7. McAuley JB. Congenital Toxoplasmosis. J Pediatric Infect Dis Soc. 2014;3(Suppl 1) Suppl 1;S30-5. https://doi.org/10.1093/jpids/piu077 PMID: 25232475

8. Hill D, Dubey JP. Toxoplasma gondii: transmission, diagnosis and prevention. Clin Microbiol Infect. 2002;8(10):634-40. https://doi.org/10.1046/j.1469-0691.2002.00485.x PMID: 12390281

9. de Barros RAM, Torrecilhas AC, Marciano MAM, Mazuz ML, Pereira-Chioccola VL, Fux B. Toxoplasmosis in human and

animals around the world. Diagnosis and perspectives in the One Health approach. Acta Trop. 2022;231:106432. https://doi.org/10.1016/j.actatropica.2022.106432 PMID: 35390311

10. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372(71):n71. https://doi.org/10.1136/bmj.n71 PMID: 33782057

11. Kohl C, McIntosh EJ, Unger S, Haddaway NR, Kecke S, Schiemann J, et al. Online tools supporting the conduct and reporting of systematic reviews and systematic maps: a case study on CADIMA and review of existing tools. Environ Evid. 2018;7(8).

12. Bouwknegt M, Devleesschauwer B, Graham H, Robertson LJ, van der Giessen JW, Euro-FBP workshop participants. Prioritisation of food-borne parasites in Europe, 2016. Euro Surveill. 2018;23(9):17-00161. https://doi.org/10.2807/1560-7917.ES.2018.23.9.17-00161 PMID: 29510783

13. Dámek F, Swart A, Waap H, Jokelainen P, Le Roux D, Deksne G, et al. Systematic review and modelling of age-dependent prevalence of Toxoplasma gondii in livestock, wildlife and felids in Europe. Pathogens. 2023;12(1):97. https://doi.org/10.3390/pathogens12010097 PMID: 36678447

14. Bartolomé Alvarez J, Martínez Serrano M, Moreno Parrado L, Lorente Ortuño S, Crespo Sánchez MD. Prevalencia e incidencia de la infección por Toxoplasma gondii en mujeres en edad fértil en Albacete (2001-2007). [Prevalence and incidence in Albacete, Spain, of Toxoplasma gondii infection in women of childbearing age: differences between immigrant and non-immigrant (2001-2007)]. Rev Esp Salud Publica. 2008;82(3):333-42. Spanish. https://doi.org/10.1590/S1135-57272008000300009 PMID: 18711647

15. Antolová D, Janičko M, Halánová M, Jarčuška P, Gecková AM, Babinská I, et al. Exposure to Toxoplasma gondii in the Roma and non-Roma inhabitants of Slovakia: A cross-sectional seroprevalence study. Int J Environ Res Public Health. 2018;15(3):408. https://doi.org/10.3390/ijerph15030408 PMID: 29495474

16. Antoniou M, Tzouvali H, Sifakis S, Galanakis E, Georgopoulou E, Tselentis Y. Toxoplasmosis in pregnant women in Crete. Parassitologia. 2007;49(4):231-3. PMID: 18689233

17. Asencio MA, Herraez O, Tenias JM, Garduño E, Huertas M, Carranza R, et al. Seroprevalence survey of zoonoses in Extremadura, southwestern Spain, 2002-2003. Jpn J Infect Dis. 2015;68(2):106-12. https://doi.org/10.7883/yoken.JJID.2014.181 PMID: 25420654

18. Berger F, Goulet V, Le Strat Y, Desenclos JC. Toxoplasmosis among pregnant women in France: risk factors and change of prevalence between 1995 and 2003. Rev Epidemiol Sante Publique. 2009;57(4):241-8. https://doi.org/10.1016/j.respe.2009.03.006 PMID: 19577390

19. Birgisdóttir A, Asbjörnsdottir H, Cook E, Gislason D, Jansson C, Olafsson I, et al. Seroprevalence of Toxoplasma gondii in Sweden, Estonia and Iceland. Scand J Infect Dis. 2006;38(8):625-31. https://doi.org/10.1080/00365540600606556 PMID: 16857606

20. Bobić B, Milosavić M, Guzijan G, Djurković-Djaković O. First report on Toxoplasma gondii infection in Bosnia and Herzegovina: study in blood donors. Vector Borne Zoonotic Dis. 2016;16(12):807-9. https://doi.org/10.1089/vbz.2016.2028 PMID: 27797684

21. Bobić B, Nikolić A, Klun I, Vujanić M, Djurković-Djaković O. Undercooked meat consumption remains the major risk factor for Toxoplasma infection in Serbia. Parassitologia. 2007;49(4):227-30. PMID: 18689232

22. Brkić S, Gajski G, Bogavac M, Marić D, Turkulov V, Tomić S. Серопреваленција токсоплазмозе у Војводини. [Seroprevalence of toxoplasmosis in Vojvodina]. Srp Arh Celok Lek. 2010;138(5-6):333-6. Serbian. https://doi.org/10.2298/SARH1006333B PMID: 20607979

23. Burrells A, Opsteegh M, Pollock KG, Alexander CL, Chatterton J, Evans R, et al. The prevalence and genotypic analysis of Toxoplasma gondii from individuals in Scotland, 2006-2012. Parasit Vectors. 2016;9(1):324. https://doi.org/10.1186/s13071-016-1610-6 PMID: 27267112

24. Capretti MG, De Angelis M, Tridapalli E, Orlandi A, Marangoni A, Moroni A, et al. Toxoplasmosis in pregnancy in an area with low seroprevalence: is prenatal screening still worthwhile? Pediatr Infect Dis J. 2014;33(1):5-10. https://doi.org/10.1097/INF.0000000000000006 PMID: 24064557

25. Czyzewski K, Fraczkiewicz J, Salamonowicz M, Pieczonka A, Zajac-Spychala O, Zaucha-Prazmo A, et al. Low seroprevalence and low incidence of infection with Toxoplasma gondii (Nicolle et Manceaux, 1908) in pediatric hematopoietic cell transplantation donors and recipients: Polish nationwide study. Folia Parasitol (Praha). 2019;66:66. https://doi.org/10.14411/fp.2019.019 PMID: 31823860

26. Daković Rode O, Židovec Lepej S, Vodnica Martucci M, Lasica Polanda V, Begovac J. Prevalencija protutijela na Toxoplasma gondii u bolesnika zaraženih virusom humane imunodeficijencije u Hrvatskoj. [Prevalence of antibodies against Toxoplasma gondii in patients infected with human immunodeficiency virus in Croatia]. Infektol Glas. 2010;30(1):5-10. Croatian.

27. De Paschale M, Agrappi C, Clerici P, Mirri P, Manco MT, Cavallari S, et al. Seroprevalence and incidence of Toxoplasma gondii infection in the Legnano area of Italy. Clin Microbiol Infect. 2008;14(2):186-9. https://doi.org/10.1111/j.1469-0691.2007.01883.x PMID: 18034857

28. de Witte LD, Snijders G, Litjens M, Kamperman AM, Kushner SA, Kahn RS, et al. Are infectious agents involved in the pathogenesis of postpartum psychosis? J Affect Disord. 2018;229:141-4. https://doi.org/10.1016/j.jad.2017.12.069 PMID: 29310062

29. de Witte LD, van Mierlo HC, Litjens M, Klein HC, Bahn S, Osterhaus AD. The association between antibodies to neurotropic pathogens and schizophrenia: a case-control study. NPJ Schizophr. 2015;1(1):15041. https://doi.org/10.1038/npjschz.2015.41 PMID: 27336045

30. Diza E, Frantzidou F, Souliou E, Arvanitidou M, Gioula G, Antoniadis A. Seroprevalence of Toxoplasma gondii in northern Greece during the last 20 years. Clin Microbiol Infect. 2005;11(9):719-23. https://doi.org/10.1111/j.1469-0691.2005.01193.x PMID: 16104986

31. Dzitko K, Malicki S, Komorowski J. Effect of hyperprolactinaemia on Toxoplasma gondii prevalence in humans. Parasitol Res. 2008;102(4):723-9. https://doi.org/10.1007/s00436-007-0824-0 PMID: 18092180

32. Fanigliulo D, Marchi S, Montomoli E, Trombetta CM. Toxoplasma gondii in women of childbearing age and during pregnancy: seroprevalence study in Central and Southern Italy from 2013 to 2017. Parasite. 2020;27:2. https://doi.org/10.1051/parasite/2019080 PMID: 31934847

33. Findal G, Barlinn R, Sandven I, Stray-Pedersen B, Nordbø SA, Samdal HH, et al. Toxoplasma prevalence among pregnant women in Norway: a cross-sectional study. APMIS. 2015;123(4):321-5. https://doi.org/10.1111/apm.12354 PMID: 25628065

34. Flatt A, Shetty N. Seroprevalence and risk factors for toxoplasmosis among antenatal women in London: a re-examination of risk in an ethnically diverse population. Eur J Public Health. 2013;23(4):648-52. https://doi.org/10.1093/eurpub/cks075 PMID: 22696530

35. Flegr J, Hrušková M, Hodný Z, Novotná M, Hanušová J. Body height, body mass index, waist-hip ratio, fluctuating asymmetry and second to fourth digit ratio in subjects with latent toxoplasmosis. Parasitology. 2005;130(Pt 6):621-8. https://doi.org/10.1017/S0031182005007316 PMID: 15977898

36. Gutiérrez-Zufiaurre N, Sánchez-Hernández J, Muñoz S, Marín R, Delgado N, Sáenz MC, et al. Seroprevalencia de anticuerpos frente a Treponema pallidum, Toxoplasma gondii, virus de la rubéola, virus de la hepatitis B y C y VIH en mujeres gestantes. [Seroprevalence of antibodies against Treponema pallidum, Toxoplasma gondii, rubella virus, hepatitis B and C virus, and HIV in pregnant women]. Enferm Infecc Microbiol Clin. 2004;22(9):512-6. Spanish. https://doi.org/10.1016/S0213-005X(04)73152-3 PMID: 15511391

37. Hofhuis A, van Pelt W, van Duynhoven YTHP, Nijhuis CDM, Mollema L, van der Klis FRM, et al. Decreased prevalence and age-specific risk factors for Toxoplasma gondii IgG antibodies in The Netherlands between 1995/1996 and 2006/2007. Epidemiol Infect. 2011;139(4):530-8. https://doi.org/10.1017/S0950268810001044 PMID: 20492743

38. Holec-Gasior L, Kur J. Badania epidemiologiczne populacji kobiet gminy Przodkowo w kierunku toksoplazmozy. [Epidemiological studies of toxoplasmosis among women from Przodkowo commune]. Przegl Epidemiol. 2009;63(2):311-6. Polish. PMID: 19799267

39. Kaňková Š, Procházková L, Flegr J, Calda P, Springer D, Potluková E. Effects of latent toxoplasmosis on autoimmune thyroid diseases in pregnancy. PLoS One. 2014;9(10):e110878. https://doi.org/10.1371/journal.pone.0110878 PMID: 25350671

40. Kolbekova P, Kourbatova E, Novotna M, Kodym P, Flegr J. New and old risk-factors for Toxoplasma gondii infection: prospective cross-sectional study among military personnel in the Czech Republic. Clin Microbiol Infect. 2007;13(10):1012-7. https://doi.org/10.1111/j.1469-0691.2007.01771.x PMID: 17617185

41. Lassen B, Janson M, Viltrop A, Neare K, Hütt P, Golovljova I, et al. Serological evidence of exposure to globally relevant zoonotic parasites in the Estonian population. PLoS One.

2016;11(10):e0164142. https://doi.org/10.1371/journal.
pone.0164142 PMID: 27723790

42. Lobo ML, Patrocinio G, Sevivas T, DE Sousa B, Matos
O. Portugal and Angola: similarities and differences in
Toxoplasma gondii seroprevalence and risk factors in pregnant
women. Epidemiol Infect. 2017;145(1):30-40. https://doi.
org/10.1017/S0950268816001904 PMID: 27608967

43. Lopes AP, Dubey JP, Moutinho O, Gargaté MJ, Vilares A,
Rodrigues M, et al. Seroepidemiology of Toxoplasma gondii
infection in women from the North of Portugal in their
childbearing years. Epidemiol Infect. 2012;140(5):872-7.
https://doi.org/10.1017/S0950268811001658 PMID: 21878147

44. López-Fabal F, Gómez-Garcés JL. Marcadores serológicos de
gestantes españolas e inmigrantes en un área del sur de
Madrid durante el periodo 2007-2010. [Serological markers
of Spanish and immigrant pregnant women in the south of
Madrid during the period 2007-2010]. Rev Esp Quimioter.
2013;26(2):108-11. Spanish. PMID: 23817647

45. Maggi P, Volpe A, Carito V, Schinaia N, Bino S, Basho M, et al.
Surveillance of toxoplasmosis in pregnant women in Albania.
New Microbiol. 2009;32(1):89-92. PMID: 19382673

46. Marcinek P, Nowakowska D, Szaflik K, Spiewak E, Małafiej
E, Wilczyński J. Analiza wybranych powikłatń w przebiegu
ciazy u kobiet z serologicznymi cechami ostrej toksoplazmozy
lub ostrej parwowirozy. [Analysis of complications
during pregnancy in women with serological features of
acute toxoplasmosis or acute parvovirosis]. Ginekol Pol.
2008;79(3):186-91. Polish. PMID: 18592853

47. Mihu AG, Balta C, Marti DT, Paduraru AA, Lupu MA, Olariu
TR. Seroprevalence of Toxoplasma gondii infection among
women of childbearing age in an endemic region of Romania,
2016-2018. Parasite. 2020;27:59. https://doi.org/10.1051/
parasite/2020057 PMID: 33198884

48. Mizgajska-Wiktor H, Jarosz W, Andrzejewska I, Krzykała M,
Janowski J, Kozłowska M. Differences in some developmental
features between Toxoplasma gondii-seropositive and
seronegative school children. Folia Parasitol (Praha).
2013;60(5):416-24. https://doi.org/10.14411/fp.2013.044
PMID: 24471283

49. Motoi S, Navolan DB, Malita D, Ciohat I, Nemescu D,
Manciuc C, et al. A decreasing trend in Toxoplasma gondii
seroprevalence among pregnant women in Romania - results
of a large scale study. Exp Ther Med. 2020;20(4):3536-40.
https://doi.org/10.3892/etm.2020.9012 PMID: 32905270

50. Nash JQ, Chissel S, Jones J, Warburton F, Verlander NQ. Risk
factors for toxoplasmosis in pregnant women in Kent, United
Kingdom. Epidemiol Infect. 2005;133(3):475-83. https://doi.
org/10.1017/S0950268804003620 PMID: 15962554

51. Niemiec KT, Raczyński P, Markiewicz K, Leibschang J, Ceran A.
Czestość wystepowania zarazeń pierwotniakiem Toxoplasma
gondii u 2016 kobiet ciezarnych oraz ich dzieci urodzonych
w Instytucie Matki i Dziecka w Warszawie. [The prevalence of
Toxoplasma gondii infection among 2016 pregnant women and
their children in the Institute of Mother and Child in Warsaw].
Wiad Parazytol. 2002;48(3):293-9. Polish. PMID: 16888975

52. Nowakowska D, Stray-Pedersen B, Śpiewak E, Sobala W,
Małafiej E, Wilczyński J. Prevalence and estimated incidence
of Toxoplasma infection among pregnant women in Poland:
a decreasing trend in the younger population. Clin Microbiol
Infect. 2006;12(9):913-7. https://doi.org/10.1111/j.1469-
0691.2006.01513.x PMID: 16882298

53. Nowakowska D, Wujcicka W, Sobala W, Śpiewak E, Gaj Z,
Wilczyński J. Age-associated prevalence of Toxoplasma gondii
in 8281 pregnant women in Poland between 2004 and 2012.
Epidemiol Infect. 2014;142(3):656-61. https://doi.org/10.1017/
S0950268813001179 PMID: 23721799

54. Olariu TR, Petrescu C, Darabus G, Lighezan R, Mazilu O.
Seroprevalence of Toxoplasma gondii in Western Romania.
Infect Dis (Lond). 2015;47(8):580-3. https://doi.org/10.3109/23
744235.2015.1028098 PMID: 25851242

55. Olariu TR, Ursoniu S, Hotea I, Dumitrascu V, Anastasiu D,
Lupu MA. Seroprevalence and risk factors of Toxoplasma
gondii infection in pregnant women from Western Romania.
Vector Borne Zoonotic Dis. 2020;20(10):763-7. https://doi.
org/10.1089/vbz.2019.2599 PMID: 32589521

56. Piffer S, Lauriola AL, Pradal U, Collini L, Dell'Anna L, Pavanello
L. Toxoplasma gondii infection during pregnancy: a ten-
year observation in the province of Trento, Italy. Infez Med.
2020;28(4):603-10. PMID: 33257637

57. Pinto B, Castagna B, Mattei R, Bruzzi R, Chiumiento L,
Cristofani R, et al. Seroprevalence for toxoplasmosis in
individuals living in north west Tuscany: access to Toxo-test in
central Italy. Eur J Clin Microbiol Infect Dis. 2012;31(6):1151-6.
https://doi.org/10.1007/s10096-011-1422-8 PMID: 21964589

58. Pribakovic JA, Katanic N, Radevic T, Tasic MS, Kostic M, Stolic
B, et al. Serological status of childbearing-aged women for

Toxoplasma gondii and cytomegalovirus in northern Kosovo
and Metohija. Rev Soc Bras Med Trop. 2019;52:e20170313.
https://doi.org/10.1590/0037-8682-0313-2017 PMID:
30652782

59. Prusa AR, Kasper DC, Olischar M, Husslein P, Pollak A,
Hayde M. Evaluation of serological prenatal screening to
detect Toxoplasma gondii infections in Austria. Neonatology.
2013;103(1):27-34. https://doi.org/10.1159/000342625 PMID:
23018152

60. Puccio G, Cajozzo C, Canduscio LA, Cino L, Romano A,
Schimmenti MG, et al. Epidemiology of Toxoplasma and CMV
serology and of GBS colonization in pregnancy and neonatal
outcome in a Sicilian population. Ital J Pediatr. 2014;40(1):23.
https://doi.org/10.1186/1824-7288-40-23 PMID: 24559197

61. Ramos JM, Milla A, Rodríguez JC, Padilla S, Masiá M, Gutiérrez
F. Seroprevalence of Toxoplasma gondii infection among
immigrant and native pregnant women in Eastern Spain.
Parasitol Res. 2011;109(5):1447-52. https://doi.org/10.1007/
s00436-011-2393-5 PMID: 21541753

62. Robinson E, de Valk H, Villena I, Le Strat Y, Tourdjman
M. National perinatal survey demonstrates a decreasing
seroprevalence of Toxoplasma gondii infection among
pregnant women in France, 1995 to 2016: impact for screening
policy. Euro Surveill. 2021;26(5):1900710. https://doi.
org/10.2807/1560-7917.ES.2021.26.5.1900710 PMID: 33541484

63. Rodrigues FT, Sousa AP, Escoval MA, Condeço J, Cardoso L,
Lopes AP. Seroepidemiology of Toxoplasma gondii in blood
donors in Portugal. Transfus Apher Sci. 2020;59(4):102777.
https://doi.org/10.1016/j.transci.2020.102777 PMID: 32487512

64. Rudin C, Hirsch HH, Spaelti R, Schaedelin S, Klimkait T. Decline
of seroprevalence and incidence of congenital toxoplasmosis
despite changing prevention policy-three decades of cord-
blood screening in north-western Switzerland. Pediatr
Infect Dis J. 2018;37(11):1087-92. https://doi.org/10.1097/
INF.0000000000001978 PMID: 29561516

65. Sagel U, Krämer A, Mikolajczyk RT. Incidence of maternal
Toxoplasma infections in pregnancy in Upper Austria,
2000-2007. BMC Infect Dis. 2011;11(1):348. https://doi.
org/10.1186/1471-2334-11-348 PMID: 22168604

66. Salamon D, Bulanda M. Toxoplasma gondii and women
of reproductive age: an analysis of data from the Chair of
Microbiology, Jagiellonian University Medical College in
Cracow. Ann Parasitol. 2014;60(4):291-6. PMID: 25706428

67. Sampedro A, Mazuelas P, Rodríguez-Granger J, Torres E,
Puertas A, Navarro JM. Marcadores serológicos en gestantes
inmigrantes y autóctonas en Granada. [Serological markers in
immigrant and Spanish pregnant women in Granada]. Enferm
Infecc Microbiol Clin. 2010;28(10):694-7. Spanish. https://doi.
org/10.1016/j.eimc.2010.04.007 PMID: 20961669

68. Santiago B, Blázquez D, López G, Sainz T, Muñoz M, Alonso
T, et al. Perfil serológico en gestantes extranjeras frente
a VIH, VHB, VHC, virus de la rubéola, Toxoplasma gondii,
Treponema pallidum, y Trypanosoma cruzi. [Serological profile
of immigrant pregnant women against HIV, HBV, HCV, rubella,
Toxoplasma gondii, Treponema pallidum, and Trypanosoma
cruzi]. Enferm Infecc Microbiol Clin. 2012;30(2):64-9. Spanish.
https://doi.org/10.1016/j.eimc.2011.07.010 PMID: 22079225

69. Scepanovic P, Alanio C, Hammer C, Hodel F, Bergstedt J, Patin
E, et al. Human genetic variants and age are the strongest
predictors of humoral immune responses to common
pathogens and vaccines. Genome Med. 2018;10(1):59. https://
doi.org/10.1186/s13073-018-0568-8 PMID: 30053915

70. Siponen AM, Kinnunen PM, Koort J, Kallio-Kokko H, Vapalahti
O, Virtala AM, et al. Toxoplasma gondii seroprevalence in
veterinarians in Finland: older age, living in the countryside,
tasting beef during cooking and not doing small animal
practice associated with seropositivity. Zoonoses Public
Health. 2019;66(2):207-15. https://doi.org/10.1111/zph.12550
PMID: 30536784

71. Sroka J, Zwoliński J, Dutkiewicz J. Czekstość wystepowania
przeciwciał anty-Toxoplasma gondii wśród pracowników
Zakładów Miesnych w Lublinie. [The prevalence of anti-
Toxoplasma gondii antibodies among abattoir workers in
Lublin]. Wiad Parazytol. 2003;49(1):47-55. Polish. PMID:
16889017

72. Strhársky J, Klement C, Hrubá F. Seroprevalence of Toxoplasma
gondii antibodies in the Slovak Republic. Folia Microbiol
(Praha). 2009;54(6):553-8. https://doi.org/10.1007/s12223-
009-0081-y PMID: 20140726

73. Studenicová C, Bencaiová G, Holková R. Seroprevalence of
Toxoplasma gondii antibodies in a healthy population from
Slovakia. Eur J Intern Med. 2006;17(7):470-3. https://doi.
org/10.1016/j.ejim.2006.07.007 PMID: 17098589

74. Studenicová C, Ondriska F, Holková R. Séroprevalencia
Toxoplasma gondii u gravidných zien na Slovensku.
[Seroprevalence of Toxoplasma gondii among pregnant women

Check for updates

in Slovakia]. Epidemiol Mikrobiol Imunol. 2008;57(1):8-13. Slovakian. PMID: 18318393

75. Suvisaari J, Torniainen-Holm M, Lindgren M, Härkänen T, Yolken RH. Toxoplasma gondii infection and common mental disorders in the Finnish general population. J Affect Disord. 2017;223:20-5. https://doi.org/10.1016/j.jad.2017.07.020 PMID: 28715724

76. Szénási Z, Horváth K, Sárkány E, Melles M. Toxoplasmosis surveillance during pregnancy and quality assurance of methods in Hungary. Wien Klin Wochenschr. 2005;117(S4) Suppl 4;29-34. https://doi.org/10.1007/s00508-005-0444-6 PMID: 16416382

77. Thaller R, Tammaro F, Pentimalli H. Fattori di rischio per la toxoplasmosi in gravidanzain una popolazione del centro Italia. [Risk factors for toxoplasmosis in pregnant women in central Italy]. Infez Med. 2011;19(4):241-7. Italian. PMID: 22212163

78. Tomasoni LR, Sosta E, Beltrame A, Rorato G, Bigoni S, Frusca T, et al. Antenatal screening for mother to child infections in immigrants and residents: the case of toxoplasmosis in northern Italy. J Immigr Minor Health. 2010;12(6):834-40. https://doi.org/10.1007/s10903-010-9321-0 PMID: 20140516

79. Vilibic-Cavlek T, Ljubin-Sternak S, Ban M, Kolaric B, Sviben M, Mlinaric-Galinovic G. Seroprevalence of TORCH infections in women of childbearing age in Croatia. J Matern Fetal Neonatal Med. 2011;24(2):280-3. https://doi.org/10.3109/14767058.201 0.485233 PMID: 20476874

80. Wang H, Yolken RH, Hoekstra PJ, Burger H, Klein HC. Antibodies to infectious agents and the positive symptom dimension of subclinical psychosis: The TRAILS study. Schizophr Res. 2011;129(1):47-51. https://doi.org/10.1016/j.schres.2011.03.013 PMID: 21458236

81. Wilking H, Thamm M, Stark K, Aebischer T, Seeber F. Prevalence, incidence estimations, and risk factors of Toxoplasma gondii infection in Germany: a representative, cross-sectional, serological study. Sci Rep. 2016;6(1):22551. https://doi.org/10.1038/srep22551 PMID: 26936108

82. Wójcik-Fatla A, Sroka J, Zając V, Zwoliński J, Sawczyn-Domańska A, Kloc A, et al. Study on Toxoplasma gondii, Leptospira spp., Coxiella burnetii, and Echinococcus granulosus infection in veterinarians from Poland. J Vet Res (Pulawy). 2018;62(4):477-83. https://doi.org/10.2478/jvetres-2018-0069 PMID: 30729205

83. Zajkowska A, Garkowski A, Czupryna P, Moniuszko A, Król ME, Szamatowicz J, et al. Seroprevalence of parvovirus B19 antibodies among young pregnant women or planning pregnancy, tested for toxoplasmosis. Przegl Epidemiol. 2015;69(3):479-82, 597-600. PMID: 26519843

84. Sutton AJ, Abrams KR. Bayesian methods in meta-analysis and evidence synthesis. Stat Methods Med Res. 2001;10(4):277-303. https://doi.org/10.1177/096228020101000404 PMID: 11491414

85. Calero-Bernal R, Gennari SM, Cano S, Salas-Fajardo MY, Ríos A, Álvarez-García G, et al. Anti-Toxoplasma gondii antibodies in European residents: a systematic review and meta-analysis of studies published between 2000 and 2020. Pathogens. 2023;12(12):1430. https://doi.org/10.3390/pathogens12121430 PMID: 38133313

86. Meireles LR, Ekman CC, Andrade HF Jr, Luna EJ. Human toxoplasmosis outbreaks and the agent infecting form. Findings from a systematic review. Rev Inst Med Trop São Paulo. 2015;57(5):369-76. https://doi.org/10.1590/S0036-46652015000500001 PMID: 26603222

87. Bigna JJ, Tochie JN, Tounouga DN, Bekolo AO, Ymele NS, Youda EL, et al. Global, regional, and country seroprevalence of Toxoplasma gondii in pregnant women: a systematic review, modelling and meta-analysis. Sci Rep. 2020;10(1):12102. https://doi.org/10.1038/s41598-020-69078-9 PMID: 32694844

88. Rostami A, Riahi SM, Contopoulos-Ioannidis DG, Gamble HR, Fakhri Y, Shiadeh MN, et al. Acute Toxoplasma infection in pregnant women worldwide: a systematic review and meta-analysis. PLoS Negl Trop Dis. 2019;13(10):e0007807. https://doi.org/10.1371/journal.pntd.0007807 PMID: 31609966

89. Robert-Gangneux F, Dardé ML. Epidemiology of and diagnostic strategies for toxoplasmosis. Clin Microbiol Rev. 2012;25(2):264-96. https://doi.org/10.1128/CMR.05013-11 PMID: 22491772

90. Rostami A, Riahi SM, Gamble HR, Fakhri Y, Nourollahpour Shiadeh M, Danesh M, et al. Global prevalence of latent toxoplasmosis in pregnant women: a systematic review and meta-analysis. Clin Microbiol Infect. 2020;26(6):673-83. https://doi.org/10.1016/j.cmi.2020.01.008 PMID: 31972316

91. Salari N, Rahimi A, Zarei H, Abdolmaleki A, Rasoulpoor S, Shohaimi S, et al. Global seroprevalence of Toxoplasma gondii in pregnant women: a systematic review and meta-analysis.

BMC Pregnancy Childbirth. 2025;25(1):90. https://doi.org/10.1186/s12884-025-07182-2 PMID: 39885489

92. Pappas G, Roussos N, Falagas ME. Toxoplasmosis snapshots: global status of Toxoplasma gondii seroprevalence and implications for pregnancy and congenital toxoplasmosis. Int J Parasitol. 2009;39(12):1385-94. https://doi.org/10.1016/j.ijpara.2009.04.003 PMID: 19433092

93. Giese L, Seeber F, Aebischer A, Kuhnert R, Schlaud M, Stark K, et al. Toxoplasma gondii infections and associated factors in female children and adolescents, Germany. Emerg Infect Dis. 2024;30(5):995-9. https://doi.org/10.3201/eid3005.231045 PMID: 38666641

94. Tenter AM, Heckeroth AR, Weiss LM. Toxoplasma gondii: from animals to humans. Int J Parasitol. 2000;30(12-13):1217-58. https://doi.org/10.1016/S0020-7519(00)00124-7 PMID: 11113252

95. Stelzer S, Basso W, Benavides Silván J, Ortega-Mora LM, Maksimov P, Gethmann J, et al. Toxoplasma gondii infection and toxoplasmosis in farm animals: Risk factors and economic impact. Food Waterborne Parasitol. 2019;15:e00037. https://doi.org/10.1016/j.fawpar.2019.e00037 PMID: 32095611

96. Opsteegh M, Prickaerts S, Frankena K, Evers EG. A quantitative microbial risk assessment for meatborne Toxoplasma gondii infection in The Netherlands. Int J Food Microbiol. 2011;150(2-3):103-14. https://doi.org/10.1016/j.ijfoodmicro.2011.07.022 PMID: 21864927

97. Deng H, Swart A, Bonačić Marinović AA, van der Giessen JWB, Opsteegh M. The effect of salting on Toxoplasma gondii viability evaluated and implemented in a quantitative risk assessment of meat-borne human infection. Int J Food Microbiol. 2020;314:108380. https://doi.org/10.1016/j.ijfoodmicro.2019.108380 PMID: 31707174

98. Cook AJC, Gilbert RE, Buffolano W, Zufferey J, Petersen E, Jenum PA, et al. Sources of toxoplasma infection in pregnant women: European multicentre case-control study. BMJ. 2000;321(7254):142-7. https://doi.org/10.1136/bmj.321.7254.142 PMID: 10894691

99. Said B, Halsby KD, O'Connor CM, Francis J, Hewitt K, Verlander NQ, et al. Risk factors for acute toxoplasmosis in England and Wales. Epidemiol Infect. 2017;145(1):23-9. https://doi.org/10.1017/S0950268816002235 PMID: 27677229

100. van den Berg OE, Stanoeva KR, Zonneveld R, Hoek-van Deursen D, van der Klis FR, van de Kassteele J, et al. Seroprevalence of Toxoplasma gondii and associated risk factors for infection in the Netherlands: third cross-sectional national study. Epidemiol Infect. 2023;151:e136. https://doi.org/10.1017/S095026882300122X PMID: 37503608

101. Rogan WJ, Gladen B. Estimating prevalence from the results of a screening test. Am J Epidemiol. 1978;107(1):71-6. https://doi.org/10.1093/oxfordjournals.aje.a112510 PMID: 623091

102. Huertas-López A, Cantos-Barreda A, Sánchez-Sánchez R, Martínez-Carrasco C, Ibáñez-López FJ, Martínez-Subiela S, et al. A systematic review and meta-analysis of the validation of serological methods for detecting anti-Toxoplasma gondii antibodies in humans and animals. Vet Parasitol. 2024;328:110173. https://doi.org/10.1016/j.vetpar.2024.110173 PMID: 38537410

103. Greiner M, Gardner IA. Epidemiologic issues in the validation of veterinary diagnostic tests. Prev Vet Med. 2000;45(1-2):3-22. https://doi.org/10.1016/S0167-5877(00)00114-8 PMID: 10802331

104. Deng H, Devleesschauwer B, Liu M, Li J, Wu Y, van der Giessen JWB, et al. Seroprevalence of Toxoplasma gondii in pregnant women and livestock in the mainland of China: a systematic review and hierarchical meta-analysis. Sci Rep. 2018;8(1):6218. https://doi.org/10.1038/s41598-018-24361-8 PMID: 29670127

105. Berkvens D, Speybroeck N, Praet N, Adel A, Lesaffre E. Estimating disease prevalence in a Bayesian framework using probabilistic constraints. Epidemiology. 2006;17(2):145-53. https://doi.org/10.1097/01.ede.0000198422.64801.8d PMID: 16477254

106. Wilkinson MD, Dumontier M, Aalbersberg IJ, Appleton G, Axton M, Baak A, et al. The FAIR Guiding Principles for scientific data management and stewardship. Sci Data. 2016;3(1):160018. https://doi.org/10.1038/sdata.2016.18 PMID: 26978244

107. Swart A, Maas M, de Vries A, Cuperus T, Opsteegh M. Bayesian binary mixture models as a flexible alternative to cut-off analysis of ELISA results, a case study of Seoul Orthohantavirus. Viruses. 2021;13(6):1155. https://doi.org/10.3390/v13061155 PMID: 34208752

Check for updates