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Seroprevlance of *Coxiella burnetii* among abattoir and slaughterhouse workers: A meta-analysis

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ABSTRACT

Q fever caused by the gram negative bacteria, *Coxiella burnetii,* is an occupational hazard for those who live and work in rural settings and those who are in contact with animals, especially abattoir and slaughterhouse workers. Australia is the only country to register a vaccine to prevent Q fever (Q-vax®, Seqirus, Australia) that is used in high risk populations. Seroprevalence studies conducted to determine the burden of Q fever (*C. burnetii* infection) in different settings have demonstrated high levels of heterogeneity with estimates of the percent positive ranging from 30% to 70%. There is a need for a more systematic evaluation of the findings of these studies in order to provide summary estimates of the seroprevalence in different settings.

We searched for published articles using PubMed, MEDLINE-EMBASE, and Scopus databases using search terms obtained from an initial review of published reports of recent Q fever outbreaks. Data on the seroprevalence of *C. burnetii* infection (Q fever) was extracted from the selected studies and a random effects meta-analysis was performed with stratification by outbreak status, year, country and serological techniques used. Results were visualised with a forest plot with 95% CI and measures of heterogeneity (I^2) for the random effects model.

A total of 19 articles that met the search criteria were included. The reported seroprevalence rate ranged from 4.7% to 91.7% among abattoir and slaughterhouse workers. No inter-group heterogeneity was observed ($p = 0.956$), supporting the pooling of all studies into one pooled measure. The pooled estimate of seropositivity for *C. burnetii* infection in people working in abattoirs and slaughterhouses was 26% (95% CI: 18–35%) regardless of the evidence of an "outbreak", the time of year or country. Seropositivity for *C burnetii* was independent of a person's age and years of occupational experience. Within abattoirs and slaughterhouses, slaughtering of cattle, sheep and goats are the most important risk factors associated with seropositivity and for those who showed over symptoms upon infection.

We recommend that vaccination programmes are directed towards people employed in the meat processing industry to mitigate the significant health and economic impacts of Q fever.

1. Background

Q fever (Q stands for query), caused by the highly pathogenic bacteria called *Coxiella burnetii*, is a zoonotic disease [15] and has worldwide distribution [28]. Since its discovery and description in Australia in 1937 [10,13] there have been several Q fever outbreaks reported internationally and the disease is considered endemic in most regions of the world [12,22,28,43]. The Netherlands is the country which experienced the highest ever reported Q fever outbreak [35]. Intensive farming of dairy goats and dairy sheep was the main reason for the outbreaks that occurred in The Netherlands [34].

Domestic ruminants and pets and in Australia, native marsupials, are the main reservoirs of infection [8,9,37,40]. Transmission to humans occurs mainly through inhalation of contaminated aerosols originating from parturient animals and their birth products [15,29]. Humans are considered accidental and dead-end hosts as there is no evidence of human-to-human transmission [15]. The seroprevalence of *C. burnetii* infection can range from 30% to 70% in people working in high-risk occupations such as farmers, veterinarians and abattoir workers [4].

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Table 1
Characteristics of studies that included abattoir and slaughterhouse workers.

Author (Year)	Outbreak	Country	Setting	Size (n)	Seropositive	Prevalence (%)	Lab method
Gilroy [17]	Yes	Australia	Abattoir	68	29	43	CFT
Abebe [1]	No	Ethiopia	Abattoir	465	30	6.5	CFT
Adesiyun [2]	No	Trinidad	Abattoir	85	4	4.7	ELISA
Khalili [24]	No	Iran	Slaughterhouse	75	51	68	ELISA
Marrie [27]	No	Canada	Slaughterhouse	96	12	12.5	CFT
Esmaeili [14]	No	Iran	Slaughterhouse	190	43	22.5	ELISA
Aflatoonian [3]	No	Iran	Slaughterhouse	64	5	7.8	ELISA
Perez-Trallero [33]	No	Spain	Slaughterhouse	36	33	91.7	IFA
Berktaş [7]	No	Turkey	Slaughterhouse	41	27	65.9	ELISA
Htwe [21]	No	Japan	Abattoir	107	12	11.2	IFA
CDC [44]	Yes	USA	Abattoir	42	19	45.2	CFT
Beech [45]	Yes	Australia	Abattoir	516	50	9.7	CFT
Schnurrenberger [46]	No	USA	Abattoir	2091	104	5	CFT
Schonell [47]	No	UK	Abattoir	96	21	28.1	CFT
Riemann [48]	No	Brazil	Abattoir	144	42	29	AGGLUTINATION
McKelvie [30]	Yes	Australia	Abattoir	139	22	15.8	CFT
CDNANZ [49]	Yes	Australia	Abattoir	100	18	18	CFT
Donaghy [11]	Yes	UK	Abattoir	228	49	21.5	NA
Wilson [42]	Yes	UK	Slaughterhouse	179	75	41.9	IFA
Berktaş [7]	No	Turkey	Butcher house	77	33	42.9	ELISA

Note: CFT = Complement Fixation Test, IFA = Immunofluorescence Assay, and ELISA = Enzyme-Linked Immunosorbent Assay. NA refers to Not Available.

Table 2
PubMed search strategy: Articles search history and strategy for abattoirs and slaughterhouse workers.

Search	Query	Items found
#12	Search (((q fever) OR coxiella burnetii)) AND (((((((seroprevalence) OR seroepidemiology) OR serology) OR serological) OR prevalence) OR incidence) OR epidemiology)	2864
#11	Search ((((((seroprevalence) OR seroepidemiology) OR serology) OR serological) OR prevalence) OR incidence) OR epidemiology	2,745,738
#10	Search (q fever) OR coxiella burnetii	5865
#9	Search epidemiology	1,970,371
#8	Search incidence	2,343,722
#7	Search prevalence	2,189,454
#6	Search serological	56,243
#5	Search serology	194,892
#4	Search seroepidemiology	1336
#3	Search seroprevalence	25,616
#2	Search coxiella burnetii	3157
#1	Search q fever	4994

Table 3
MEDLIN-EMBASE search history: Articles search history and strategy for abattoirs and slaughterhouse workers.

No.	Query	Results
#11	'q fever'/exp. OR 'coxiella burnetii'/exp. AND ('seroprevalence'/exp. OR 'seroepidemiology'/exp. OR 'serology'/exp. OR 'prevalence'/exp. OR 'incidence'/exp. OR 'epidemiology'/exp)	2246
#10	'seroprevalence'/exp. OR 'seroepidemiology'/exp. OR 'serology'/exp. OR 'prevalence'/exp. OR 'incidence'/exp. OR 'epidemiology'/exp	2,687,691
#9	'q fever'/exp. OR 'coxiella burnetii'/exp	6631
#8	'epidemiology'/exp	2,514,169
#7	'incidence'/exp	313,776
#6	'prevalence'/exp	520,913
#5	'serology'/exp	202,792
#4	'seroepidemiology'/exp	2906
#3	'seroprevalence'/exp	15,639
#2	'coxiella burnetii'/exp	3640
#1	'q fever'/exp	5152

Prevention of Q fever in Australia is through targeted immunization especially in those working in, or associated with the meat industry using the locally produced Q Vax vaccine (Seqirus, Australia), which has high efficacy in adults [25,26]. Q Vax is reported to provide up to 93% immune protection [32] with long-lived immune responses to *C. burnetii* [23]. However, the incidence of Q fever in people working in the red meat industry remains relatively high. Therefore, the current review provides information on the variability of the prevalence of Q fever exposure and risk factors for exposure in this occupational group.

2. Materials and methods

A search for published articles was conducted using several strategies (see details in Tables 1–3 and supporting files 1–2 and Fig. 2): an online search of PubMed, MEDLINE-EMBASE, and Scopus databases was conducted using the terms Q fever, *Coxiella burnetii*, seroprevalence, sero-epidemiology, serology, incidence, prevalence, abattoir, abattoir workers, slaughterhouse, slaughterhouse workers, and butcher and meat workers. Further key words were then obtained from an initial review of reports of outbreak investigations in various countries.

One reviewer individually screened all study titles identified through database searches. An initial review of abstracts was performed to identify articles for a more detailed full text review. The final articles were selected if they met the following criteria: 1) if the full text or abstract is available, 2) articles that are published in a peer-reviewed or refereed archival journal in English, 3) articles that are based on original data; i.e., not a review article or meta-analysis, 4) articles that contained reported prevalence estimates from statistical analyses, and 5) articles of studies that were conducted on people working in the meat industry (slaughterhouse and abattoir workers, and butchers). Meta-analysis was done for abattoir and slaughterhouse workers with a total of 19 studies which met the inclusion criteria. Details of the studies' characteristics along with the number of studies included in each are summarized in supporting information Table 1.

Articles with extreme reported seroprevalence rates, that is, 0.0% and 100%, have been included in order to minimize the publication bias especially for positive findings. The prevalence of exposure was selected as the outcome variable in each of the various sub-groups. Odds and risk ratios were also extracted as measures of the strength of association between Q fever and exposures to different risk factors. Initial data extraction was done using Microsoft Excel and compiled

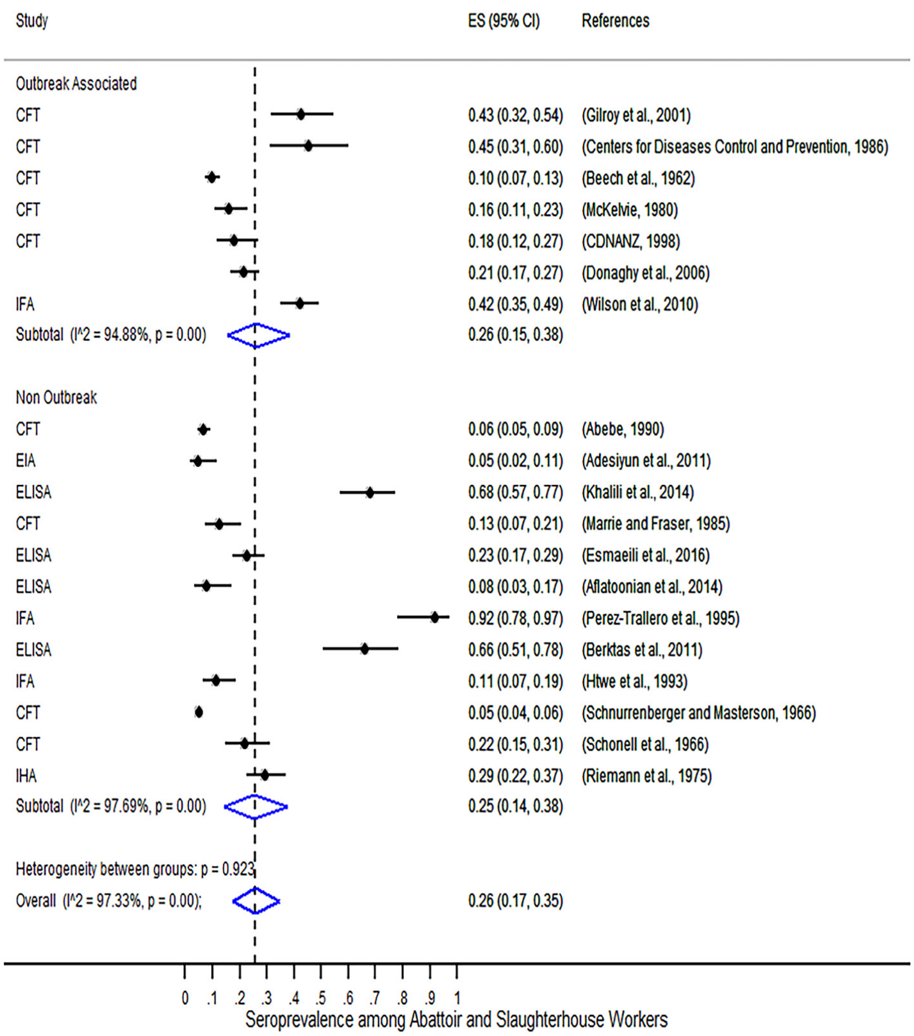

Fig. 1. Forest plot of seroprevalence of C. burnetii among abattoirs and slaughterhouse workers in 19 included studies stratified by outbreak status. Note: CFT = Complement Fixation Test, IFA = Immunofluorescence Assay, and ELISA = Enzyme-Linked Immunosorbent Assay. Also, ES(95% CI) refers to the seroprevalence point estimate (ES) with 95% CI. P = p-value and I^2 describes the percentage of total variation across studies that is due to heterogeneity rather than chance.

data was imported to Stata version 13 [39].

Stratification based on serological test type and whether the study reported findings of an outbreak investigation was performed to determine the presence of heterogeneity in terms of the seroprevalence and potential reporting bias. Random effects meta-analysis was conducted using the *metaprop* Stata package that pools proportions and presents weighted sub-group and overall pooled estimates with inverse-variance weights obtained from a random-effects model [31] (see supporting File 2). A forest plot with error bars to indicate the 95% confidence interval around each of the [true] prevalence estimates was constructed and Higgin's I2 was used to quantify the amount of heterogeneity in the prevalence estimates, across studies [19,20]. The I^2 is calculated using the following formula $I^2 = 100\% \times (Q - \mathrm{df})/Q$, where Q is Cochran's heterogeneity statistic and df the degrees of freedom [20].

Moreover, we used metafor R statistical package [41] for running meta-regression analysis for assessing presence of heterogeneity in the seroprevalences between outbreak and non-outbreak situations.

3. Results

A total of 7110 articles were identified in the initial searches of PubMed (2864), MEDLINE - EMBASE (2246) and Scopus (2000) databases. After removing duplicate articles, the title and abstracts of 4685 articles were reviewed to identify a total of 185 research articles that met our initial selection criteria. After the final screen 19 seroprevalence studies were included which met the inclusion criteria. Details on the characteristics of included studies are provided in Table 1.

Reported seroprevalence rates ranging from 4.7% to 91.7% among abattoir and slaughterhouse workers have been reported [1–3,7,14,17,21,24,27,33]. The magnitude ranged from 4.7% in Trinidad [2] to 43.0% among abattoirs in Australia [1,2,17], and 7.8% in Iran – 91.7% in Spain among slaughterhouse workers [3,7,24,33].

The outputs of the random effects meta-analysis on the seroprevalence of *C. burnetii* among abattoirs and slaughterhouse workers stratified by outbreak status is shown in Fig. 1. This figure presents the study specific proportions with 95% exact confidence intervals for each study, the sub-group and overall pooled estimate with 95% Wald confidence intervals and the I^2 statistic which provides a measure of the total amount of variation (as a percentage) in the prevalence estimates that is due to variation at the individual study level.

The result of the meta-analysis shown in Fig. 1 indicates the absence of inter-group heterogeneity on the seroprevalence of *C. burnetii* ($p = 0.932$, $I^2 = 97.33\%$), both during outbreak and non-outbreak situations, supporting the pooling of all studies into one summary

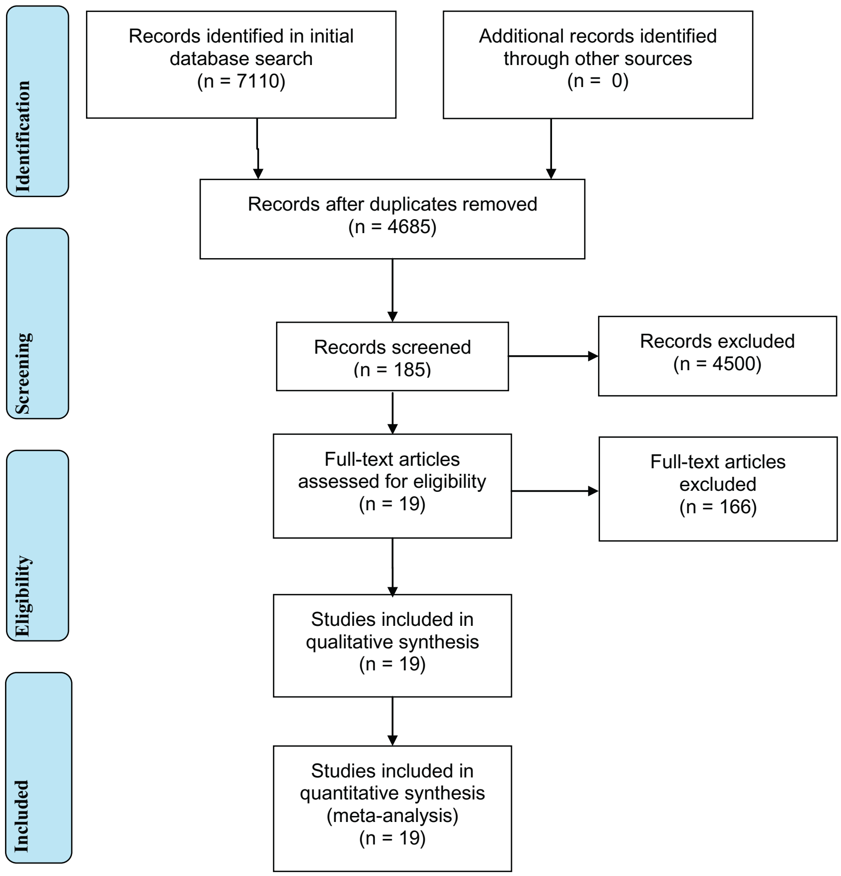

Fig. 2. Search strategy decision tree.
A total of 7110 articles were found from PubMed (2864), MEDLINE - EMBASE (2246) and Scopus (2000) databases. See Tables 2 and 3, supporting Files 1 and 2, and Fig. 2 for detailed search histories and strategies. After removing duplicated articles, 4685 articles were found and further refinement using title and abstract skimming, a total of 185 researches have retained. Finally, a total of 19 studies which fulfil the eligibility criteria were included in the meta-analysis.

Table 4
Table Mixed-effects meta-regression model results on the seroprevalence of Q fever in abattoir and slaughterhouses.

Source of variation	Category	Estimate	SE	Z	P-Value	95% CI		I^2	R^2
						Lower	Upper		
Outbreak	Intercept	0.27	0.09	3.05	0.00	0.10	0.45	99.06%	0.02%
	Outbreak	0.01	0.11	0.08	0.94	−0.21	0.23		
Diagnosis method	Intercept	0.18	0.12	1.57	0.12	−0.05	0.41	98.90%	26.86%
	CFT	0.01	0.14	0.06	0.96	−0.26	0.27		
	ELISA	0.22	0.16	1.40	0.16	−0.09	0.52		
	IFA	0.30	0.17	1.78	0.08	−0.03	0.62		

Mixed-Effects Model (k = 19; tau^2 (estimated amount of residual heterogeneity) estimator: ML (Maximum Likelihood)). I^2 (residual heterogeneity/unaccounted variability). R^2 (amount of heterogeneity accounted for).

measure: 26% (95%, CI: 17–35%). However, the seroprevalence estimates showed significant intra-group heterogeneity for the three serological tests with I^2 exceeding 94% ($p < 0.001$) for both outbreak and non-outbreak situations.

Meta-regression analysis (summarized in Table 4) indicated absence of statistical significant heterogeneity (p-value > 0.05) between outbreak and among serological methods in the seroprevalence of *C. burnetii*. Hence, we conclude that pooling the seroprevalences for outbreak and non-outbreak situations is supported through a meta-regression.

4. Discussion

The result of the seroprevalence studies showed that Q fever is endemic in meat processing industries such as abattoirs and slaughterhouses. The result of the meta-analysis indicated that, the seroprevalence of *C. burnetii* infection remained relatively constant regardless of outbreak situations. A strong association with the meat industry is confirmed [16]. This is in accordance with studies that have shown that abattoir workers are notable at-risk group for Q fever who should be fully protected from this occupational disease [6].

The overall seroprevalence of *C. burnetii* (26%) determined in this meta-analysis falls within the range of values (30–70%) reported in studies of high risk groups elsewhere [4]. Gilroy et al. [17] indicated that up to sixty-eight (66%) of employees in abattoirs are considered susceptible to primary infection and that unscreened, unvaccinated, non-immune workers developed Q fever after exposure to *C. burnetii* [17]. Furthermore, Perez-Trallero et al. showed that > 86% of slaughterhouse workers in one study had evidence of previous infection by *C. burnetii* using skin testing and serology? [33].

The detection of higher prevalence of antibodies to *C. burnetii* in abattoir workers and those who had minimal contact with animals is an indication of presence of pre-existing immunity rather than recent infection [2,17]. Infection with *C. burnetii* among abattoir and slaughterhouse workers occurs independent of the age, sex, race, years of occupational experience or the types of duties performed in the abattoir or in the offices by the workers [2,14,24]. In addition, the absence of association between seropositivity for *C. burnetii* and work history, work type, splashing of animal secretions on face or body and occupational injury have also been identified [14]. However, the results of two studies (Wilson et al. [42]; Marrie and Fraser [27]) suggest that being male [OR = 6.4, 95% CI: 1.8–23.4] is independently statistically significantly associated with an increased risk of testing positive for infection with *C. burnetii* [27,42].

The greatest risk of infection was associated with working in areas where cattle, sheep and swine are slaughtered [11,30]. Marrie and Fraser [27] showed that slaughtering cattle (working on the kill floor) was a significant risk factor for positive antibody titers among slaughterhouse workers [27]. Furthermore, A previous study by Perez-Trallero et al., [33] reported 19.25 higher [OR = 19.25, 95% CI: 5.34, 102.74] odds of Q fever infection for those working in slaughterhouses [33].

In addition, people who work in other occupations in rural settings and that have contact with animals, especially the operators of the livestock industry (veterinarians, tanners, and wool carders) are also at higher risk of seropositivity [24,36].

One published case control study confirmed the higher incidence of Q fever associated with increased level of exposure to a slaughterhouse (low exposure: OR = 3.0; moderate: OR = 4.7; high: OR = 15.0; chi2 for trend, p = 0.006) and high level of exposure to the slaughterhouse site (OR = 6.8, 95% CI: 1.1–40.3) [5]. A strong association with the meat industry was confirmed [16]. This is in accordance with studies that have shown that abattoir workers are a notable at-risk group for Q fever [6]. It is the study that supports the hypothesis of a sheep lairage being the source of potential exposure, Scottish co-located slaughterhouse and cutting plant. Passing through walkway by the sheep lairage was independently associated with an increased risk of testing positive. Those who passed through the stores were 3.2 (95% CI: 1.7–6.3) times as likely to be a confirmed case, those who passed through walkway by the sheep lairage were 2.1 (95% CI: 1.0–4.3) times as likely [42]. Bell, et al. [6] indicated that because the organism is transmitted in aerosols, it is important that not only abattoir employees but all workers who visit or work on an abattoir site are vaccinated against Q fever. This includes service providers such as electricians, plumbers, telecommunication workers, weights and measures inspectors and transport workers [6].

A randomized, blind, placebo-controlled trial of Q fever and influenza vaccines has been conducted in three Queensland abattoirs, showing occurrence of Q fever cases in unvaccinated workers in all three abattoirs during the follow-up period [38]. However, vaccination administered 10 or more days after the likely period of exposure showed no significant protective effect (RR = 0.57; 95% CI 0.13–2.57; p = 0.60) [17]. The study by Greig et al. [18] showed the average annual risk of infection among abattoir workers to be 45.0 per 1000 (95% CI 42.3–47.6), and 62.6 per 1000 (95% CI 57.5–67.7) over the first 10 years of exposure [18]. Up to 90% of new entrants in high-risk workplaces will be susceptible to Q fever and require vaccination [18].

In summary, the seroprevalence associated with *C. burnetii* infection ranged from 4.7% to 91.7% among abattoir and slaughterhouse workers was reported in the included studies. From the random effects meta-analysis, seropositivity for *C. burnetii* in abattoirs and slaughterhouses can be expected in more than a quarter of workers (26%; 95% CI: 17%–35%) regardless of evidence of an outbreak. In addition, seropositivity for *C. burnetii* is independent of age and years of occupational experience in meat abattoir and slaughterhouses but significantly associated with activities related to slaughtering of cattle, sheep and goats. Vaccination 10 days prior to exposure to environments where *C. burnetii* may be present was shown to be an effective prevention mechanism. Vaccination programmes for workers in high risk industries is highly recommended for mitigating the incidence of Q fever, and subsequent chronic sufferings and work day offs among abattoir and slaughterhouse workers.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.onehlt.2018.09.002.

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