Long-term impact of a Q-fever outbreak: An evaluation of health symptoms, health-related quality of life, participation and health care satisfaction after ten years

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ABSTRACT

Objective: To assess health symptoms, health-related quality of life, participation, and health care satisfaction in Q-fever patients up to 10 years after infection.

Methods: Cross-sectional questionnaire survey in the Netherlands. Data on health symptoms, fatigue (CIS), health-related quality of life (EQ-5D), social/work participation, health care providers and health care satisfaction were collected in patients with chronic Q-fever (CQ), Q-fever fatigue syndrome (QFS), and patients who experience QFS-like disease without a post-infection diagnosis (QLD).

Results: A vast majority of the 478 Q-fever patients (response rate 54.3%) face several health problems 10 years after infection. Fatigue was the most prevalent symptom in all groups (91.2%). The median EQ-5D index value differed significantly between the three diagnostic groups (CQ: 0.67; QFS: 0.55; QLD:0.70; $p < 0.001$). Approximately 50% of all patients had serious problems with work and physical activities, and more than 25% experienced difficulties with leisure time, household and social contacts. Also, more than one third stopped working permanently. Furthermore, GP's, internists, and physical therapists were the most often consulted health care providers. Patients gave low ratings for the overall quality of care for Q-fever, with 75% scoring a 5.0 or lower on a 10-point scale.

Conclusion: Long-term health consequences are considerable for Q-fever patients, especially for those with QFS. The majority of the patients was unsatisfied with the quality of care for Q-fever. Awareness of the long-term impact of zoonotic diseases like Q-fever is needed to offer optimal health care for these patients.

1. Introduction

In late spring of 2007, a large Q-fever outbreak occurred in the Netherlands. This zoonotic disease outbreak was the beginning of the largest Q-fever epidemic ever reported worldwide. The epidemic lasted until 2011 with annual seasonal outbreaks linked to Q-fever abortion waves on dairy goats and sheep farms. This resulted in at least 4000 known cases of acute Q-fever [1]. Outbreaks of zoonotic diseases are an emerging threat to public health [2]. The relevance of zoonoses to human health has been highlighted by the recent international COVID-19 Coronavirus outbreak [3].

Q-fever is a zoonotic disease caused by *Coxiella burnetii,* a bacteria that hosts in the placenta and reproductive tissues of infected animals and becomes aerosolized during parturition [4]. Humans acquire Q-fever when they inhale this fine particulate matter, or through inhalation of airborne contaminated dust, which can spread out over extensive areas. Acute infection develops after a median incubation period of 18 days, with 95% of cases expected to occur between 7 and 32 days after exposure [4]. In general, most infected Q-fever patients (60%) are asymptomatic, and 40% develop symptoms ranging from

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mild flu like symptoms (20%) to more severe symptoms (20%) including fever, headache, myalgia, coughing, pneumonia, hepatitis, myocarditis, and pericarditis [5]. Patients with more severe symptoms in this acute phase are recommended to be treated with antibiotics for 2–3 weeks, preferably initiated within 3 days after the onset of symptoms [6]. Sometimes hospital admission is needed for severely ill patients. Hospitalization rates for acute Q-fever patients during the Dutch epidemic were on average 21.6%. Patients who were admitted to the hospital most frequently displayed symptoms of fever or pneumonia [7].

Infected Q-fever patients may develop prolonged profound health complications. Literature describes two long-term health consequences. The first long-term health effect is the development of chronic Q-fever (CQ), which occurs in approximately 1–2% of both symptomatic and asymptomatic Q-fever patients [8]. The most common clinical manifestations of CQ are infections of aortic aneurysms or vascular prostheses and endocarditis. CQ has a high mortality rate when left untreated [9]. Timely diagnosis and starting antibiotic treatment are important for survival. Treatment for CQ consists of long-term administration of antibiotics for at least 18 to 24 months [8]. The second long-term health consequence of Q-fever is the development of Q-fever fatigue syndrome (QFS), which occurs in approximately 20% of patients with a symptomatic Q-fever infection [10,11]. Clinical presentation of QFS consists of severe fatigue lasting longer than six months, as well as musculoskeletal pain, sleeping problems, impaired memory or concentration, and headache [12]. To date, there are no evidence-based clinical treatments available for QFS. Current recommendation for treatment is cognitive behavioral therapy, as it showed positive effects in reducing fatigue in a group of QFS patients [13]. In addition, in daily clinical practice a third group of patients is seen. These patients experience very similar long-term health complaints, however, they do not meet diagnostic criteria for QFS or have not been diagnosed as QFS. Studies describing the long-term impact for this group of patients are scarce [14,15]. This group will be described in this study as patients with QFS-like disease (QLD).

Studies examining the long-term consequences of Q-fever patients mainly focused on clinical outcomes and treatment results [16]. There are only a handful of studies on self-perceived health status e.g. health-related quality of life, fatigue and health symptoms, especially at long-term. One study showed that 4 years after a Q-fever infection persisting fatigue was present in 46%, while 50% experienced a severely impaired quality of life [17]. Furthermore, a recent study on the long-term impact on psychosocial functioning demonstrated that both CQ and QFS patients experienced reduced quality of life, more anxiety and lower levels of social functioning five to nine years after the acute infection compared to the general population [16]. Additionally, only a limited number of studies examined the impact of CQ and QFS on social and work participation. For example, Morroy et al. [5] found that Q-fever patients with persisting fatigue at 12–26 months also reported more long-term absence from work and sick leave. One in ten patients were unable to function at pre-Q-fever infection level at work. This was mainly due to fatigue and concentration problems. In addition, more than 30% of these patients reported that they had not resumed their daily activities. In line with these findings, van Loenhout et al. [18] showed that almost one in five Q-fever patients (19%) had a reduced work participation after one year.

Besides the lack of knowledge on long-term health and social consequences, little is known about health care use and satisfaction with care of Q-fever patients. However, to further improve the health care for patients who have been affected by a major zoonotic disease outbreak like Q-fever, it is imperative to learn more about health care use and satisfaction with care. Therefore, the aims of this study were to assess health symptoms, health-related quality of life, social/work participation, health care use and satisfaction with care in patients with CQ, QFS or QLD up to 10 years after infection.

2. Methods

2.1. Study design and participants

In December 2018, an online questionnaire was sent by two Q-fever patient organizations (Q-uestion and Q-support) via email to eligible Q-fever patients. Patients were eligible for inclusion if they met the following inclusion criteria: a member of Q-uestion or Q-support, aged 18 years or older at data collection, and able to read Dutch. Membership of patient organization Q-uestion or Q-support required the submission of a positive test result for a Q-fever infection. A reminder to complete the questionnaire was sent after four weeks by email. All participants gave online consent to use the collected data for scientific research. The Medical Ethics Review Board of Erasmus MC approved the study protocol (MEC-2018-1605).

2.2. Measures

2.2.1. Socio-demographic characteristics

Socio-demographic variables that were collected in the online questionnaire included age, gender, educational level, living situation, and having a partner. Educational level was categorized as low (primary education, lower or middle general secondary education), middle (higher secondary education, middle vocational education) and high (higher vocational education, university) education. Living situation was dichotomized as living with children (1) vs. without children (0). Partnership (or having a partner) was dichotomized as living with (1) vs. without a significant other (0).

2.2.2. Medical characteristics

Medical data were self-reported and included year of Q-fever infection, hospitalization (yes/no) during acute infection, self-reported medical diagnosis, use of antibiotics in acute phase and number of hospitalizations since being infected with Q-fever. Patients were classified according to three diagnosis groups based on their self-reported diagnosis: chronic Q-fever (CQ) patients, Q-fever fatigue syndrome (QFS) patients, and patients who experience QFS-like disease (QLD).

2.2.3. Health symptoms

A total of 27 common health complaints based on QFS guidelines [12] were assessed, such as concentration problems, dizziness, headache, and an option 'other'. Patients could select which health complaints were a significant problem for them since the primary Q-fever infection. 'Which of the following health symptoms have you experienced since you have Q-fever?'

2.2.4. Fatigue

Fatigue was measured with the subscale 'subjective experience of fatigue' of the Checklist Individual Strength (CIS) [19]. This scale consists of 8 items (e.g. "I feel tired", "I have trouble concentrating") scored on a 7-point Likert scale ranging from 1 (yes, that is true) to 7 (no, that is not true). Total scores can range from 8 to 56; higher scores indicate more fatigue. A score of 35 or more is indicative of severe fatigue [20].

2.2.5. Health related quality of life (HRQOL)

HRQOL was measured with the EQ-5D-5L, a generic HRQOL questionnaire with five dimensions: mobility, self-care, usual activities (e.g. work, study, housework, family or leisure activities), pain/discomfort, and anxiety/depression. In the current study, the EQ-5D-5L was extended with a cognition dimension covering aspects of memory, understanding, coherence, and thinking [21]. Each dimension of the EQ-5D-5L has five response levels ranging from no problems (Level 1) to extreme problems (Level 5). Based on the five dimensions (without the cognition dimension), a summary score (utility index) can be calculated [22]. The utility index is anchored from 1 (full health) to 0 (death), and

Table 1
Patient characteristics of all respondents (*n* = 478) and for chronic Q-fever patients (CQ), Q-fever fatigue syndrome patients (QFS) and patients with QFS-like disease (QLD).

	Total	CQ	QFS	QLD	
	N = 478	*N* = 52	*N* = 282	*N* = 144	
	n (%)	n (%)	n (%)	n (%)	χ^2 (*p*)
Sociodemographic characteristics					
Age in years, *median (IQR)*	58.0 (48.0–65.0)	69.0 (61.0–73.0)	56.0 (47.0–63.0)	57.0 (47.8–65.0)	52.93 (**< 0.001**)
Gender					14.08 (**0.001**)
Male	246 (51.5)	38 (73.1)	129 (45.7)	79 (54.9)	
Female	232 (48.5)	14 (26.9)	153 (54.3)	65 (45.1)	
Education					13.45 (**0.009**)
Low	144 (30.1)	24 (46.2)	76 (27.0)	44 (30.6)	
Middle	174 (36.4)	11 (21.2)	118 (41.8)	45 (31.3)	
High	160 (33.5)	17 (32.7)	88 (31.2)	55 (38.2)	
Partnership					0.63 (0.732)
Living with significant other	371 (77.8)	42 (80.8)	216 (76.6)	113 (79.0)	
Living without significant other	106 (22.2)	10 (19.2)	66 (23.4)	30 (21.0)	
Living situation					9.64 (**0.008**)
Living with children	144 (30.2)	6 (11.5)	92 (32.6)	46 (32.2)	
Living without children	333 (69.8)	46 (88.5)	190 (67.4)	97 (67.8)	
Employment status before Q-fever					7.24 (**0.027**)
Paid work	365 (76.4)	32 (61.5)	222 (78.7)	111 (77.1)	
No paid work	113 (23.6)	20 (38.5)	60 (21.3)	33 (22.9)	
Medical characteristics					
Hospitalization when infected					22.91 (**< 0.001**)
Yes	109 (22.8)	25 (48.1)	61 (21.6)	23 (16.0)	
No	369 (77.2)	27 (51.9)	221 (78.4)	121 (84.0)	
Hospitalizations since infection, *median (IQR)*	1.0 (1.0–2.0)	3.0 (1.0–4.0)	1.0 (1.0–2.0)	1.0 (1.0–2.0)	15.45 (**< 0.001**)
Antibiotics					17.97 (**0.001**)
Yes	329 (72.3)	44 (95.7)	193 (71.2)	92 (66.7)	
No	106 (23.3)	1 (2.2)	63 (23.2)	42 (30.4)	
Not sure	20 (4.4)	1 (2.2)	15 (5.5)	4 (2.9)	

Note. Kruskal-Wallis H tests were used for continuous variables, and χ^2 tests for binary or ordinal/nominal variables.

can be interpreted as a judgment on the relative desirability of a health status compared with perfect health. In addition, participants were asked to score how they perceived their overall health status on a VAS scale ranging from 0 ("worst possible health") to 100 ("best possible health").

2.2.6. Social participation

Social participation was measured with eight self-developed items on the following domains: work, finance, household, sports, hobbies, social relationships, relationship with partner and family role. For each domain, participants were asked to rate the number of problems they experience due to Q-fever. Items were scored on a 4-point scale ranging from no problems (0) to slight (1), moderate (2) or severe problems (3). The sum score can range from 0 to 33; a higher score represents greater problems in participation.

2.2.7. Work participation

To measure work participation the following items were formulated. At first, employment status at the moment of the infection was evaluated ('What was your employment status before the Q-fever infection?'). If employed, a question on the number of working hours per week followed ('How many hours a week did you work before the Q-fever infection?'). Then, the patient's current working status was evaluated ('Did your work status changed due to Q-fever?'). The answer options were as follows: I stopped working permanently due to Q-fever; I currently work less due to Q-fever; I worked less for a period, but resumed work to their normal working hours; I continued to work the same number of hours after infection; my working status changed due to reasons unrelated to Q-fever. If patients worked less hours than before the infection, they reported their current working hours ('How many hours a week do you currently work?'). Furthermore, patients

were asked two questions about work disability. Patients had to indicate if they were officially recognised as disable for work and whether they received a disability benefit. In the Netherlands, after two years of prolonged sick leave, individuals can apply for a disability benefit by the Dutch Institute for Employee Benefits Schemes (UWV), a semi-autonomous agency of the Ministry of Social Affairs and Employment [23].

2.2.8. Health care providers

Patients were asked which health care providers they have visited since they had Q-fever-related health complaints. They could make a selection in a list with 21 different health care providers (e.g., general practitioners (GP), medical specialists, physiotherapists, nurse specialists, occupational physicians), and an option 'other'. They also had to indicate how often they visited this health care provider.

2.2.9. Satisfaction with care

Patients were asked how satisfied they were with the care and support they received for Q-fever during the following time periods: i) in first 12 months after infection, ii) in the period between and iii) in the last 12 months. In addition, they were asked how satisfied they were with the care for patients with Q-fever in general, measured on a 10-point scale (1 = not satisfied at all, 10 = very satisfied). In an additional open ended question patients could clarify their rating. Two researchers (MB and LB) coded these answers independently into categories. Consensus on the categories was reached in a consecutive meeting between the researchers.

2.3. Statistical analyses

Statistical analysis was performed using SPSS software (version

22.0). Descriptive statistics were performed to describe the socio-demographic and medical characteristics of the study sample. Internal consistency (Cronbach's α) was calculated for subscale 'subjective experience of fatigue' of the CIS. Next, the number (proportions) of patients or median and IQR were calculated for all outcome measures. Differences between the three diagnosis groups were tested with Kruskal-Wallis H tests or Wilcoxon signed rank tests for not normally distributed continuous variables. χ^2 tests were used for binary or ordinal/nominal variables. This was done consecutively for health symptoms, fatigue scores, EQ-5D-5L scores, social participation, work participation, health care use, and satisfaction with care. Gender and age differences for EQ-5D-5L index values were performed by a Mann-Whitney U test and a Kruskal-Wallis H test. For all analysis, a p-value of < 0.05 was considerate as statistically significant.

3. Results

3.1. Patient and medical characteristics

A total of 880 patients were invited to participate in the questionnaire survey, of which 478 patients completed the online questionnaire (response rate 54.3%). Data of the non-responders were not available. The median (IQR) age of the participants was 58.0 (48.0–65.0) years and 51.5% was male (Table 1). The majority of the participants lived with a significant other (77.8%) and without children (69.8%). The median (IQR) number of years since the initial Q-fever infection was 9 years (8–10). Most patients (35.1%) were infected in the year 2009. During the initial infection, 22.8% of the participants were hospitalized and the majority (72.3%) received treatment with antibiotics. Of the 478 participants, 10.9% had CQ (N = 52), 59.0% QFS (N = 282), and 30.1% QLD (N = 144). There were significant differences between the three diagnosis groups on sociodemographic and medical characteristics (Table 1).

3.2. Health symptoms

The median total number of health symptoms was 12.0 (8.0–17.0), QFS reported significantly more health symptoms than CQ and QLD patients (Table 2). Fatigue was the most prevalent health symptom (91.2%), followed by concentration problems (81.4%), physical exhaustion when exercising (78.5%), and joint pain (74.3%). There were significant differences in the proportion of patients with specific health symptoms between the groups (Fig. 1). Main statistically significant differences were found on memory problems, muscle soreness, cardiovascular problems, fatigue, joint pain and physical exhaustion.

3.3. Fatigue

The majority (87.1%) of the participants was severely fatigued (score ≥ 35). The median fatigue score of all participants was 49.1 (41.1–53.7). The three groups differed significantly in total fatigue score, as well as in the proportion participants who were severely fatigued (score ≥ 35), indicating that relatively more QFS patients were severely fatigued compared to CQ and QLD patients (Table 2). The internal consistency of this scale in the present study was good (Cronbach's α = 0.87).

3.4. Health-related quality of life

HRQOL (EQ-5D) scores are shown in Fig. 2. Most problems were reported on the dimensions usual activities, cognition, and pain/discomfort, with respectively 89.6%, 89.6%, and 88.5% reporting at least some problems (slight, moderate, severe, and extreme). These percentages are respectively 14.7%, 8.4%, 34.4% for the average Dutch population [24]. There were significant differences between the three diagnosis groups on usual activities ($\chi^2(2) = 33.29$, $p < 0.001$), cognition ($\chi^2(2) = 49.98$, p < 0.001), pain/discomfort ($\chi^2(2) = 30.96$, p < 0.001), mobility ($\chi^2(2) = 10.93$, $p = 0.004$), and self-care ($\chi^2(2) = 9.35$, $p = 0.009$) but not on anxiety/depression.

Furthermore, the median EQ-5D index value for all Q-fever patients was 0.60 (0.32–0.74) and the median VAS score was 45.0 (30.0–62.0). Scores differed significantly between the three diagnosis groups (Table 2). QFS patients had the lowest scores, but CQ and QLD patients also had very low scores in comparison with the average Dutch index value of 0.87 [25]. In general, EQ-5D index scores in our study sample were significantly lower for women than for men (U = 1999.50, z = −2.62, $p = 0.014$), as well as for younger patients (< 40 years) and patients in their fifties (50–59 years) compared to patients in their forties (40–49 years), sixties (60–69 years) or older patients (> 70 years), $\chi^2(4) = 13.159.347$, $p = 0.011$.

3.5. Social participation

The median sum score on the social participation scale was 15.0

Table 2
Health symptoms, fatigue and health-related quality of life scores of all Q-fever patients, chronic Q-fever patients (CQ), Q-fever fatigue syndrome patients (QFS) and patients with QFS-like disease (QLD).

|	Total	CQ	QFS	QLD	Difference
	median (IQR)	median (IQR)	median (IQR)	median (IQR)	χ^2 (p)
Health symptoms					
Total number of health symptoms	12.0 (8.0–17.0)	10.0 (6.0–13.0)	13.0 (10.0–18.0)	10.0 (6.3–15.0)	34.17 (< 0.001)
Fatigue					
Total fatigue score	49.1 (41.1–53.7)	48.0 (34.3–52.6)	50.3 (44.6–53.7)	45.7 (35.4–52.6)	22.36 (< 0.001)
Severely Fatigued (n ≥ 35)					31.29 (< 0.001)
Yes	377 (87.1)	34 (73.9)	242 (94.5)	101 (77.1)	
No	56 (12.9)	12 (26.1)	14 (5.5)	30 (22.9)	
Health-related quality of life					
EQ index score	0.60 (0.32–0.74)	0.67 (0.31–0.81)	0.55 (0.24–0.71)	0.70 (0.45–0.80)	27.57 (< 0.001)
EQ VAS score	45.0 (30.0–62.0)	49.5 (30.8–69.3)	40.0 (28.0–60.0)	55.0 (40.0–68.0)	21.46 (< 0.001)
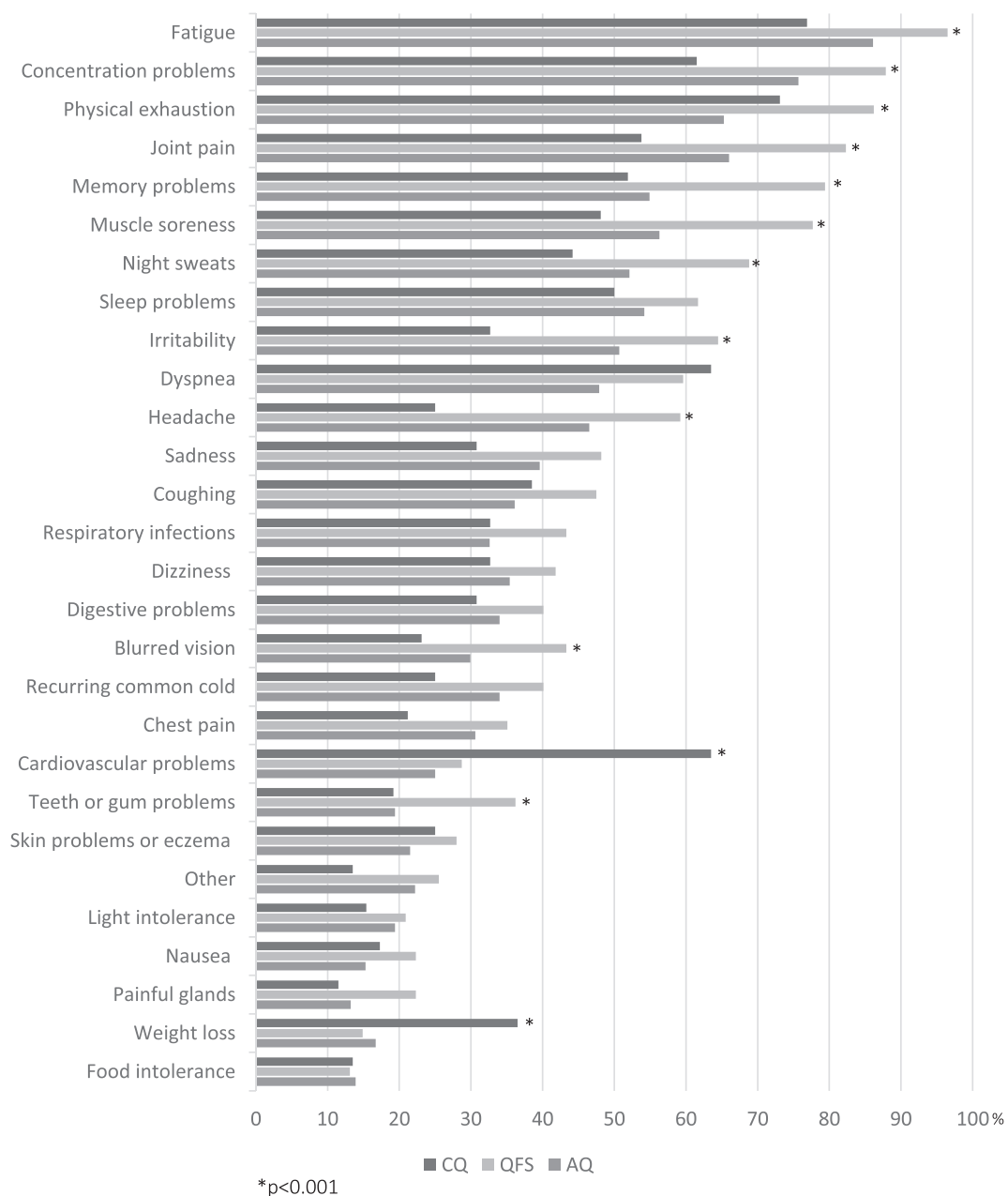
Fig. 1. Health symptoms (%) for chronic Q-fever patients (CQ), Q-fever fatigue syndrome patients (QFS) and patients with QFS-like disease (QLD).

(9.0–20.0). Particularly in the domains work, exercise, and study participants experienced severe problems, 52.6%, 51.5%, and 42.4% respectively. There was a significant difference in the sum score between the three diagnosis groups (QFS:17.0 (IQR 12.0–21.0) vs. CQ:11.0 (IQR 6.0–16.5) vs. QLD:11.0 (IQR 6.0–17.0); $\chi^2(2) = 34.61, p < 0.001$). The groups also differed significantly on each separate domain of the social participation questionnaire (Fig. 3). QFS patients experienced most difficulties with social participation compared to CQ and QLD patients.

3.6. Work participation

In total, 76.4% of all patients had paid work before the Q-fever infection. The median number of hours they worked per week was 40.0 (30.0–40.0). The majority (38.7%) of these patients stopped working permanently due to Q-fever and 33.2% had to work less. A further 12.1% reported that they worked less for a period, but resumed work to

their normal working hours. Only a small subsample continued to work the same number of hours after infection (8.8%). For the remainder of patients (7.3%) their working status changed due to reasons unrelated to Q-fever. To date, the median number of working hours was 17.8 (9.8–30.0), which is more than 50% less than before being infected with Q-fever (Wilcoxon Z = −9.11, $p < 0.001$). In addition, 31.8% of the participants reported that they were officially disabled for work due to Q-fever and 24.7% received a disability benefit by the Dutch Institute for Employee Benefit Scheme (UWV). QFS patients were more often disabled for work $\chi^2(2) = 22.23, p = 0.001$) and more often received a disability benefit ($\chi^2(2) = 10.74, p = 0.030$) than QLD and CQ patients. Furthermore, there were differences in the proportion of participants that stopped working, worked less hours and worked less for a period ($\chi^2(2) = 36.36, p < 0.001$). Relatively more CQ patients (65.4%) stopped working (vs. QFS:42.2% vs. QLD:24.5%), more QFS patients (37.9%) worked less (vs. CQ:11.5% vs. QLD:29.4%), and more QLD patients (22.5%) worked less temporarily (vs. CQ:3.8% vs. QFS:5.9%).
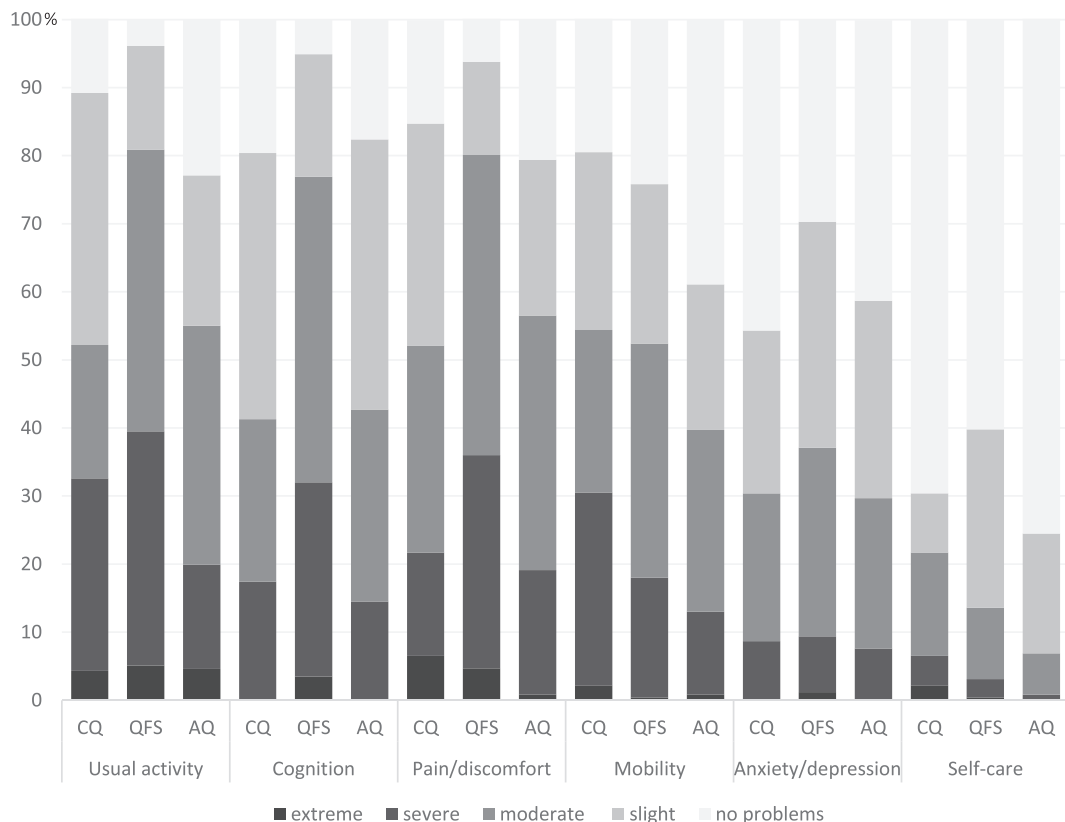
Fig. 2. Health-related quality of life in proportion of responses by level of severity (problems) for EQ-5D-5L dimensions for chronic Q-fever patients (CQ), Q-fever fatigue syndrome patients (QFS) and patients with QFS-like disease (QLD).
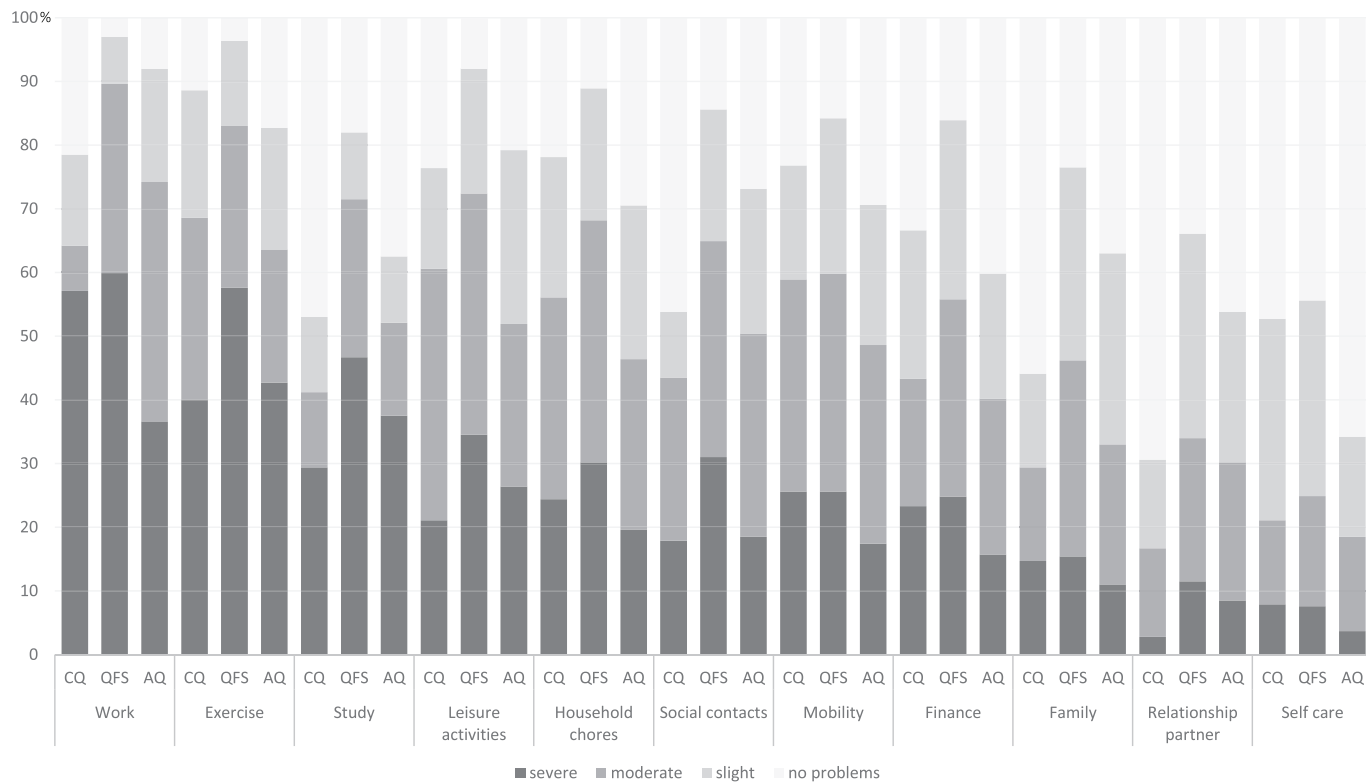

Fig. 3. Problems (%) in social participation per domain for chronic Q-fever patients (CQ), Q-fever fatigue syndrome patients (QFS) and patients with QFS-like disease (QLD).
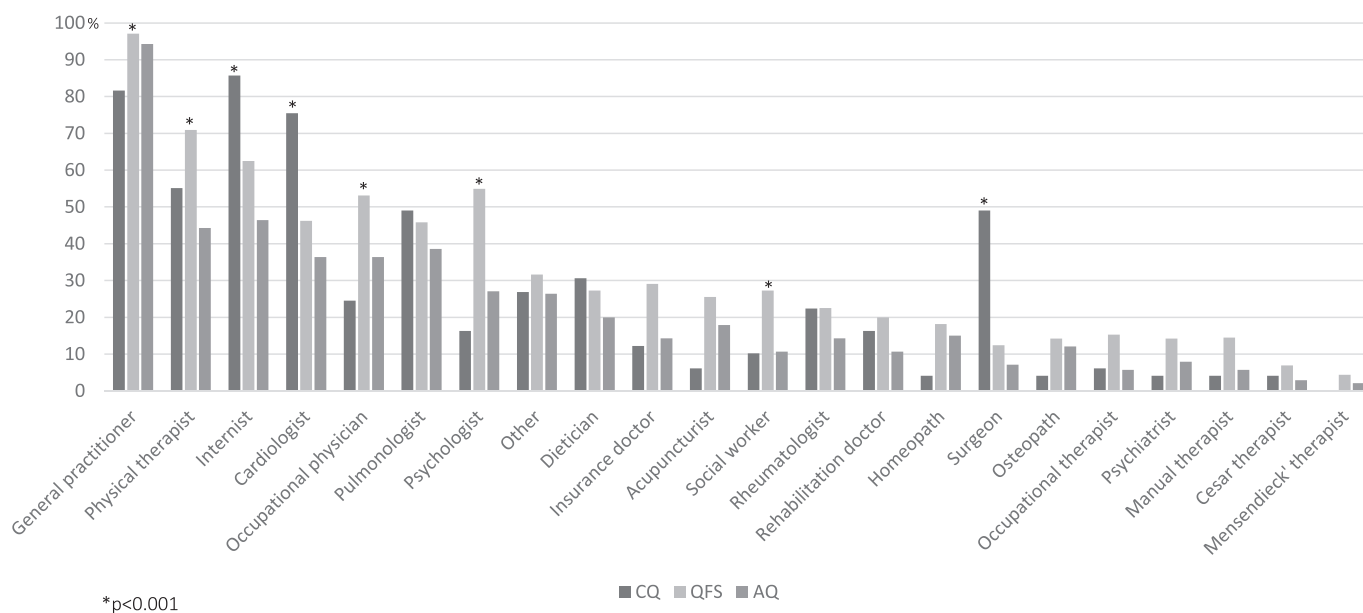
Fig. 4. Health care use (%) of chronic Q-fever patients (CQ), Q-fever fatigue syndrome patients (QFS) and patients with QFS-like disease (QLD).

*p<0.001

3.7. Health care providers

The median number of different health care providers the participants consulted for Q-fever related issues was 6.0 (4.0–8.0). There was a significant difference in the number of consulted health care providers between the three diagnosis groups ($\chi^2(2) = 42.08$, p < 0.001). QFS patients had the highest diversity in health care providers they consulted (median = 7.0, IQR 5.0–9.0) and QLD patients the least (median = 4.0, IQR 3.0–7.0). GP's, internists, and physical therapists were the three most often consulted health care providers, CQ patients also frequently consulted a cardiologist (75.5%). Fig. 4 shows the percentages and differences of the type of health care providers consulted by the three diagnosis groups. In addition, patients also indicated how often they visited these health care providers. On average, GP's were visited 27 times since they had Q-fever-related health complaints, while internists and physical therapists were visited respectively 10 and 73 times. Occupational physicians (12 times) and psychologist (22 times) were also frequently visited. There was a significant difference between the three diagnosis groups in the frequency of the visits to their health care providers ($\chi^2(2) = 58.06$, p < 0.001). QLD patients visited less frequently health care providers than QFS and CQ patients.

3.8. Health care satisfaction

On a scale of 1 to 10, Q-fever patients in this study awarded the care and support they received in the first 12 months after the infection with a median score of 3.0 (1.0–6.0), whereas the care in the period thereafter was awarded a median score of 5.0 (IQR 3.0–7.0) and in the last 12 months a 6.0 (IQR 3.5–8.0). There were significant differences in all three time periods between the three diagnosis groups (Table 3). Notably, CQ patients were most satisfied compared to the other two groups. Similarly, when asked how they would rate overall quality of care for Q-fever, CQ patients were most positive. On average, 75.0% of all patients gave a score of 5.0 or lower, on a 10-point scale (median 4.0, IQR 2.0–5.0). Most frequently mentioned barriers in health care included: lack of knowledge of Q-fever (28.6%), not feeling heard or understood (27.1%), and lack of availability of services (20.9%).

4. Discussion

The results of this study show that Q-fever has a considerable long-

term impact on health symptoms, health-related quality of life and participation. The majority of the Q-fever patients in the present study still faced several health problems 10 years after being infected. Fatigue, concentration problems, physical exhaustion and joint pain were most prevalent health problems. Health-related quality of life was low, especially regarding daily activities, cognition and pain. In addition, half of the Q-fever patients in this study reported serious problems with work and exercise, and more than a quarter experienced difficulties with leisure time, household and social contacts. Besides, more than one third (38.7%) stopped working permanently due to Q-fever. Patients that still worked, had to reduce their working hours by 50% on average. Overall, QFS patients reported the most problems, but CQ and QLD patients experienced similar long-term consequences.

Fatigue was the most reported health symptom within the three groups, which is in line with previous research [10,16,17]. The majority (87.1%) of Q-fever patients was severely fatigued. As expected, relatively more QFS patients were severely fatigued (94.5%) compared to CQ (73.9%) and QLD patients (77.1%). The mechanisms of post-infection fatigue are increasingly studied, however much is still unknown. Moreover, evidence-based treatment for chronic fatigue after infection is lacking. This is also reflected in patients' ratings on health care satisfaction. Three quarters of the patients was unsatisfied with the overall quality of care for Q-fever. Noteworthy, CQ patients were more satisfied compared to the other two groups. A possible explanation for this finding could be that chronic Q-fever is a recognised life-threatening disease while debate remains regarding the entity of post-infectious fatigue syndromes.

Recently, the concept of 'positive health' as proposed by Huber and colleagues is gaining ground within daily health care practice [26]. Positive health defines health not merely as 'the absence of disease' but as a broader concept that comprises different dimensions: bodily functions, mental functions, spiritual dimension, quality of life, social and societal participation and daily functioning. Literature shows a large discrepancy in the perception of health between patients and physicians [27]. Patients consider all health dimensions as equally important whereas physicians mainly assess health biomedically. More attention to quality of life, participation and daily functioning in medical practice may improve communication and patients' satisfaction. This may be particularly relevant for Q-fever patients in whom problems on all those dimensions are prominent, and current satisfaction with health care was extremely low.

Table 3
Health care satisfaction of all Q-fever patients, chronic Q-fever patients (CQ), Q-fever fatigue syndrome patients (QFS) and patients with QFS-like disease (QLD).

	Total	CQ	QFS	QLD	Difference
	median (IQR)	median (IQR)	median (IQR)	median (IQR)	χ^2 (p)
Satisfaction with received care and support					
In first 12 months	3.0	5.0	3.0	3.0	13.73
	(1.0–6.0)	(2.0–8.0)	(1.0–6.0)	(1.0–6.3)	(0.001)
Period in between	5.0	8.0	5.0	5.0	25.04
	(3.0–7.0)	(6.0–9.0)	(3.0–7.0)	(2.0–6.0)	(< 0.001)
In last 12 months	6.0	8.0	6.0	6.0	25.46
	(3.5–8.0)	(6.0–10.0)	(3.0–8.0)	(3.0–7.0)	(< 0.001)
Satisfaction with overall quality of care for Q-fever					
Total score (1 − 10)	4.0	5.5	3.0	4.0	13.34
	(2.0–5.0)	(2.8–7.0)	(2.0–5.0)	(2.0–6.0)	(0.001)

Note. Health care satisfaction is measured on a 10-point scale (1 = not satisfied at all, 10 = very satisfied).

Quality of life of our study population was much lower than that of the general Dutch population [24]. The problems reported with usual activities like work, study, housework, family or leisure activities were 6-fold higher for Q-fever patients than for individuals in the Dutch population [24]. Cognitive problems (memory and concentration) were even 10-fold higher in Q-fever patients than in the Dutch population. Pain or discomfort was also frequently reported by Q-fever patients in the present study, 88.5% reported pain compared to one-third of the Dutch population. In addition, health-related quality of life index scores were severely impaired compared to the average Dutch index score (0.88). Particularly in women, younger patients and patients in their fifties. Overall, QFS patients reported poorer quality of life than QLD and CQ patients. Nevertheless, QLD and CQ patients also showed severe quality of life problems compared to the healthy population. Concerning participation, half of the Q-fever patients had serious problems with work, study and exercise, while more than a quarter experienced difficulties with leisure time, household and social contacts. This underlines the immense consequences for participation as well. Findings are in line with a recent comparable study in The Netherlands [16] that showed Q-fever patients had a lower quality of life, more anxiety, and lower levels of social functioning compared to the general population. In addition, QFS patients had significantly higher levels of anxiety and lower levels of social functioning compared to patients with chronic Q-fever, which was similar to our study.

One of the most striking findings of this study was the impact on work participation. More than one third (38.7%) of the patients with a paid job stopped working permanently. Patients that were still working, had on average a 50% reduction of their working hours. In addition, a quarter received a disability benefit at the time of data collection. There were some differences between the subgroups on work participation. First of all, prior to the Q-fever infection more CQ patients were already retired. Nevertheless, the majority of CQ patients had to stop working due to Q-fever. QLD patients generally worked less for a period but were able to return to pre-infection working hours later. QFS patients were most often disabled for work and received a disability benefit. According to a study on the economic consequences of the Q-fever outbreak in The Netherlands [28], the estimated income loss due to QFS was one of the major economic costs during the outbreak. Altogether, alongside the major negative impact on health status, Q-fever has significant socioeconomic implications.

The socioeconomic burden of QFS is not only caused by the absence from work but also by increased health care consumption [5]. Health care use in our study was high, within all patient subgroups. On average, patients consulted six health care providers for Q-fever related problems in the last 10 years. The health care providers most frequently seen were GP's, physical therapists, and internists. Patients were most satisfied with the health care they received in the last year. Knowledge of the long-term consequences of Q-fever is crucial for health care providers to enable them to understand and support these patients

adequately and refer them to specialised health care e.g. Q-fever expertise centre.

The present study has several strengths, including the relatively large sample size, the examination of three different diagnosis groups, the long follow-up, and the availability of normative data of the Dutch population. This study also has some shortcomings that should be mentioned. At first, recall bias could have occurred as participants were asked to recollect past events within a 10-year recall period. Recall bias can be defined as a systematic measurement error, due to selective memory or other content-related reporting effects [29]. The usual direction of recall bias is that poor health in the past is memorized as even more deteriorated as it actually was. However, the reverse may also happen. As such, true health impact might be overestimated or underestimated. Another concern related to bias was the non-response. A total of 54.3% responded to our questionnaire, which may not be representative for all Q-fever patients, however this response rate is comparable with other long-term Q-fever studies [5,17]. Furthermore, the classification of the diagnosis groups was based on self-report and not on a clinical diagnosis. This may be particularly difficult for patients, when even international clinical definitions of long-term post-infectious fatigue syndromes are not uniform. Finally, we did not study the underlying mechanism for the development of long-term health consequences of Q-fever. For future studies, examining aetiology and predictors for long-term reduced health status would be of interest.

Despite these shortcomings, this study extends the existing literature on the long-term consequences after a Q-fever outbreak. This study highlights the enormous health impact of Q-fever even after ten years, and shows Q-fever has significant long-term socioeconomic implications as well. In light of the recent international COVID-19 Coronavirus outbreak these findings are even more important, and underline the importance of effective public health strategies to prepare for, and respond to the long-lasting consequences of zoonotic disease outbreaks.

Authors' contributions

Study conception and design: AOL, AG, JH, VE and SP; Data collection: MB, RK, LB and VE; Analysis and interpretation of data: MB, MD, JH, LB and SP; First drafting of the manuscript: MB, MD, JH and SP; Critical revision for important intellectual content: MB, JH, MD, LB, RK, AOL, AG, VE and SP; final approval of the version to be published: MB, JH, MD, LB, RK, AOL, AG, VE and SP. All authors participated sufficiently in the work to take public responsibility for appropriate portions of the content; and agree to be accountable for all aspects of the work.

Ethics approval and consent to participate

The Ethics Review Board of Erasmus MC - Rotterdam approved the study protocol (METC 2018–1605); Online informed consent was obtained from all participants.

Availability of data and materials

Anonymised datasets can be made available on reasonable request to the corresponding author.

Consent for publication

Not applicable.

Declaration of Competing Interest

The authors declare that they have no competing interests.

Acknowledgments

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