



National Institute for Public Health
and the Environment
Ministry of Health, Welfare and Sport

PH impact Lyme disease: approach in the Netherlands

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2. Doctors and patient questionnaires
3. Web-based prospective surveillance
4. Clinical study

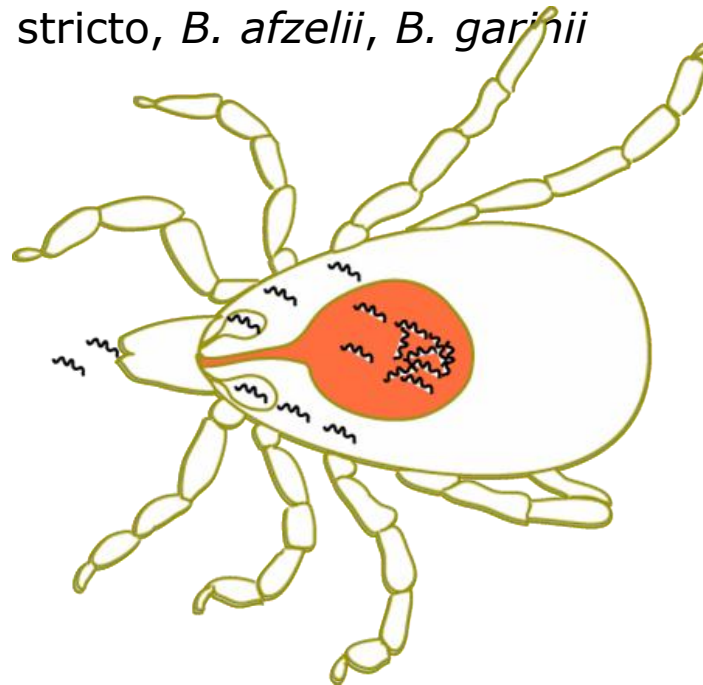


Lyme in the Netherlands



Transmission of Lyme disease

Lyme disease in Europe is caused by the *Borrelia burgdorferi* sensu lato group; *B. burgdorferi* sensu stricto, *B. afzelii*, *B. garinii*

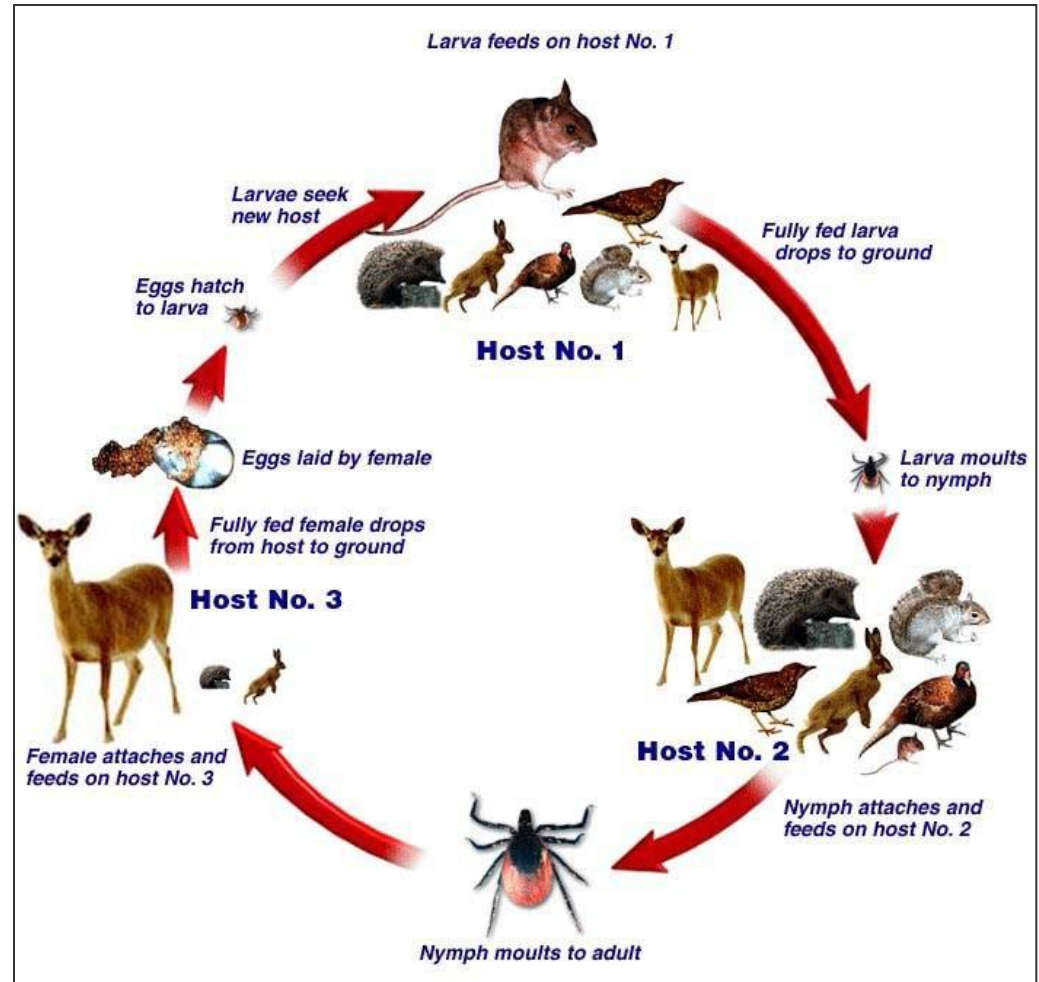


Transmission by the sheep tick (*Ixodes ricinus*).



Tick Cycle

Humans are
dead-end
hosts for
*Borrelia
burgdorferi* s.l.





Lyme disease

- Early local infection: erythema migrans (EM) 75 - 90% of *B. burgdorferi* infections
- Early disseminated infection: symptoms of nervous system, skin, joints and heart
- Chronic Lyme borreliosis...





Retrospective GP-study: postal questionnaire

All (\pm 9.000) general practitioners (GP's) in 1995, 2002, 2006 & 2010 received pre-coded questionnaire about previous year

Graag verzoek ik u de volgende vragen te beantwoorden:

1. **Hoeveel keer bent u in 2005 geconsulteerd voor een tekenbeet?**

- | | |
|----------------------------------|--------------------------------------|
| <input type="checkbox"/> 0 - 1 | <input type="checkbox"/> 25 - 49 |
| <input type="checkbox"/> 2 - 4 | <input type="checkbox"/> 50 - 99 |
| <input type="checkbox"/> 5 - 14 | <input type="checkbox"/> 100 of meer |
| <input type="checkbox"/> 15 - 24 | |

2. **Hoeveel keer bent u in 2005 geconsulteerd voor Erythema Migrans (EM)?**

- | | |
|--------------------------------|-------------------------------------|
| <input type="checkbox"/> 0 | <input type="checkbox"/> 5 - 9 |
| <input type="checkbox"/> 1 | <input type="checkbox"/> 10 of meer |
| <input type="checkbox"/> 2 - 4 | |

3. **Hoeveel keer heeft in 2005 uw vermoeden van Lyme geresulteerd in behandeling in het ziekenhuis?**

- | | |
|--------------------------------|-------------------------------------|
| <input type="checkbox"/> 0 | <input type="checkbox"/> 5 - 9 |
| <input type="checkbox"/> 1 | <input type="checkbox"/> 10 of meer |
| <input type="checkbox"/> 2 - 4 | |

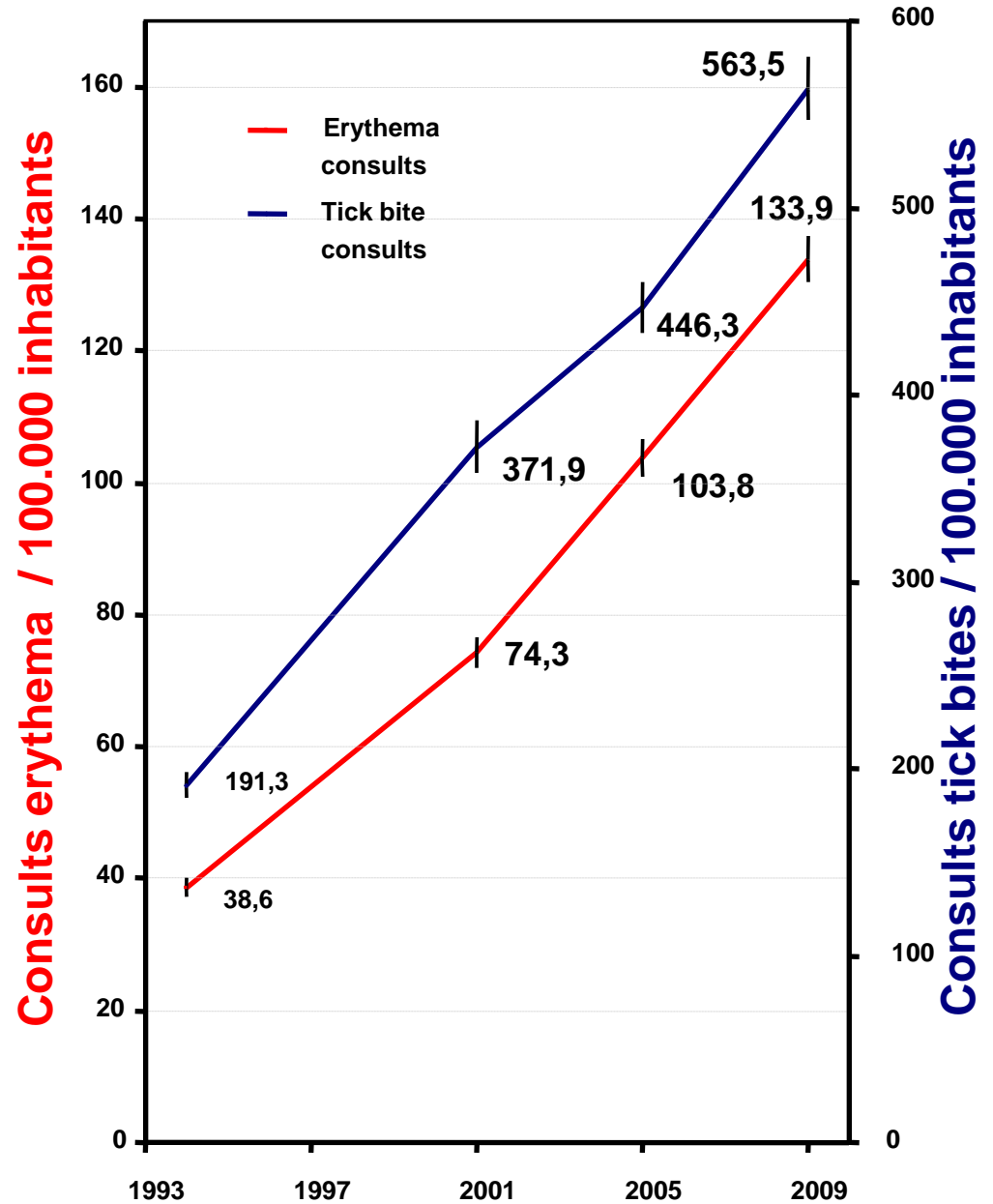
4. **Om voornoemde gegevens te interpreteren is het zeer behulpzaam als u uw praktijkomvang wilt aangeven. Hoeveel patiënten staan er ingeschreven in uw praktijk?**

- | | |
|--------------------------------------|---------------------------------------|
| <input type="checkbox"/> < 1500 | <input type="checkbox"/> 2500 - 2999 |
| <input type="checkbox"/> 1500 - 1999 | <input type="checkbox"/> 3000 of meer |
| <input type="checkbox"/> 2000 - 2499 | |



Retrospective GP-study: results

- Population coverage:
88% in 1994
↓
65% in 2009
- Tick bite consultations:
30.000 in 1994
↓
93.000 in 2009
- EM consultations:
6.000 in 1994
↓
22.000 in 2009



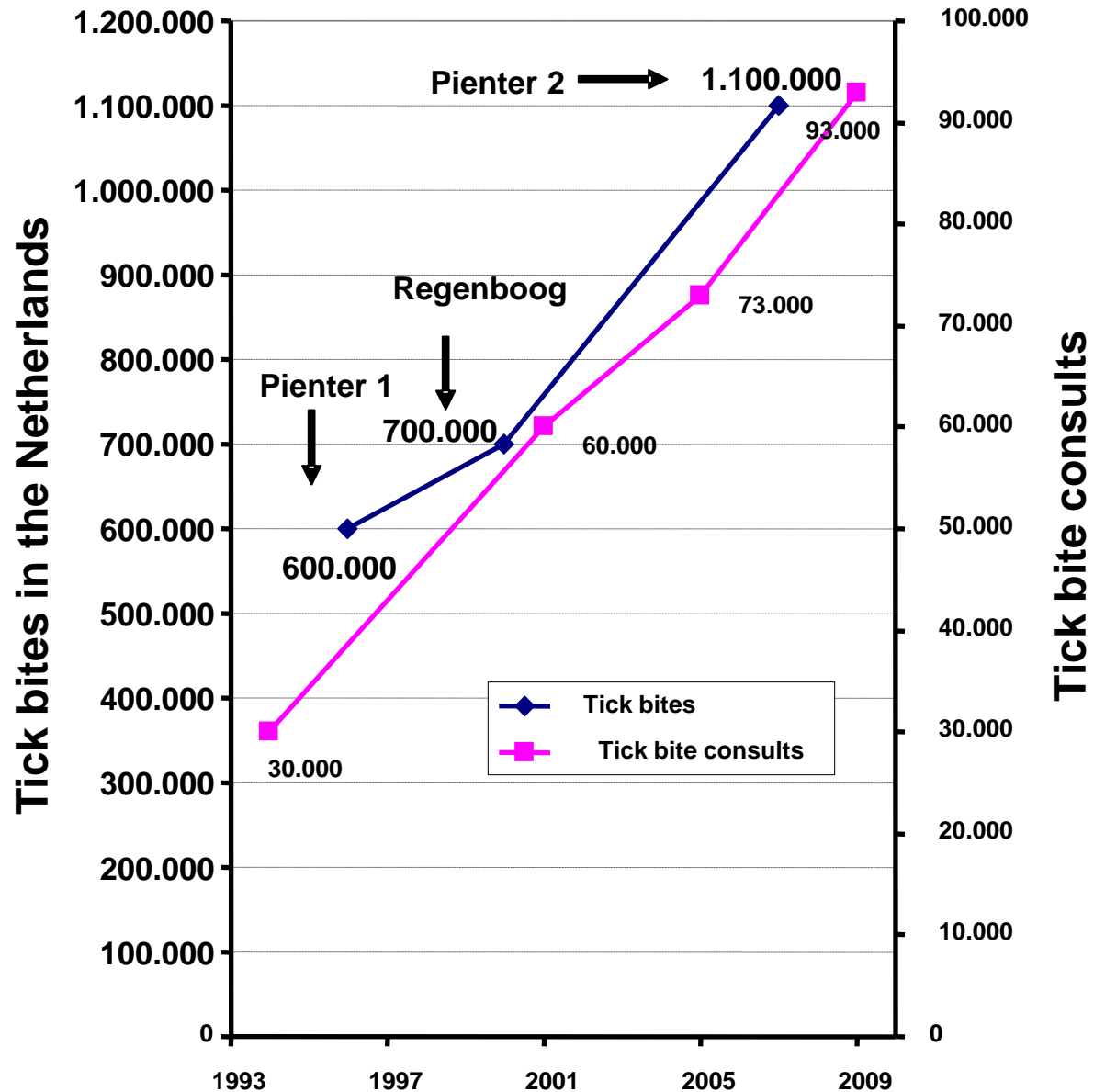


Tickbite question in 3 large population studies (>7000)

Tickbite consultations:
30.000 in 1994
↓
93.000 in 2009

Tickbites estimated:
450.000 in 1994
↓
1.400.000 in 2009

Tick bite risk on
EM ~ Lyme: 1994: 1/75 (1.3~1.6%)
↓
2009: 1/65 (1.5~1.8%)



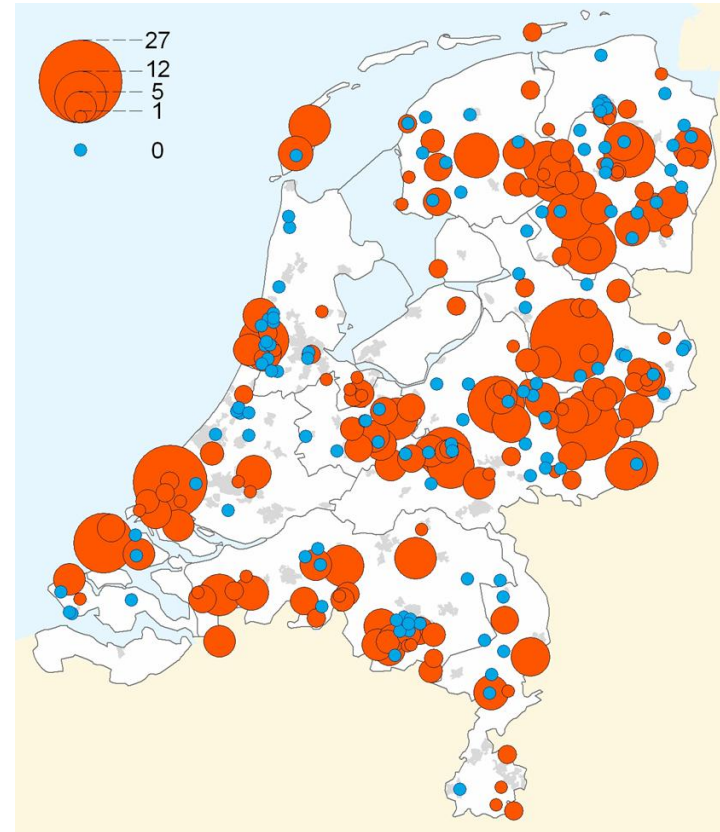


National Tick Bites Study → GP-based prospective study

- 2007 & 2008
 - 700 cases & 500 controls
 - from 300 selected GPs in hotspot areas for tick bites and EM
 - Ticks collected and tested
- Some results
 - 1.8% (9/499) participants with tickbites developed EM
 - 3.7% (3/82) if Borrelia contaminated
 - 0.55% (1/182) if not Borrelia contaminated

In line with GP retrospective study vs 3 large population studies!

- Tick bite risk on Lyme (EM).
2009: 1/65 (1.5~1.8%)





Intensified Lyme Project, started in 2011

- Work packages
 - Intervention study
 - Mandatory reporting
 - Public Health Impact
 - Communication to the Public
 - Diagnostics
 - Protocol for medical officers



Intensified Lyme Project, started in 2011

- Work packages
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 - **Public Health Impact**
 - Retrospective doctors and patient questionnaires
 - Web-based prospective surveillance
 - Clinical study
 - Communication to the Public
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After GP-based tick-bites/EM studies

→ Why further study PH impact?

- Acute manifestations other than EM?
 - Late manifestations?
 - Higher risk if no EM?
 - Burden of disease?
 - Cost-of-illness?
- } Policy-makers



PH impact: Retrospective doctors and patient questionnaires

incidence & prevalence

burden of disease & cost-of-illness

.....for all Lyme manifestations



Lyme manifestations (acute and late, frequent and rare)

- Erythema migrans (EM)
- Borrelia-lymphocytoma
- Acrodermatitis chronica atrophicans (ACA)
- Neuroborreliosis
- Lyme-arthritis
- Lyme-carditis
- Ocular manifestations
- Lyme-encefalopathy
- Persisting Lyme borreliosis
- Persisting complaints after Lyme borreliosis (“post-Lyme” syndrome)



Doctors questionnaires

- ±9000 GPs
 - ±1500 Medical officers
 - ±5500 Specialists
- } 16.000 total
- Similar questions as in earlier GP-questionnaires
 - + number of patients per Lyme manifestation (2009/2010)
 - + request to send questionnaires to Lyme patients

→Should result in:

annual **incidence** estimates **for all Lyme manifestations**

and.....recruitment of patients



Patient questionnaire

- Patients invited by their doctors
 - Lyme complaints in last 12 months
 - 1000-9000 patients....??

→Should result in:

- Risk factors for (more severe) manifestations
- Duration of Lyme manifestations and complaints
- **Burden of disease** (Health status)
- **Costs of illness** (Health-care consumption, sick leave)



- Also 9000 controls invited
 - normal incidence of (aspecific) complaints
 - not used for burden of disease and cost of illness



Burden of disease

- DALY's (Disability Adjusted Life Years)

– DALY = YLL + YLD

(YLL=Years of Life Lost, YLD=Years Lived with Disability)

mortality $YLL = \sum d1 * e1$

d1 = number of fatal Lyme cases

e1 = expected life span at age of death

morbidity $YLD = \sum n1 * t1 * dw1$

n1 = number of cases with Lyme manifestation x

t1 = duration of Lyme manifestation x

dw1 = disability (severity) weight of manifestation x

0 = healthy

1 = dead (maximum disability)

Disability weights for Lyme.....?



Defining disability weights (0=healthy;1=dead)

- Valuation of e.g. neuroborreliosis
 - Panel of judges
 - > Experts
 - > Public
 - Patients
 - Depicting the disease
 - > Disease specific
e.g. valuating disease specific descriptions by a panel
 - Generic
Validated health state questionnaires
 - Valuation method
 - > Visual analogue scale (VAS)
 - > Time trade off (TTO)
for not having a disease/disability, e.g. trade-off 10 years with disease, for 8 healthy years → disability weight=0.2

Disability weights for diseases are available, e.g.:

-Global Burden of Disease study

-Dutch Disability weights study

But Lyme was not included.....

(Haagsma, 2010, DALYs and acute onset disorders)



EQ-5D health status questionnaire

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today.

Mobility

- I have no problems in walking about
- I have some problems in walking about
- I am confined to bed

Self-Care

- I have no problems with self-care
- I have some problems washing or dressing myself
- I am unable to wash or dress myself

Usual Activities (e.g. work, study, housework, family or leisure activities)

- I have no problems with performing my usual activities
- I have some problems with performing my usual activities
- I am unable to perform my usual activities

Pain/Discomfort

- I have no pain or discomfort
- I have moderate pain or discomfort
- I have extreme pain or discomfort

Anxiety/Depression

- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed

•5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression)

•3 levels per dimension (no problems, moderate problems, extreme problems)

$$3^5 = 243 \text{ health states}$$

From health state to disability weight?

•Time-trade-off derived population weight for each element of EQ-5D

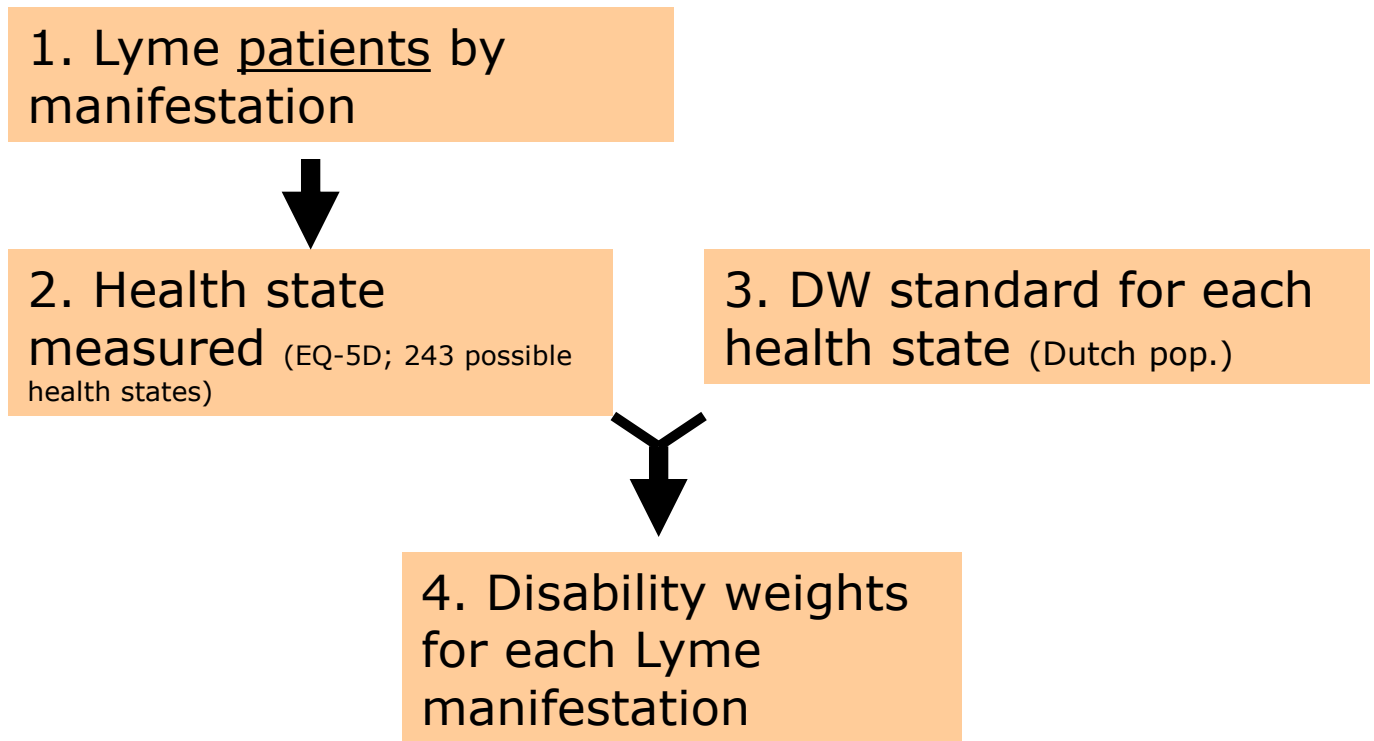
E.g. $DW_{\text{confined to bed}} = 0.2$

(trade-off 10 years confined to bed, for 8 healthy years; and thus give up 2 years of life for avoiding 10 years confined to bed)



Defining Lyme disability weights (0=healthy;1=dead)

- In summary





Burden of disease

- DALY's (Disability Adjusted Life Years)

$$- \text{DALY} = \text{YLL} + \text{YLD}$$

(YLL=Years of Life Lost, YLD=Years Lived with Disability)

mortality

$$\text{YLL} = \sum d1 * e1$$



morbidity

$$\text{YLD} = \sum n1 * t1 * dw1$$

Disability weights for Lyme manifestations

d1 = number of fatal Lyme cases

e1 = expected life span at age of death

n1 = number of cases with Lyme manifestation x

t1 = duration of Lyme manifestation x

dw1 = disability (severity) weight of manifestation x

0=healthy

1=dead (maximum disability)



Cost-of-illness (COI)

- Attributing costs to a disease
 - Measure all costs for patients and controls
 - > $COI = C_{\text{patients}} - C_{\text{controls}}$
 - > E.g. for Alzheimer
 - Measure costs directly related to disease
 - > Only patients, no controls
 - > Assuming:
 - patients can distinguish Lyme related costs
 - less recall bias than all costs (12 months in retrospective)



Cost-of-illness (COI)

For each Lyme manifestation

- > Direct health-care costs
 - Health care consumption

- > Direct non-health-care costs
 - Transport, housekeeper etc.

- > Indirect non-health-care costs
 - Production loss to society: sick leave

Approach and cost-prices derived from Dutch manual for economical evaluations in health care
(www.cvz.nl)



Intensified Lyme Project, started in 2011

- Work packages

- Intervention study
- Mandatory reporting
- **Public Health Impact**

- Retrospective doctors and patient questionnaires

→ started last week

- Web-based prospective surveillance
 - Clinical study



Plans for 2012

- Communication to the Public
- Diagnostics
- Protocol for medical officers



PH impact: Web-based prospective surveillance



Web-based prospective surveillance

- Tick-bite/EM patients recruited by internet
 - “Natuurkalender” tick-bite concept
 - + collection of ticks
 - + collection EM pictures
 - + skin samples EM
 - + questionnaires
 - › Entering the study
 - › 3 months
 - › 1 year (or more)

→This should result in:

- Risk factors for acute and disseminated LB manifestations
 - validation of incidences measured by doctors questionnaire
- Health state over time, medical consumption, sick leave
 - validation of Disease Burden and Cost-of-Illness, no recall bias



PH impact: Clinical study



Clinical study

- In collaboration with Hospitals with a Lyme specialization center
- Inclusion of patients with acute and disseminated LB

→Should result in:

- Risk factors to develop long-term sequelae
 - Persisting infection/post-Lyme syndrome?

Multi-disciplinary expertises {
Neuropsychology
Clinical symptoms/treatment
Microbiology
Immunology
Genetics



Intensified Lyme Project, started in 2011

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In summary PH impact Lyme study:

- Incidence of Lyme manifestations other than EM
- Risk factors for more severe disease
- Burden of Disease
- Cost-of-illness

Toolkit for
disease control

Conclusions and results

Next year and the years to come.....



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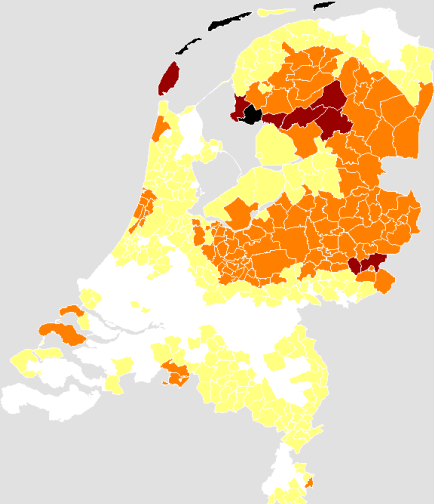
- Juanita Haagsma (burden of disease/cost-of-illness)

Stigas

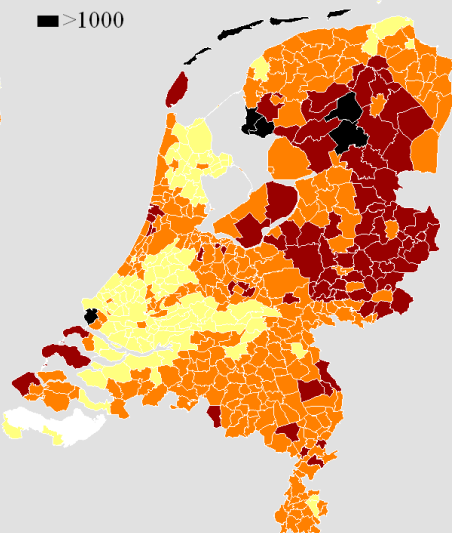
- Ad de Rooij (medical officers point of view)

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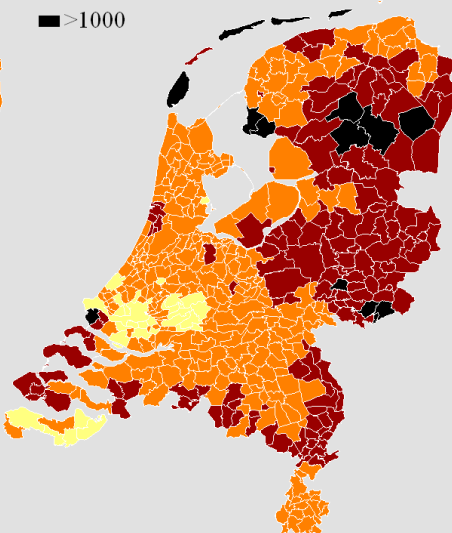
1994: Tickbites / 100.000



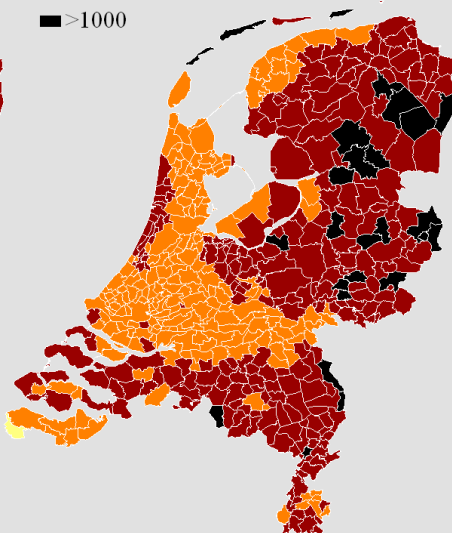
2001: Tickbites / 100.000



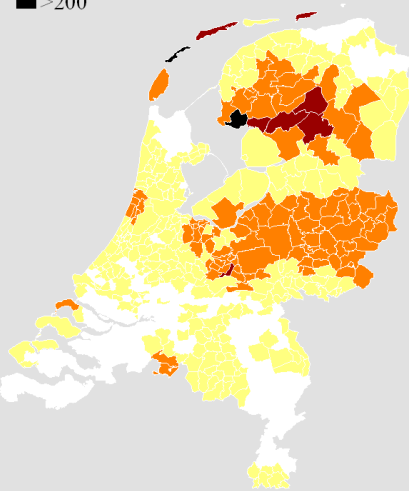
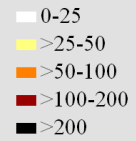
2005: Tickbites / 100.000



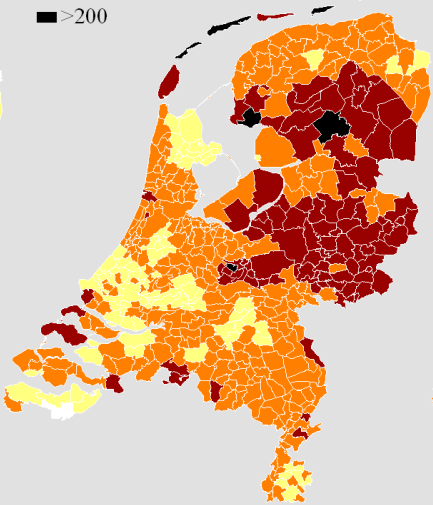
2009: Tickbites / 100.000



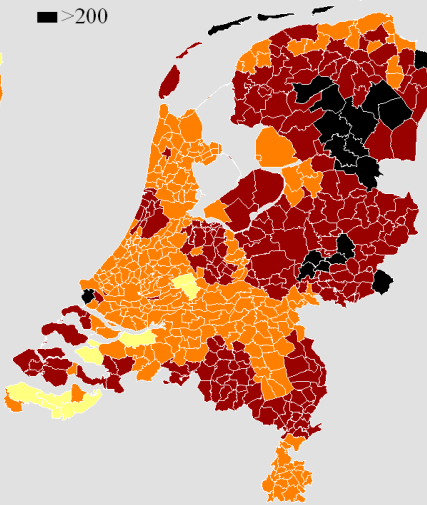
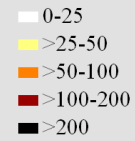
1994: Erythema / 100.000



2001: Erythema / 100.000



2005: Erythema / 100.000



2009: Erythema / 100.000

