



Universiteit Utrecht



# Vaccination of small ruminants to prevent Q fever in humans: evidence from the Dutch context

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Based on work by  
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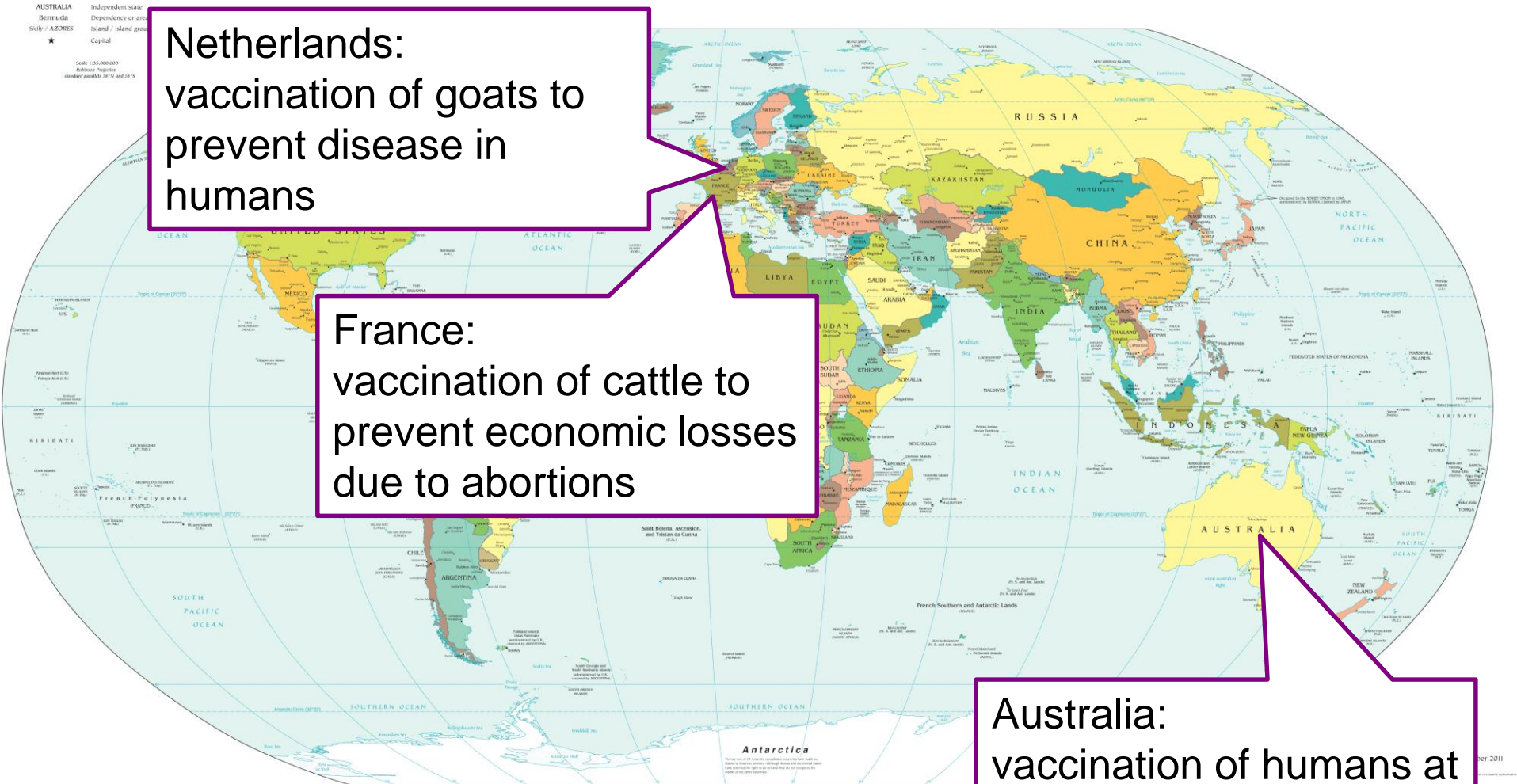


# Q fever vaccination worldwide

Netherlands:  
vaccination of goats to  
prevent disease in  
humans

France:  
vaccination of cattle to  
prevent economic losses  
due to abortions

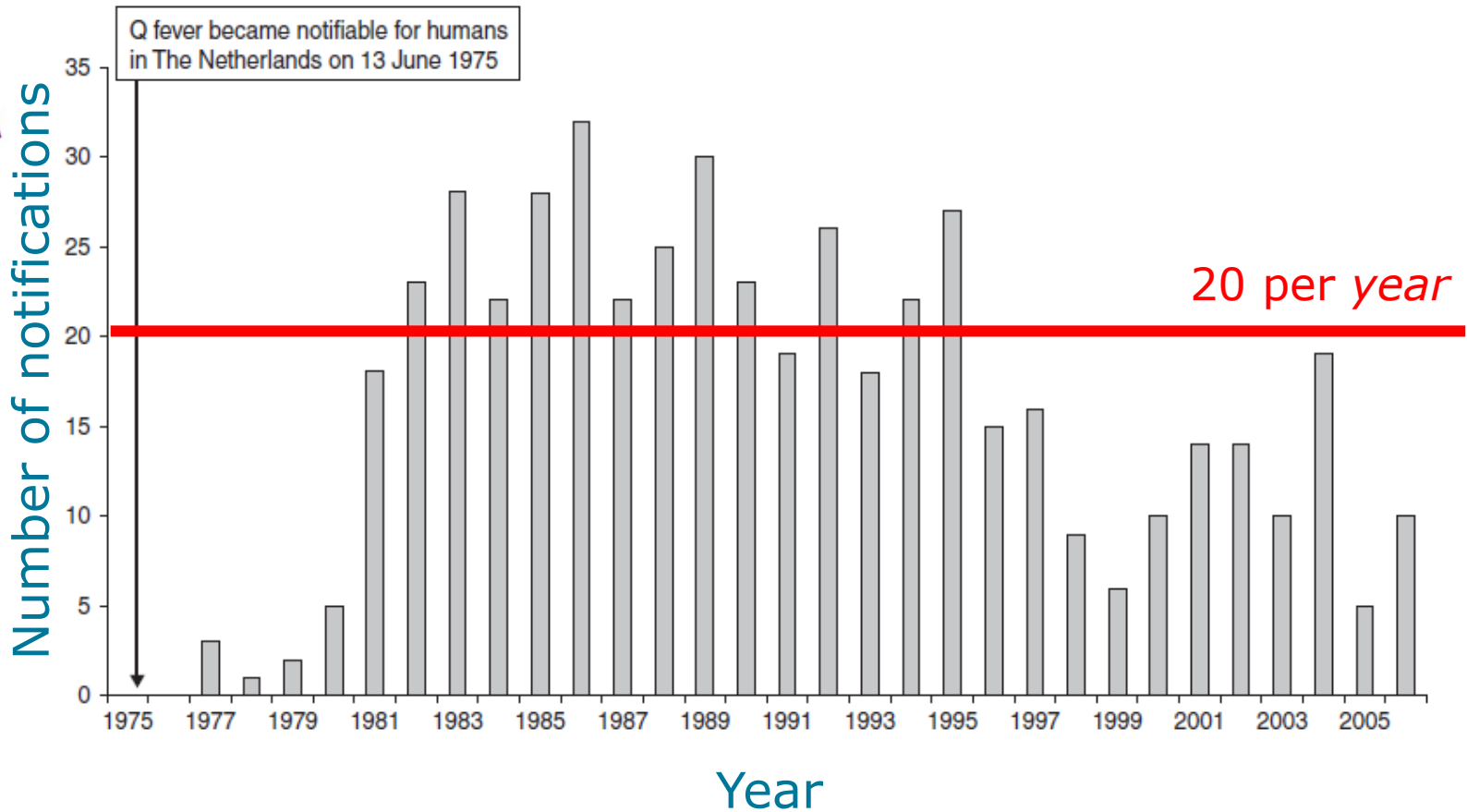
Australia:  
vaccination of humans at  
risk by occupation





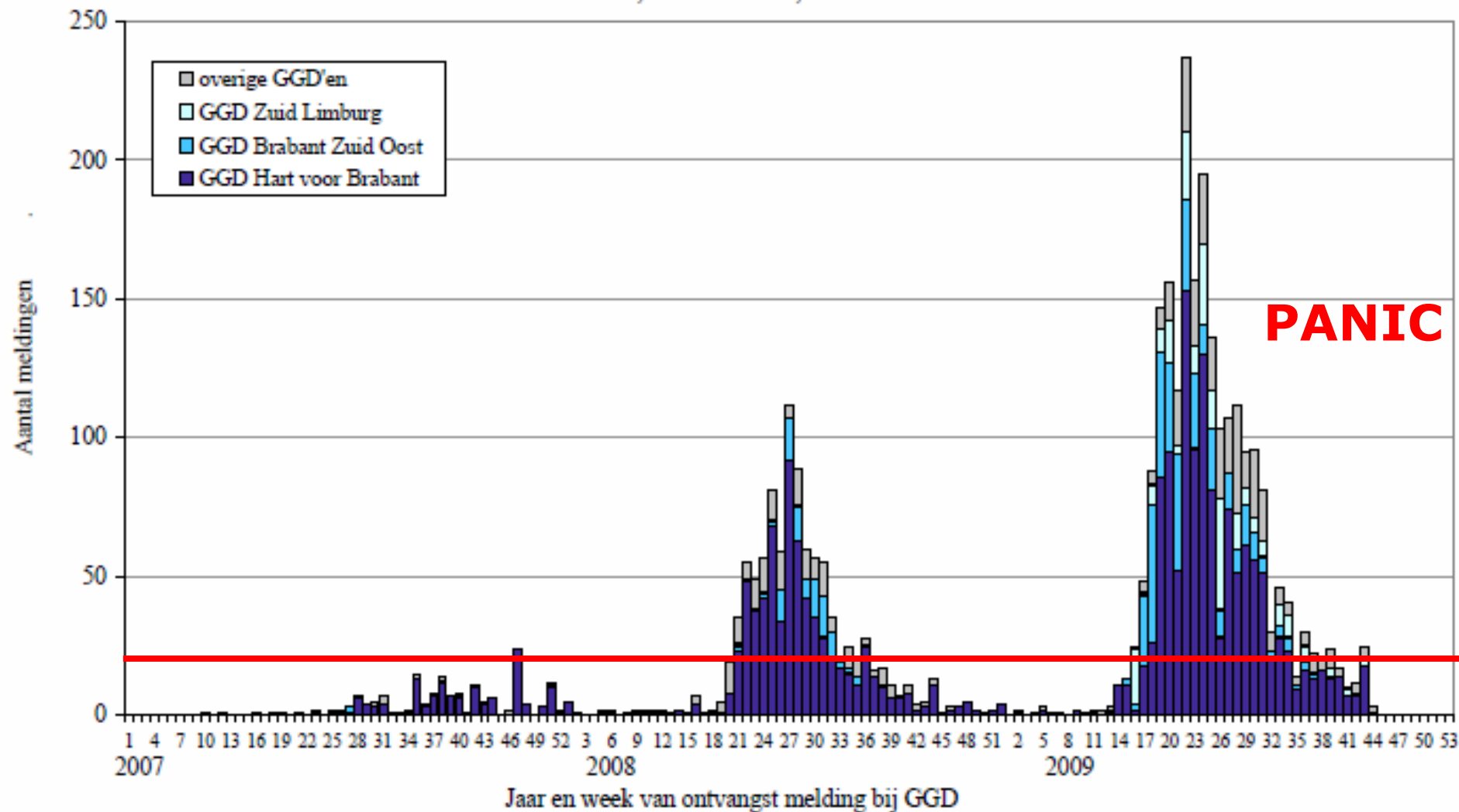
# Human situation 1975-2006

~20 notifications/yr in The Netherlands,  
sporadic, often occupational



Aantal gemelde patiënten met Q-koorts naar week van ontvangst melding bij de GGD,  
periode 01-01-2007 t/m 28-10-2009.

2007: N=168, 2008: N=1000, 2009: N=2236





# Q-fever damage control end 2009, for dairy goats/sheep

- Vaccination zone (before breeding)
  - Coxevac (phase 1, inactivated Cb)
- Bulk milk tank surveillance (Oct.)
  - PCR, twice monthly
  - positive and negative herds
- Movement control & breeding ban
- **Culling of all pregnant animals (Dec.)**
  - **From PCR bulk milk positive herds**

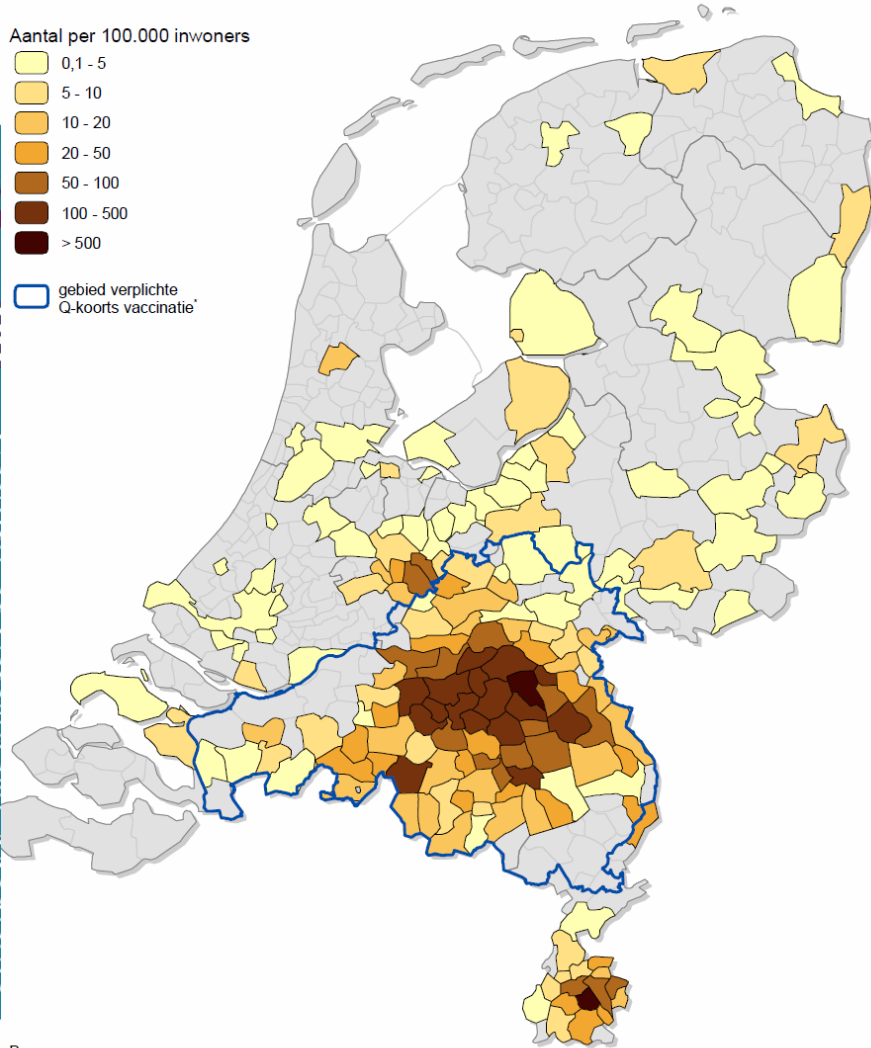
# Gemeelde Q-koortspatiënten 2009

Incidentie per gemeente  
1-1-2009 t/m 27-10-2009 (17:00)

Aantal per 100.000 inwoners

- 0,1 - 5
- 5 - 10
- 10 - 20
- 20 - 50
- 50 - 100
- 100 - 500
- > 500

gebied verplichte  
Q-koorts vaccinatie\*



Bronnen:  
- OSIRIS  
- CBS (2009)

\*) Gebied waar in 2009 vaccinatie tegen Q-koorts verplicht is voor schapen en geiten op professionele melkgeiten- en melkschapebedrijven en op bedrijven met een publieksfunctie.  
Bron: Ministerie van LNV

**rivm**

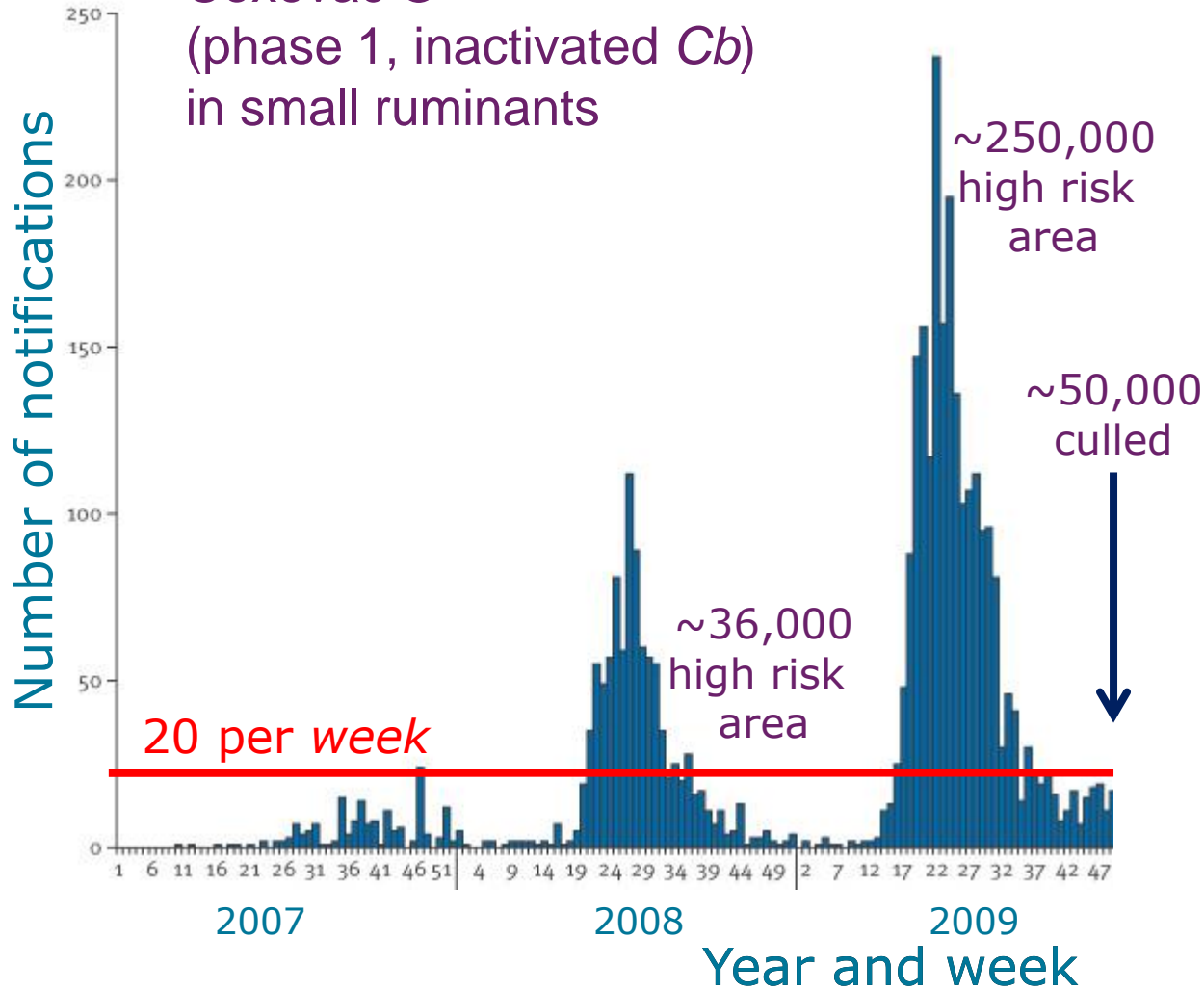


Faculty of Veterinary Medicine



# Q-fever vaccination campaign

Coxevac<sup>®</sup>  
(phase 1, inactivated *Cb*)  
in small ruminants



(Figure: van der Hoek et al, 2012)



# Q-fever vaccination effect ? In small ruminants (in 2009)

Effect on clinical disease ~ control

- Less abortion (Arricau et al, 2005)

Effect on infection process ~ transmission

- Less susceptibility (Cattle: Guatteo et al, 2008)
- Less infectivity (shedding) (Rousset et al, 2009)

Impossible to study in spring 2010: culling...

- Test culled animals ?
- Vaccinated versus unvaccinated herds
- Nulliparous versus older animals





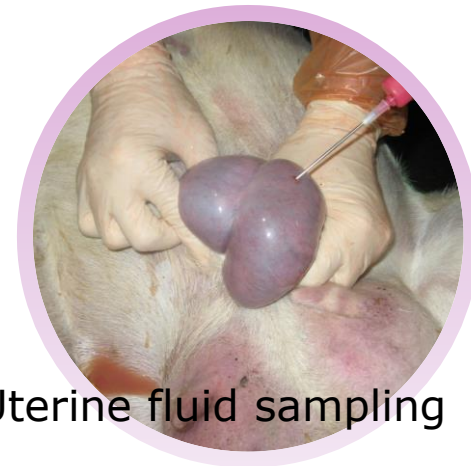
# Sampling at rendering plant

## Purpose

to quantify the effect of vaccination on prevalence and bacterial load in uterine fluid, vaginal mucus and milk of culled pregnant animals

## Samples

- ~ 1000 pregnant animals from 13 bulk milk positive herds
- 7 vaccinated and 6 unvaccinated herds
- Old (parous) and young (nulliparous) animals
- Split into 4 analysis groups
  - Unvaccinated young
  - Unvaccinated old
  - Vaccinated young
  - Vaccinated old



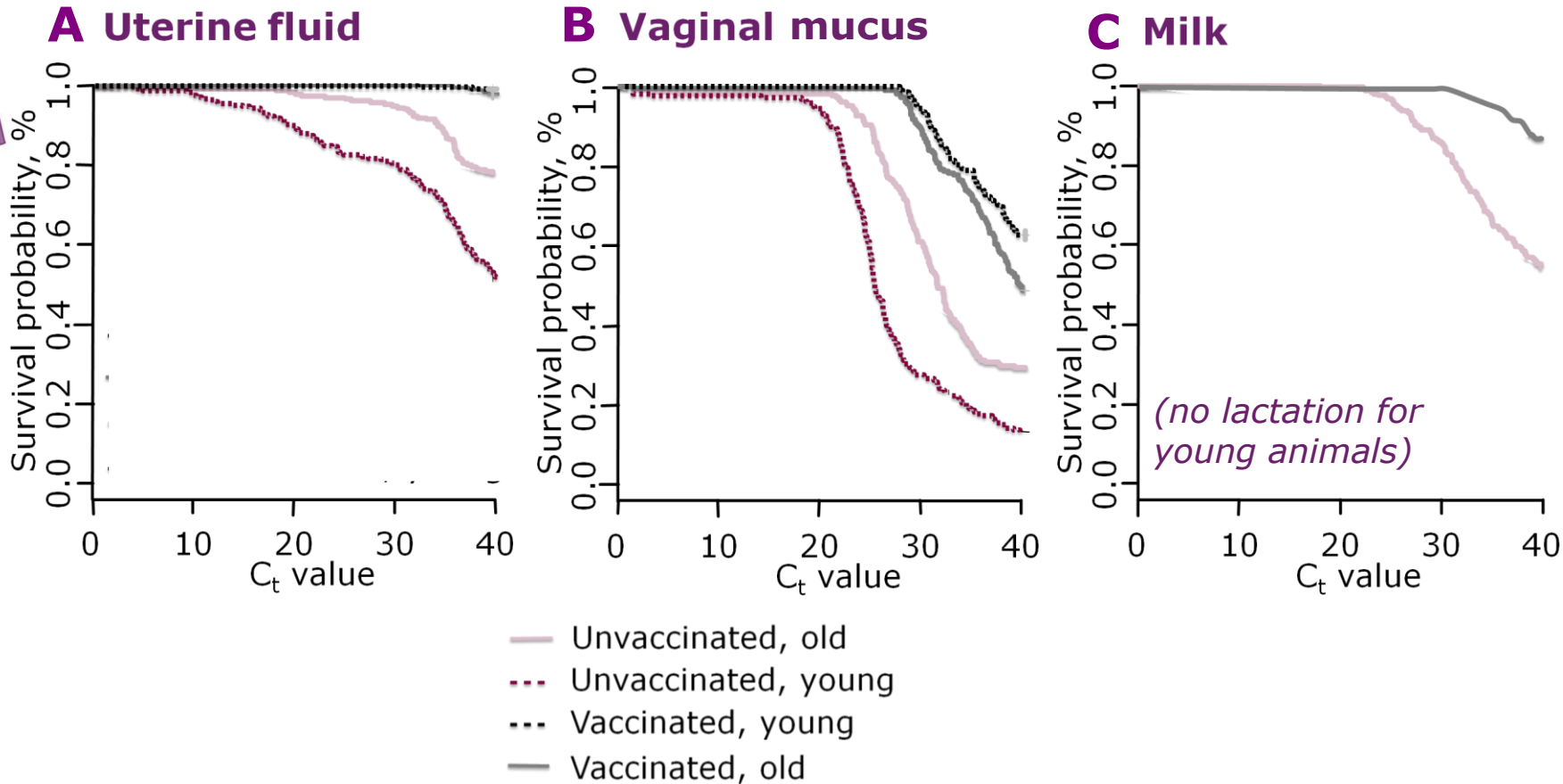
Uterine fluid sampling

# Sampling at Rendac





# Sampling at rendering plant – Quantitative PCR results



*Kaplan-Meier curves for cycle threshold (C<sub>t</sub>) values for C. burnetii*



# Sampling at rendering plant

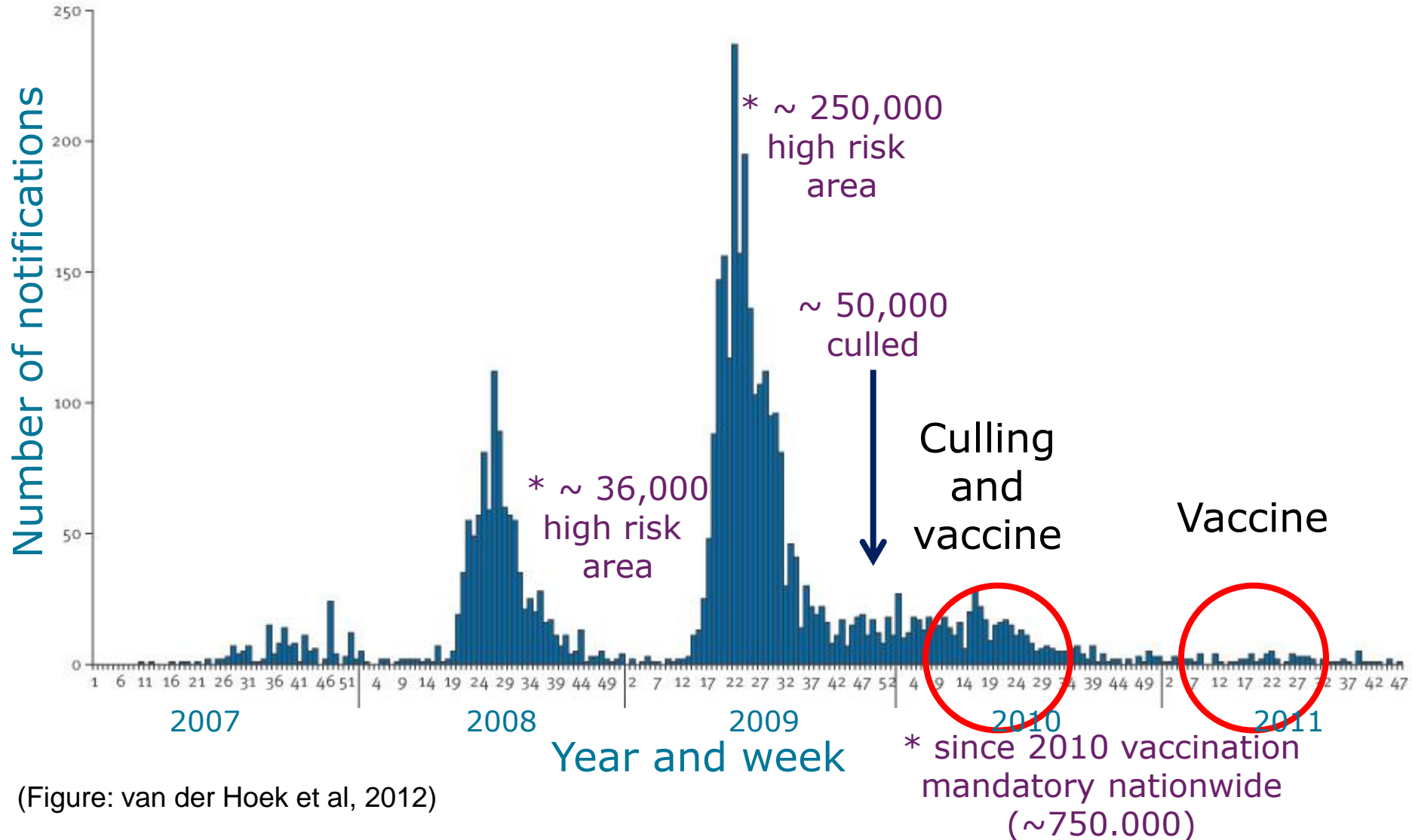
## Results

- Prevalence and bacterial load reduced in vaccinated animals
- Effects most pronounced in animals during their first pregnancy

Does this imply that this may reduce the load in the environment and human exposure to *Coxiella burnetii*?

- *How strong is this evidence ?*
- *How often/long vaccination of dairy animals ?*
- *Scale down strategy possible ?*

# Q-fever vaccination campaign



(Figure: van der Hoek et al, 2012)

# Drawbacks of vaccination ?

## in small ruminants

### Side effects (Vellema and v.d. Brom, oral communication)

- local reaction near to the injected area: common
- clinical signs: (very) mild
- feed intake and milk yield: farmers report problems
- possibly depending on previous exposure/vaccination?

### May not be effective in animals that are

- pregnant → not proven effective (Guatteo et al, 2008 (cattle))
- already infected → less effective (de Cremoux et al, 2012)

### Costs

- In non-infected herds



# When to start vaccination? in small ruminants

## **Herd health management perspective:**

- Common infection in ruminants, usually asymptomatic
- Vaccination in response to disease problem
- Individual strategy per farm by farmer and veterinarian

## **Public health perspective:**

- Outbreak in the general population
- Precautionary principle
- Preventive vaccination in goats
- Vaccination obligatory



# Is a vaccinated herd free ?

- Technical problems with
  - Serology: all animals titer
  - Clinical symptoms: very few/no
  - Pathogen detection: bulk milk PCR ?

→ Not easy to declare a vaccinated herd free of Q fever





# When to stop vaccination? in small ruminants

## Consequences of stopping vaccination

- Infection is still present → increase (Modeling work: Courcoul et al 2011 (cattle))
- Free of Q fever → (re-)introduction?
  - if animals are immune → little risk
  - if no immunity → possible risk of epidemic
- In Netherlands stopping no option
  - Risk for human infection perceived high
  - Political sensitive
  - ‘Cheap’ solution for human health (van Asseldonk et al 2013)



# Risk of (re-)introduction into free, non-vaccinated herd without immunity

Risk of introduction unknown

Detection mainly around kidding / abortion

→ Detection too late to intervene ?

→ Contingency plan ?

- Vaccine in pregnant animals ?
- Culling ?
- Antibiotic treatment ?

Switzerland Tessin 2019

movement restriction

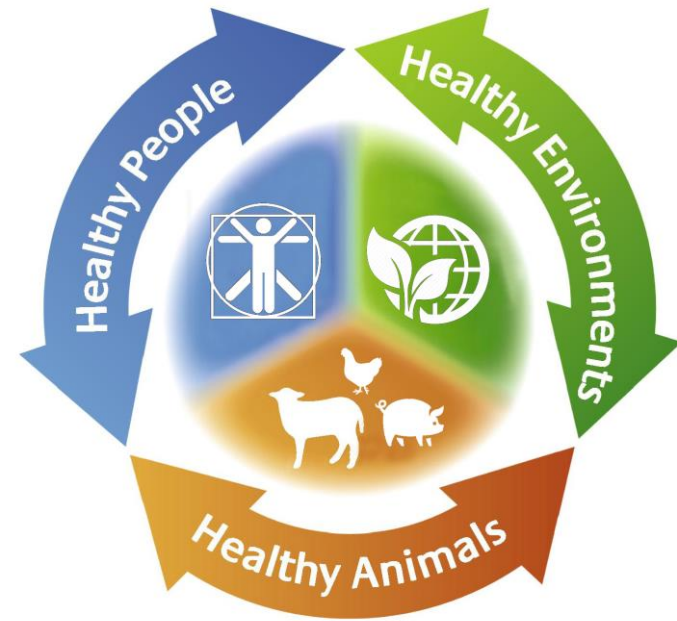
cull infected animals

vaccination ?

The screenshot shows a news article from FM1 Today. The headline is "Tessin: Mehrere Personen an Q-Fieber erkrankt". Below the headline, there are social media sharing icons for Facebook, Twitter, and Email. The date "03.06.2019" and "Kommentare" are visible. The main image shows two goats standing on a rocky outcrop in a mountainous landscape. Below the image, there is a caption: "Meist tragen die Ziegen das Bakterium in sich, welches das Q-Fieber auslöst. (Archivbild) © KEYSTONE/ALEXANDRA WEY". The article text below the image reads: "Im Tessiner Maggiatal sind in den vergangenen Wochen mehrere Fälle von Lungenentzündungen aufgetreten. Die Betroffenen sind mit dem Q-Fieber infiziert worden. Die Lage ist aber gemäss den Gesundheitsbehörden unter Kontrolle. Das Q-Fieber wird von einem Bakterium übertragen, das sich bei den Ziegen findet. Die Tessiner Gesundheitsbehörden haben deshalb die Impfung von exponierten Tieren angeordnet. Zudem wurde der Transport der Tiere von einem Betrieb zum anderen untersagt. Die Infektion über die Milch der Ziegen wird als sehr wenig wahrscheinlich eingestuft. Auch von Mensch zu Mensch wird die Krankheit nicht übertragen. Das Q-Fieber äussert sich in grippeähnlichen Erkrankungen, allerdings ohne Schnupfen oder Halsschmerzen. In ein bis zwei Prozent der Fälle..."



# Take Home OH



- Goat system changed
- Pathogen 'multiplied'
- Environmental contamination (de Rooij et al 2018)
- General population exposed & ill
- Culling & Vaccination goats
- Vaccination goats
- General population protected



**Thank you!**



# Sampling at rendering plant

## A: Prevalence uterine fluid

Group	OR (95% CI)
Unvaccinated, young	1
Unvaccinated, old	0.44 (0.25–0.78)
Vaccinated, young	0.005 (0.0002–0.12)
Vaccinated, old	0.03 (0.002–0.58)

*Multivariate logistic regression of prevalence of *C. burnetii* in uterine fluid. A random herd effect was included. OR= odds ratio.*



# Sampling at rendering plant

## A: Bacterial load uterine fluid

Group	HR (95% CI)
Unvaccinated	1
Vaccinated	0.49 (0.39 – 0.70)

*Univariate survival analysis of PCR  $C_t$  values for *Coxiella burnetii* in positive uterine fluid samples ( $C_t \leq 40$ ). HR= hazard ratio.*