

# Q fever

**Chantal Bleeker-Rovers**  
**Radboud Expertise Center for Q fever**  
**Nijmegen, the Netherlands**

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# History

1935 - Edward Holbrook Derrick, Queensland

- Severe outbreaks among abattoir workers: **Query** fever



Derrick

1936 – Simultaneous isolation

- **Cox** & Davis – ticks from ‘Nine Mile creek’ in Montana
- **Burnet** – patients Edward Holbrook Derrick



Cox

1938 – Microorganisms **Cox** & **Burnet** identical

Q fever, zoonotic disease resulting in outbreaks caused by intracellular coccobacillus *Coxiella burnetii*



Burnet

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# Epidemiology and disease in animals

## Epidemiology

- Found world-wide, most likely endemic everywhere but New-Zealand
- >40 tick species
- Birds, deer, wild boars, hares, raccoons, skunks, seals, sea lions, kangaroos
- Domestic ruminants (seroprevalence in cattle 82%, sheep and goats 73%)
- Cats and dogs

## Symptoms:

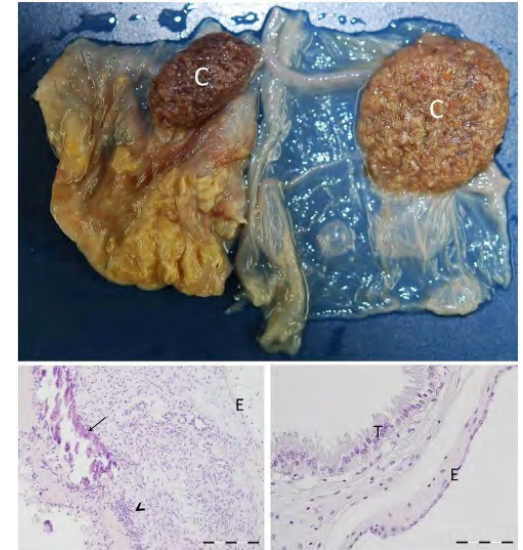
- In non-pregnant animals virtually asymptomatic
- Most important clinical presentations: abortion and stillbirth
- Abortion most frequently at the end of gestation without previous symptoms



# Burden of disease in animals

Excretion routes:

- Massive excretion of bacteria during abortions
- But: excretion of comparable numbers of bacteria during normal parturition in goats, also in sheep
- Also excretion in feces, vaginal mucus and milk



During the Dutch Q fever outbreak:

- Abortion in 40% of the pregnant goats on Q fever infected farms
- Aborting animals recover rapidly, milk production hardly affected

# Human infection

- Most often infection by inhalation of infected aerosols
- Airborne spread over a range of many kilometers
- A single bacterium can cause seroconversion
- No human to human transmission except during child birth and with blood transfusion, very rarely sexual transmission



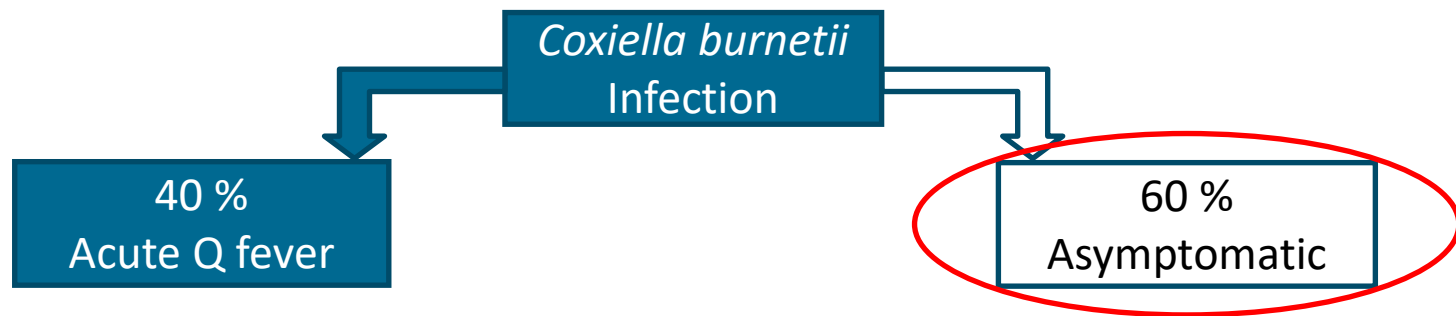
# Human infection

- Highest exposure rates in people with frequent livestock contacts:
  - 65 and 72% of persons living and/or working on dairy cattle farms seropositive (Canada and NL)
  - 74% of goat farmers seropositive (NL)
  - 65% of veterinarians seropositive (NL)
- Multiple outbreaks involving laboratory staff
- But also in humans without any animal contacts (in the Netherlands many people live < 5km of a goat farm)!



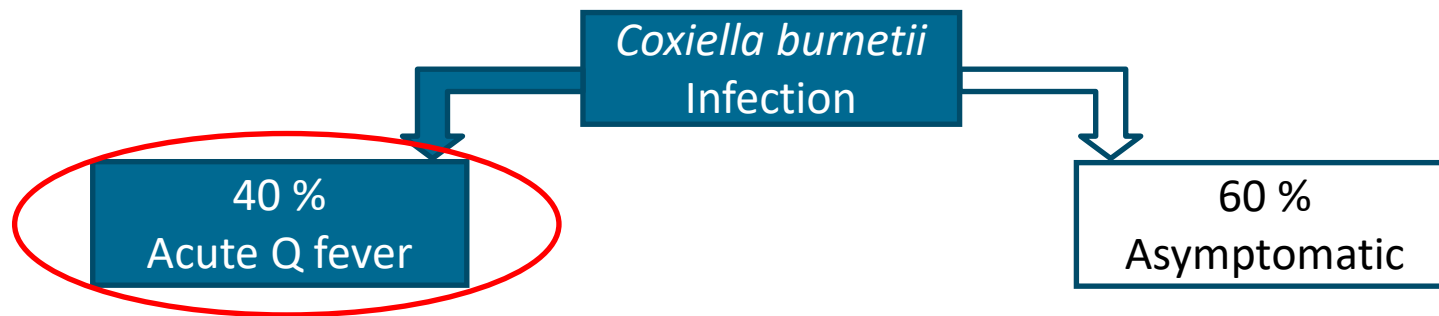
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# Human infection



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# Human infection





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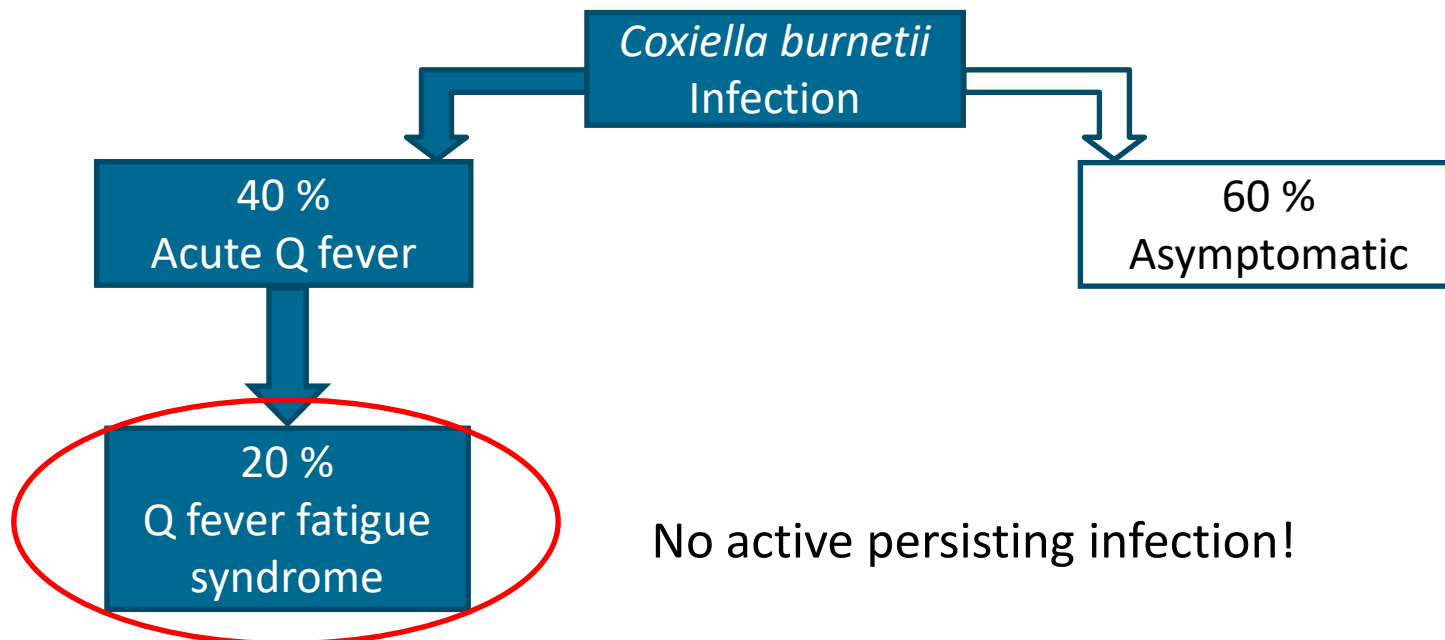
# Acute Q fever

- Often: fever, headache, fatigue
- Sometimes: nausea, vomiting, diarrhea, cough, rash
- Pneumonia, hepatitis
  
- Hospitalization around 20%, mortality <2%
  
- Diagnosis:
  - Positive PCR with compatible symptoms
  - Multiple serological samples with significant rise in titer or seroconversion
  
- Treatment: 2 weeks doxycycline (alternatives: quinolone, co-trimoxazole)



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# Q fever fatigue syndrome



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# Q fever fatigue syndrome

## Diagnosis:

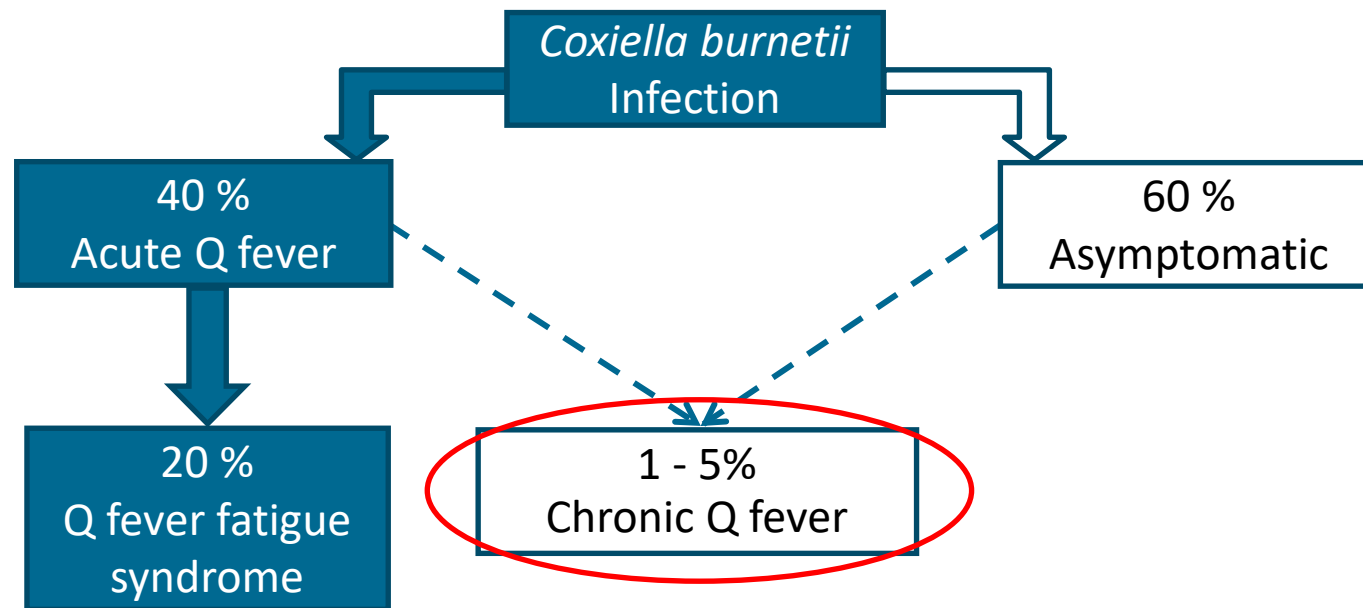
- Severe fatigue >6 months following a symptomatic acute Q fever
- Severe limitations due to fatigue
- No chronic Q fever
- No other explanation for the fatigue

## Treatment and prognosis:

- Long-term doxycycline not effective
- Cognitive behavioral therapy partly effective, effect disappears after 1 year
- No significant improvement over time
- High impact on quality of life and work status

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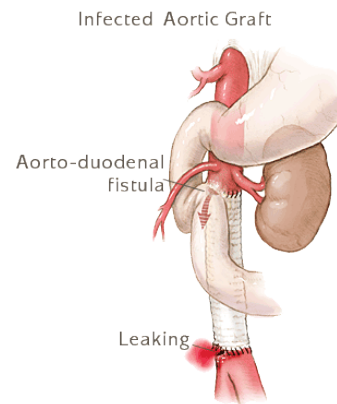
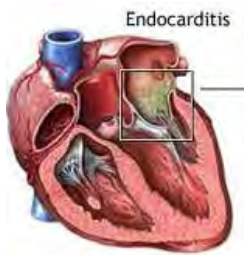
# Chronic Q fever



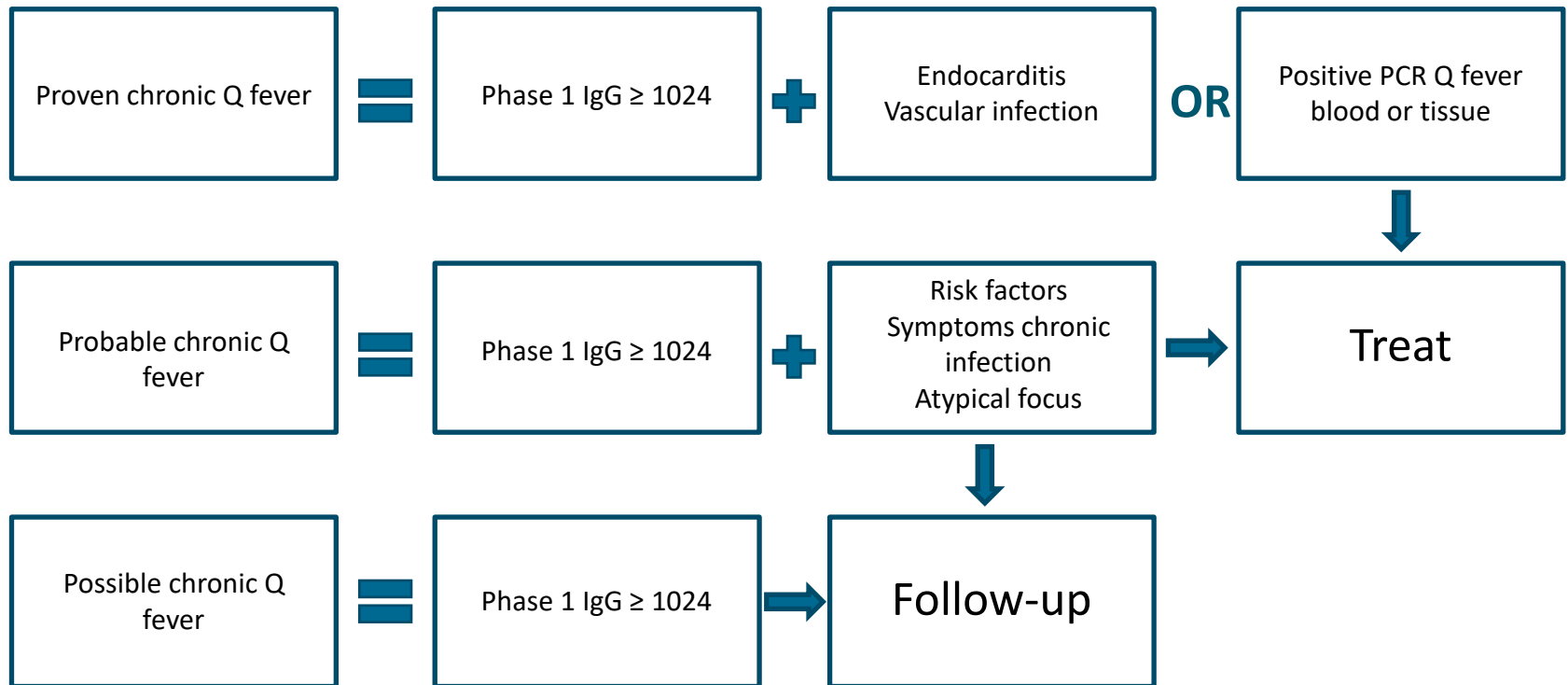
# Symptoms chronic Q fever



- Months to years following the acute infection
- >50% no symptoms
- Clinical manifestations:
  - Endocarditis (NL 35% of all chronic Q fever, underlying valve disease)
  - Mycotic aneurysms, infected vascular prostheses (NL 65%)
  - Chronic Q fever in pregnancy
  - Bone and joint infections



# Definition/diagnosis chronic Q fever



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# Treatment of chronic Q fever

- First choice: doxycycline with hydroxychloroquine (increases pH in phagolysosome) but many side effects:
  - Gastrointestinal
  - Phototoxicity (>90%)
  - Cutaneous hyperpigmentation
- Alternative regimens:
  - Moxifloxacin
  - Co-trimoxazole



# Treatment of chronic Q fever

- Treatment duration endocarditis at least 18 months
- Prosthetic heart valve at least 24 months
- Treatment duration in vascular infection unknown, in clinical practice (much) longer
- Mortality 26.5% in proven chronic Q fever



“Q fever deadlier than expected”





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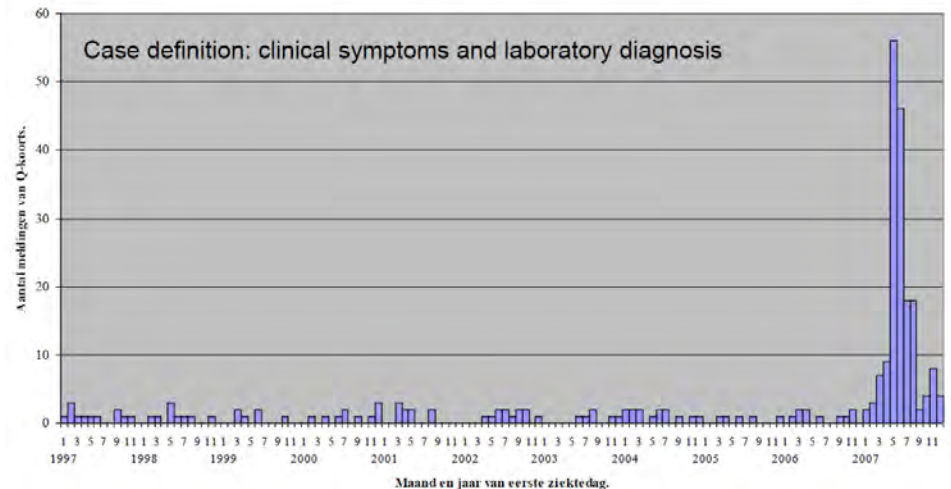
# Q fever outbreaks

- Outbreaks from a few to 400 laboratory-confirmed human cases are reported frequently world-wide
- Number of human infections estimated to be 10 times higher
- Usually geographically localised and restricted to one episode
- Source of outbreaks:
  1. Sheep
  2. Goats
- No association between cattle farms and outbreaks while seroprevalence is high: cattle related genotypes less virulent for humans, why?

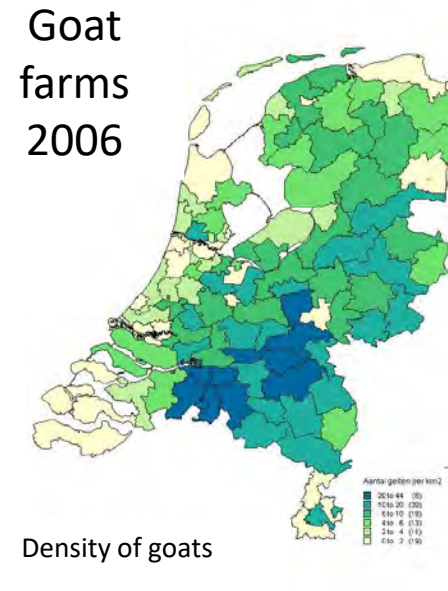
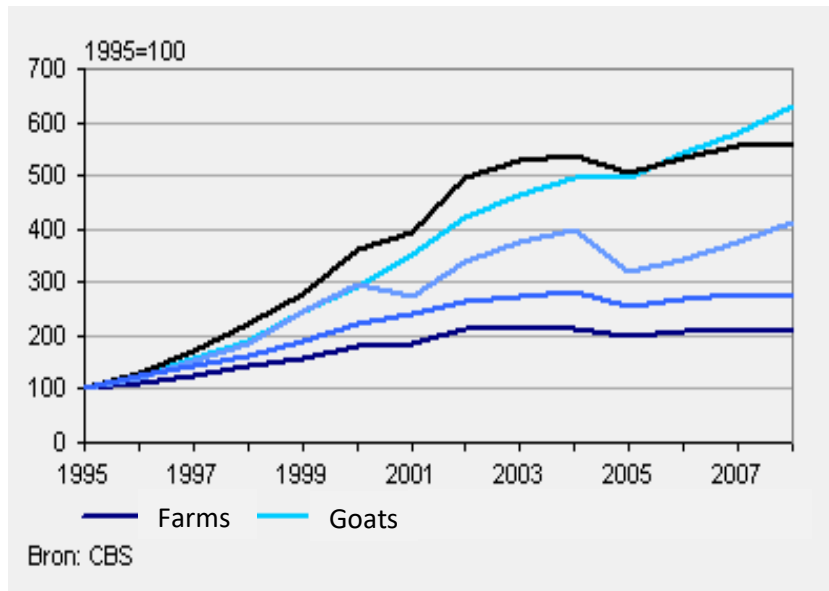


# Dutch outbreak

- Village of Herpen, May 2007: local family doctor reports an unusually high number of patients with atypical pneumonia
- Serology: Q fever



# Cause of the outbreak



- Strong increase in the number of dairy goat herds and goat numbers in recent years in close proximity to highly populated areas
- Epidemiological link
- Confirmed by genotyping data

# Dutch outbreak

	2005	2006	2007	2008	2009	2010	2011	2012	Total
Goats									
Number of confirmed Q fever abortion farms (dairy goats and dairy sheep) each year	2	7	7	8	6	0	0	0	30
Number of BTM <i>Coxiella burnetii</i> DNA positive farms					62	32	8	3	105
Culled animals	0	0	0	0	7,755	50,395	0	0	58,150
Breeding prohibition	0	0	0	0	0	46,130	n.k.	n.k.	46,130
Vaccinated animals	0	0	0	0	158,019	346,463	344,424	n.k.	848,906

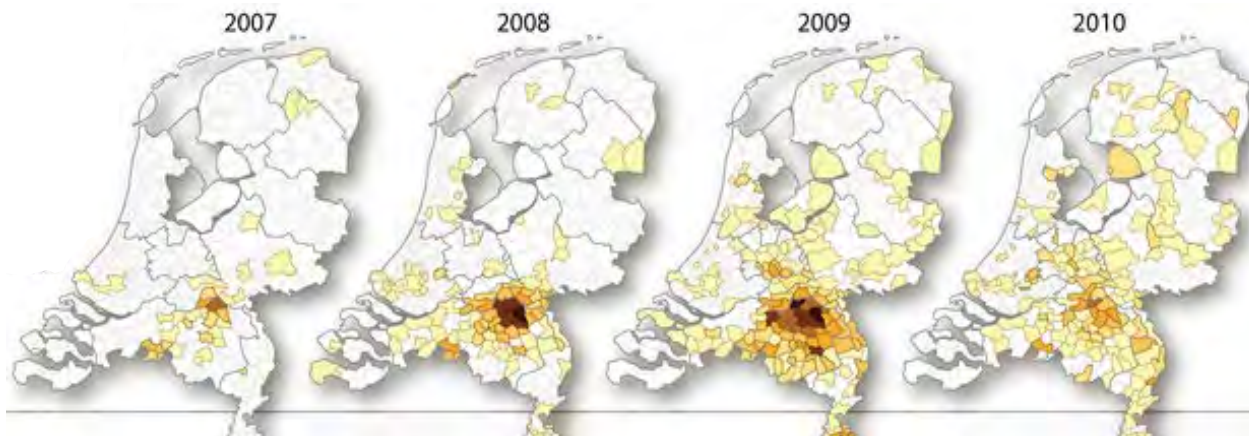
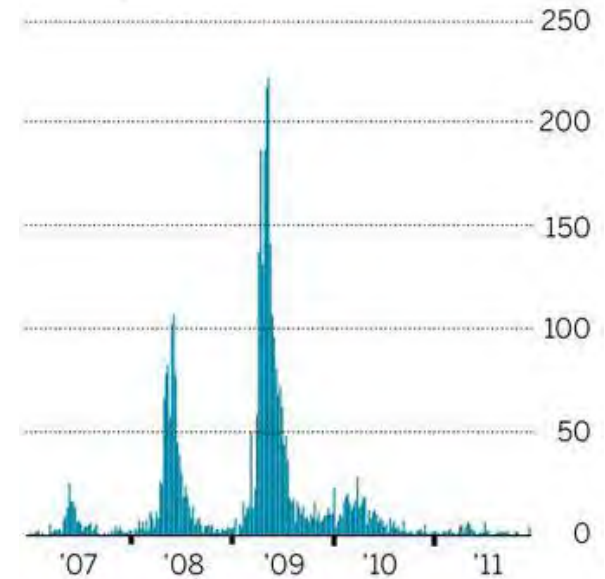
- Outbreak recognized 2 years earlier in dairy goat and sheep farms
- Hygiene measures and voluntary vaccination not enough to stop human infections
- Culling of all pregnant goats on Q fever positive farms and mandatory vaccination ended the outbreak



# Dutch outbreak

Largest outbreak ever described worldwide:

- > 4000 reported cases of acute Q-fever (9†)
- > 44,000 people infected
- > 500 patients diagnosed with chronic Q fever (update 2018: 86†)



# Costs Dutch outbreak

Results of social-economic assessment Q fever outbreak in the Netherlands 2007–2011.

Variable	Value <sup>2</sup>	Unit
Production loss agricultural sector	≈0	Million Euro/outbreak
Loss public sector	222	Million Euro/outbreak
Intervention costs	85	Million Euro/outbreak
Loss total	307	Million Euro/outbreak
Disease burden	2462	DALY
Disease burden total acute Q fever	22	DALY
Disease burden total chronic fatigue syndrome	1481	DALY
Disease burden total chronic Q fever	806	DALY
Disease burden deceased	153	DALY

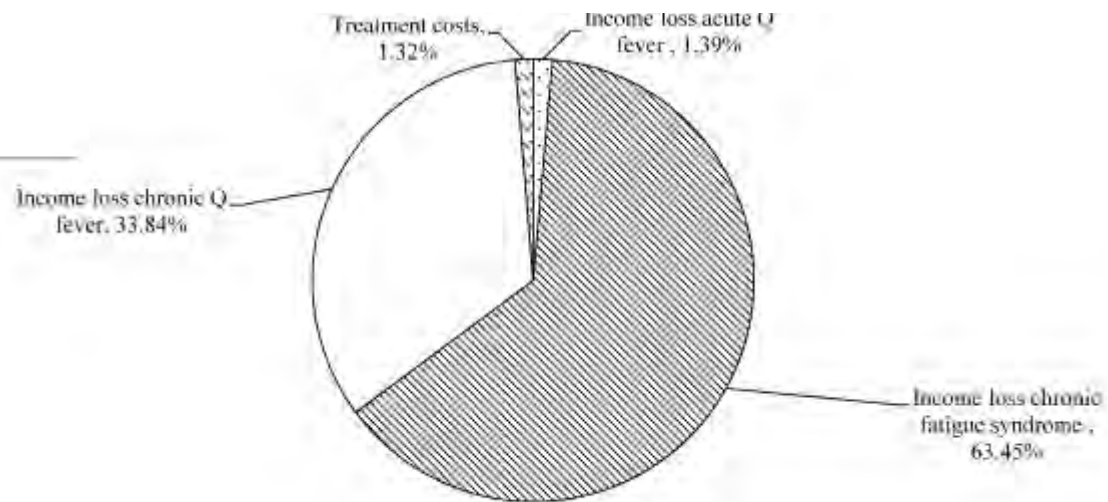


Fig. 2. Decomposition of public health costs.

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# Conclusions

- *C. burnetii* can be excreted without clinical signs of Q fever in the herd
- Acute Q fever occurs in humans without animal exposure
- Q fever outbreaks:
  - Major impact on public health with severe long-term effects and deaths
  - High costs in both livestock sector and health sector
- Early recognition: abortion storms on farms, unusual cluster of human atypical pneumonia cases
- Quick source identification: epidemiological examination, confirmed by genotyping
- Fast response: one health approach!
- Prevention: vaccination of sheep and goats in highly populated areas very effective in preventing human cases