Rijksinstituut voor Volksgezondheid
en Milieu
*Ministerie van Volksgezondheid,
Welzijn en Sport*

Van dier naar mens, zoönosen in een snel veranderde wereld

Lezing projectgroep veterinaire informatie voor senior dierenartsen

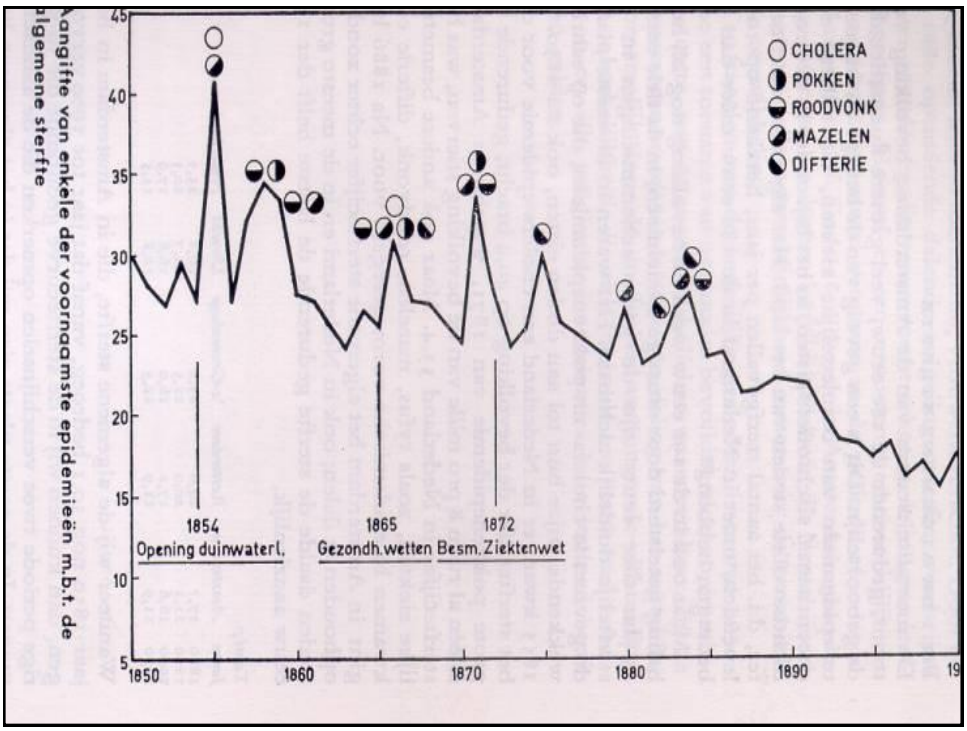
Utrecht, 17 april 2013

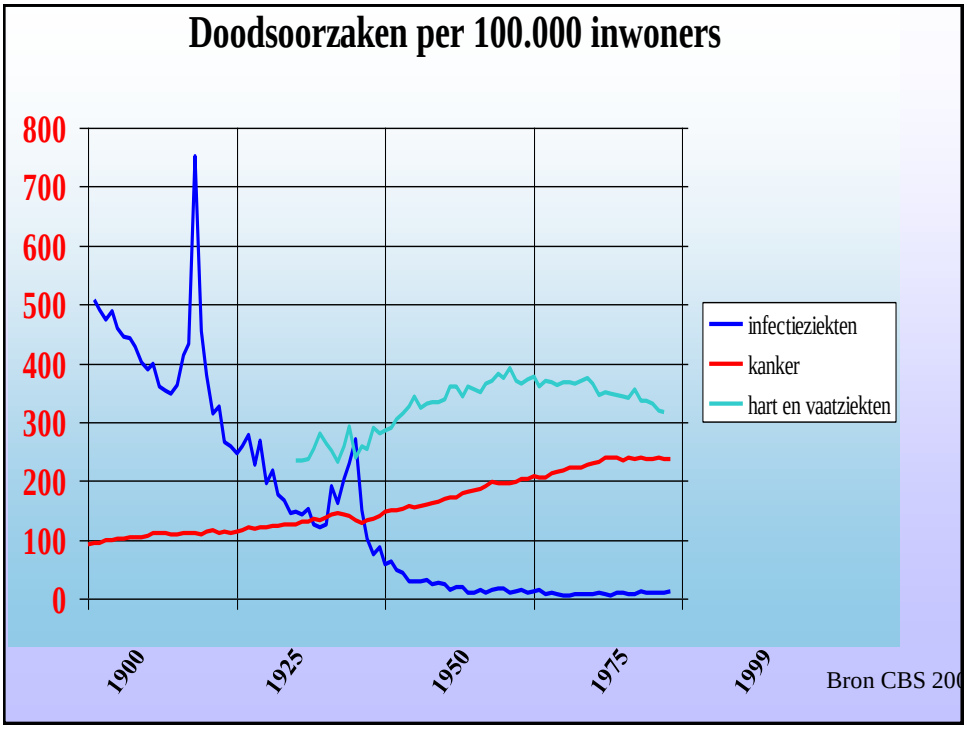
Roel A. Coutinho

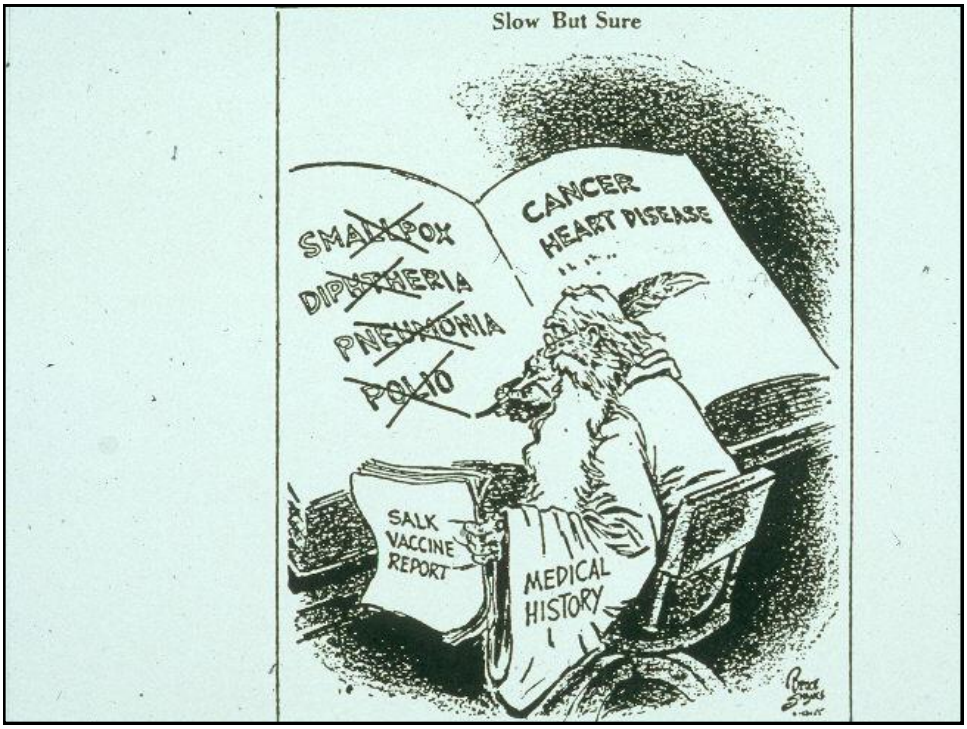
Center for Infectious Disease Control
National Institute for Public Health and the Environment
Bilthoven

Julius Center for Health Science and Primary Care
University Medical Center Utrecht

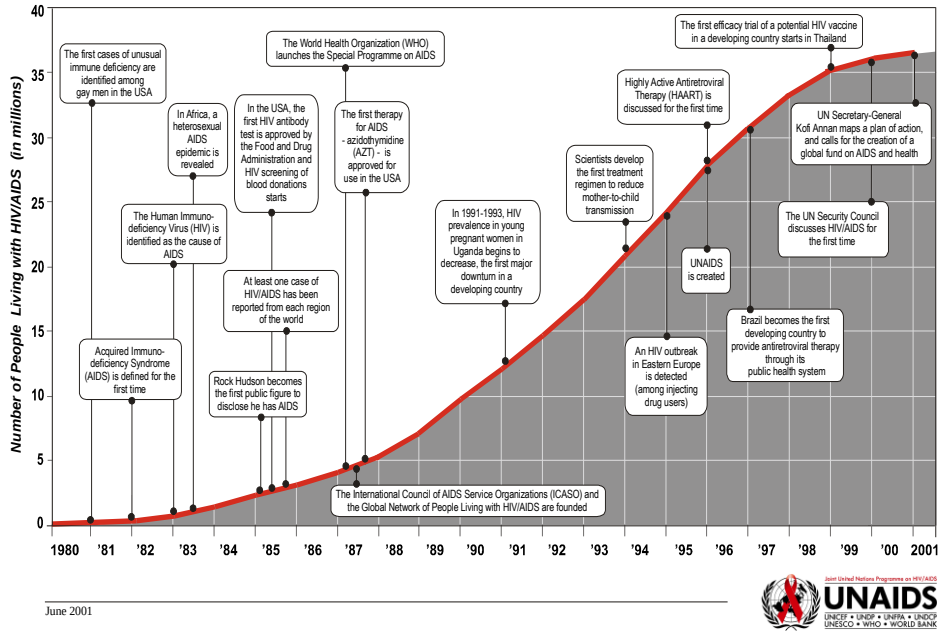
17 april 2013

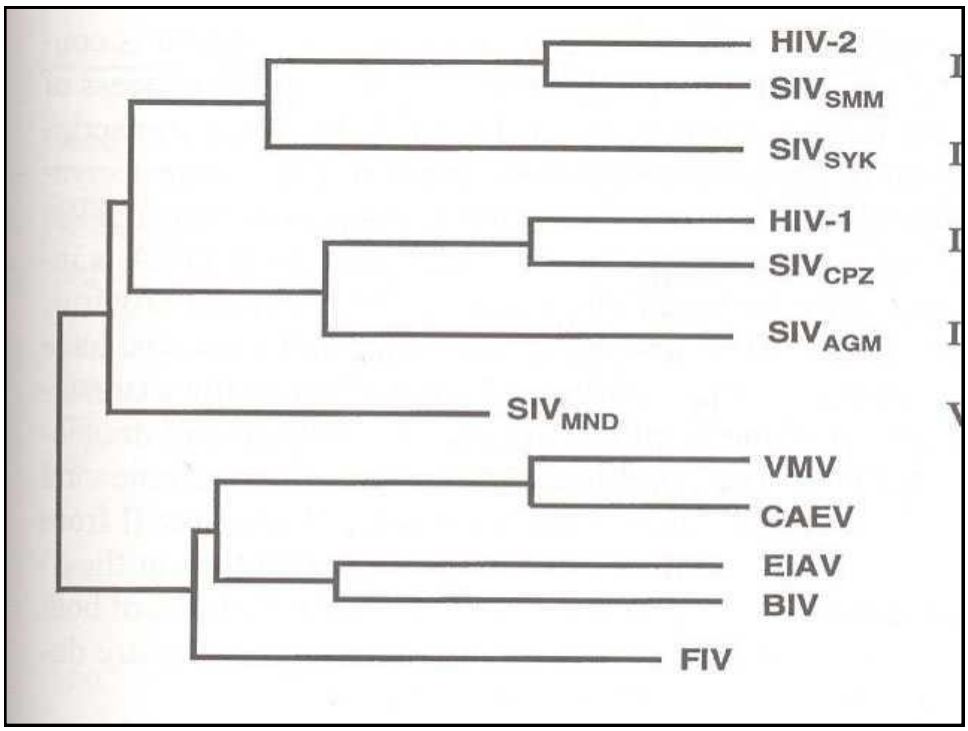



Doodsoorzaken per 100.000 inwoners
800
700
600
500
400
300
200
100
0
1900
1925
1950
1975
1999
infectieziekten
kanker
hart en vaatziekten
Bron CBS 200


Slow But Sure
SMALLPOX
DIPHTHERIA
PNEUMONIA
POLIO
CANCER
HEART DISEASE
SALK VACCINE REPORT
MEDICAL HISTORY

20 years of HIV/AIDS

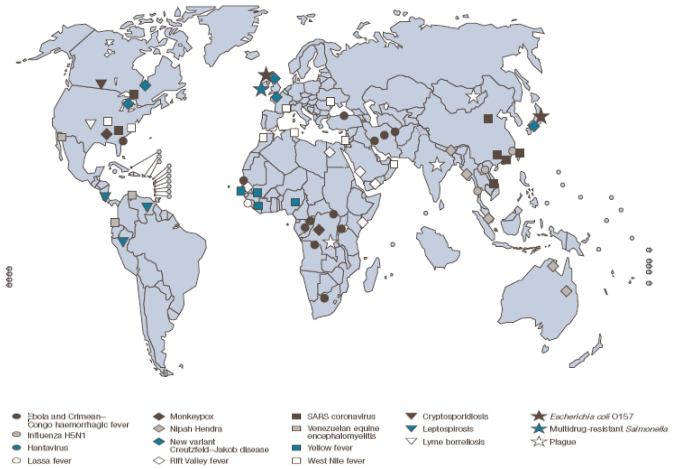




Factors in the emergence of infectious diseases

- population growth
- speed and ease of travel
- expansion into forests
- global climate change
- war and social disruption
- we get older
- Increased susceptibility of humans (HIV and immunosuppression)
- antibiotic (mis)use
- bioterrorism

Figure 1.4 Selected emerging and re-emerging infectious diseases: 1996–2004



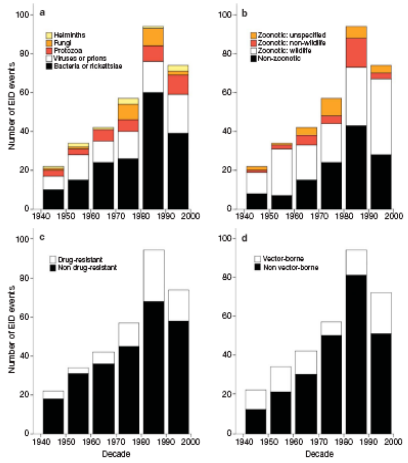


Figure 1 | Number of EID events per decade. EID events (defined as the temporal origin of an EID, represented by the original case or cluster of cases that represents a disease emerging in the human population—see Methods) are plotted with respect to a, pathogen type, b, transmission type, c, drug resistance and d, transmission mode (see keys for details).

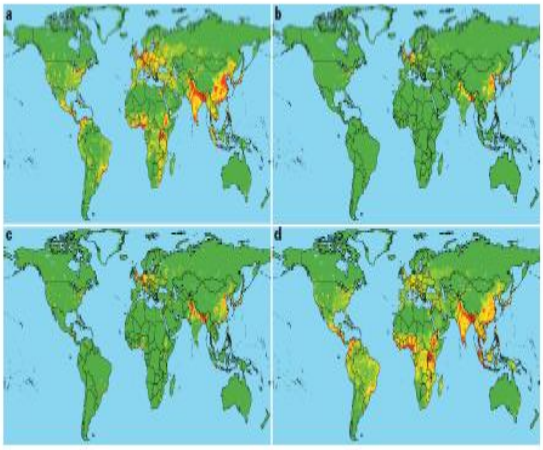


Figure 3 | Global distribution of relative risk of an EID event. Maps are derived for EID events caused by **a**, zoonotic pathogens from wildlife, **b**, zoonotic pathogens from non-wildlife, **c**, drug-resistant pathogens and **d**, vector-borne pathogens. The relative risk is calculated from regression coefficients and variable values in Table 1 (omitting the variable measuring reporting effort), categorized by standard deviations from the mean and mapped on a linear scale from green (lower values) to red (higher values).

Staff called for the Prince of Wales Hospital to be closed

Klinisch beeld van SARS

- begint met griepachtig ziektebeeld: koorts, algemene malaise, hoesten, spierpijn, kortademig, longinfiltraten
- week 2: verergering met terugkerende koorts, toenemende afwijkingen op longfoto, diarree (immunologische reactie)
- ongeveer eenderde had intensive care nodig en 20% kunstmatige beademing
- behandeling: ribavirine (?) en corticosteroïden
- sterfte hoog: <60: 7-13%; >60 43-55%
- kinderen hebben een mild beeld
- diagnose met kweek, PCR of serologie
- klinisch beeld niet specifiek

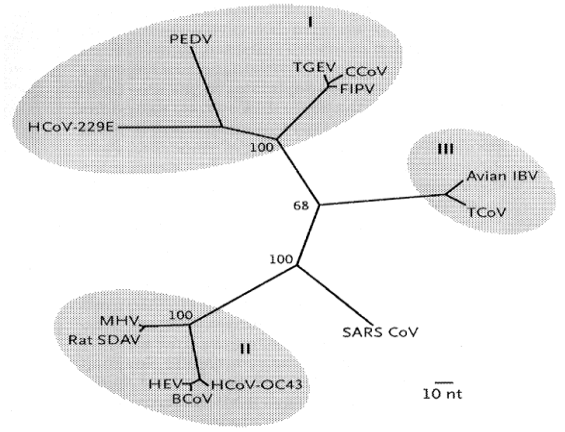


Figure 3. Estimated Maximum-Parsimony Tree Based on the Sequence Alignment of 405 Nucleotides of the Coronavirus Polymerase Gene Open Reading Frame 1b (Nucleotide Numbers 15173 to 15578 Based on Bovine Coronavirus Complete Genome Accession Number NC_003045) Comparing SARS Coronavirus with Other Human and Animal Coronaviruses.

Rijksinstituut voor Volksgezondheid en Milieu
Ministerie van Volksgezondheid, Welzijn en Sport

Home | Thema's | Bibliotheek | Onderwerpen | Ziekten & Aandoeningen | RIVM

zoek

Home > Bibliotheek > 2012 > Nieuw type coronavirus ontdekt

Nieuw type coronavirus ontdekt

Publicatiedatum: 24-09-2012
Wijzigingsdatum: 18-10-2012

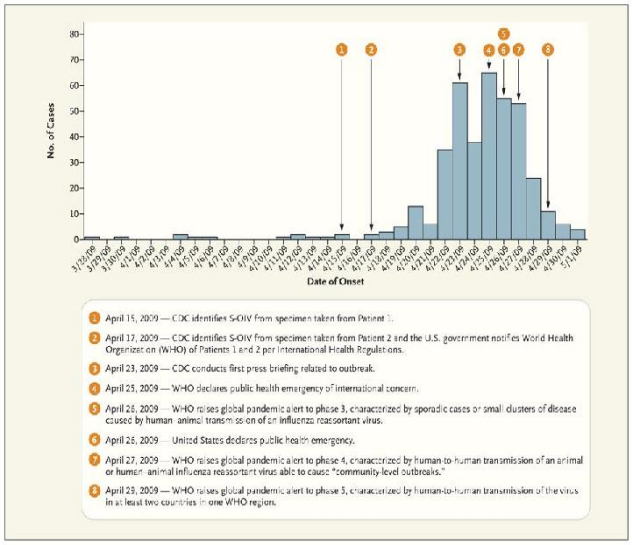
Saoedi-Arabië en het Verenigd Koninkrijk hebben beide een patiënt met een nieuw type coronavirus gemeld. Beide patiënten zijn in Saoedi-Arabië geweest. Eén patiënt is ernstig ziek, de andere is inmiddels overleden. Hoe besmettelijk dit virus is is onbekend, maar overdracht van mens-op-mens is vooralsnog niet aannemelijk. In Nederland zijn geen mensen ziek van dit virus. Het RIVM volgt nauwgezet de ontwikkelingen.

De twee patiënten zijn tussen juli en september ziek geworden. De eerste patiënt is afkomstig uit Saoedi-Arabië en is daar overleden. De tweede patiënt is gemeld door het Verenigd Koninkrijk. Deze heeft eerder Saoedi-Arabië en Quatar bezocht. De tweede patiënt wordt behandeld in een ziekenhuis in het Verenigd Koninkrijk. Vooralsnog lijkt er een link te zijn met Saoedi-Arabië.

Volg ons:

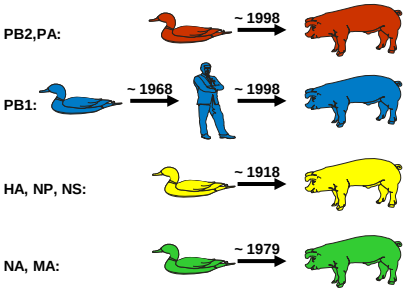
Download

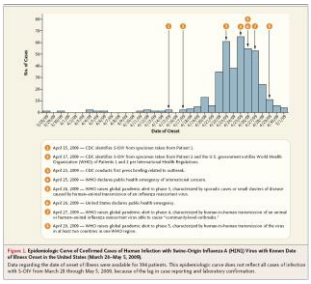
› Veelgestelde vragen nieuw coronavirus


No. of Cases
Date of Onset
1 April 15, 2009 — CDC identifies S-OIV from specimen taken from Patient 1.
2 April 17, 2009 — CDC identifies S-OIV from specimen taken from Patient 2 and the U.S. government notifies World Health Organization (WHO) of Patients 1 and 2 per International Health Regulations.
3 April 23, 2009 — CDC conducts first press briefing related to outbreak.
4 April 25, 2009 — WHO declares public health emergency of international concern.
5 April 26, 2009 — WHO raises global pandemic alert to phase 3, characterized by sporadic cases or small clusters of disease caused by human–animal transmission of an influenza reassortant virus.
6 April 26, 2009 — United States declares public health emergency.
7 April 27, 2009 — WHO raises global pandemic alert to phase 4, characterized by human-to-human transmission of an animal or human–animal influenza reassortant virus able to cause "community-level outbreaks."
8 April 29, 2009 — WHO raises global pandemic alert to phase 5, characterized by human-to-human transmission of the virus in at least two countries in one WHO region.

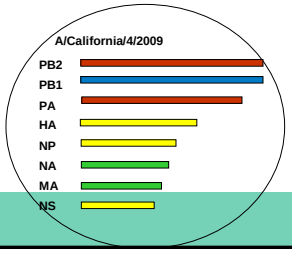

NOS.nl

Nieuwe griep virus is ontstaan door mengen van genen



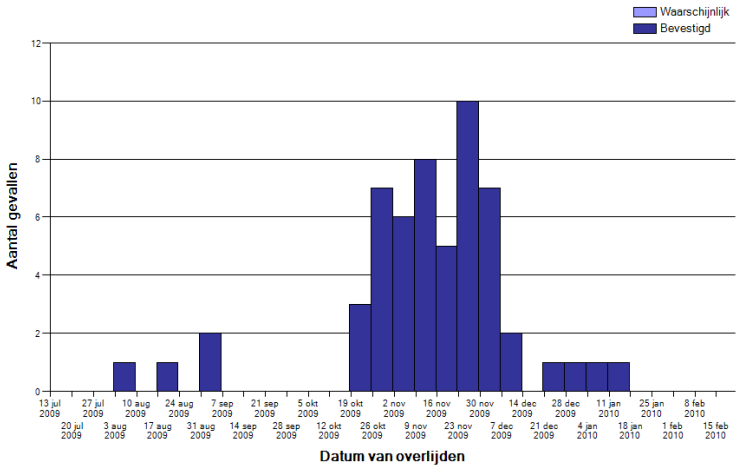


Vermoedelijke samenstelling van het H1N1 Mexicaanse griep virus



Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team*, New England Journal of Medicine, 2009

Aantal sterfgevallen met laboratorium bevestigde Nieuwe Influenza A (H1N1) per week t/m 10 maart 2010 (n=56)*



Bron: Osiris / Pandora / CIb

** Van 2 sterfgevallen zijn nog niet alle gegevens bekend waardoor deze niet in de grafiek worden getoond.*

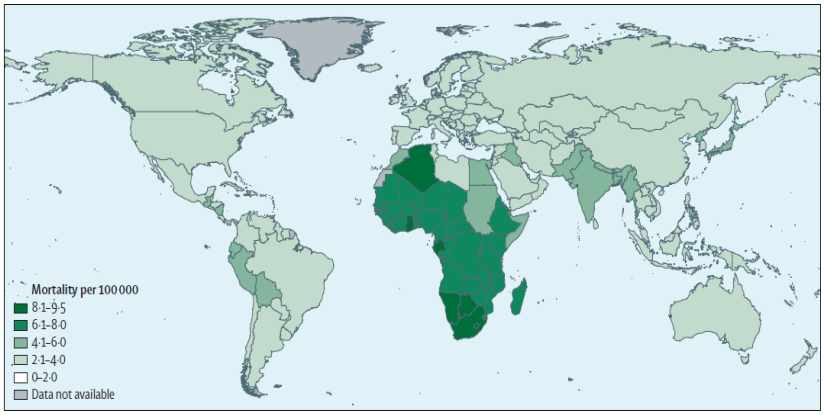


Figure 2: Estimated age-adjusted respiratory and cardiovascular mortality rate associated with 2009 pandemic influenza A H1N1 per 100 000 individuals by country

WEEKLY EPIDEMIOLOGICAL RECORD
RELEVÉ ÉPIDÉMIOLOGIQUE HEBDOMADAIRE

Epidemiological Surveillance of Communicable Diseases
Telegraphic Address: EPIDNATIONS GENEVA *Telex 27821*

Service de la Surveillance épidémiologique des Maladies transmissibles
Adresse télégraphique: EPIDNATIONS GENÈVE *Télex 27821*

Automatic Telex Reply Service
Telex 28150 Geneva with ZCZC and ENGL for a reply in English

Service automatique de réponse
Télex 28150 Genève suivi de ZCZC et FRAN pour une réponse en français

26 OCTOBER 1979 — 54th YEAR — 54e ANNÉE — 26 OCTOBRE 1979

NO SMALLPOX
26 October 1977
to
26 October 1979

2
YEARS / ANS

SANS VARIOLE
26 octobre 1977
au
26 octobre 1979

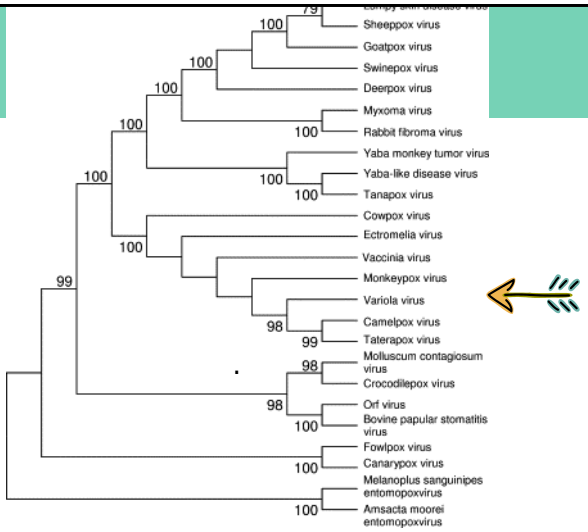


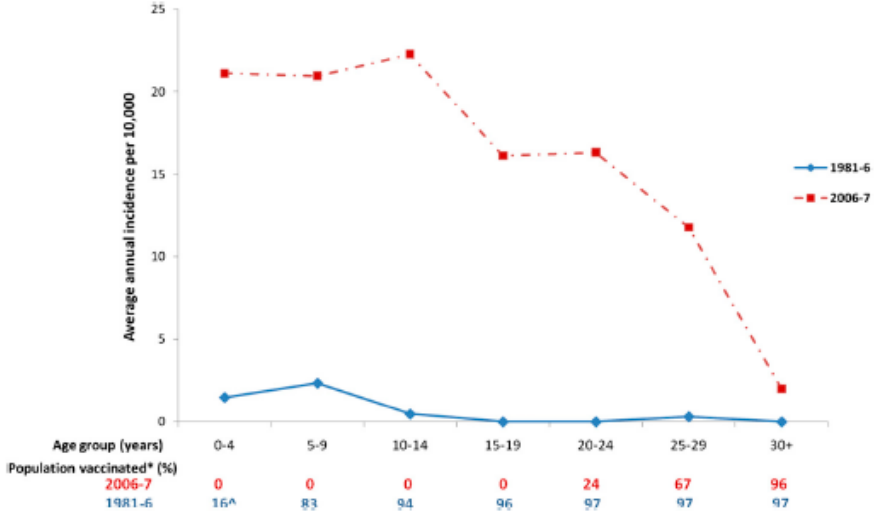
Fig.1 NJ tree (topology only) of poxviruses based on concatenated amino acid sequences from 29 conserved orthologous proteins (13, 475 aligned sites). The tree was constructed on the basis of the JTT amino acid distance, assuming that rate variation among sites follows a gamma distribution (shape parameter *a* = 0.86). Numbers on the branches represent percentages of 1000 bootstrap samples supporting each branch; only values ≥50% are shown. For accession numbers of genome sequences, see Supplementary S1

AL Hughes et al, The evolutionary biologiy of poxviruses. Infection, genetics and evolution 2010:10;50-59

Typical clinical presentation of human monkeypox in a 7-y-old female child, Sankuru District, Democratic Republic of Congo.

27

17 april 2013 Rimoin A W et al. PNAS 2010;107:16262-16267



28

17 april 2013 Rimoin et al. PNAS 2010;107:37 (16265)

LA-MRSA

NEWSFOCUS

INFECTIOUS DISEASE

From Pigs to People: The Emergence of a New Superbug

The discovery of a novel strain of MRSA able to jump from livestock to humans has sparked a multicountry effort to see how dangerous it might be

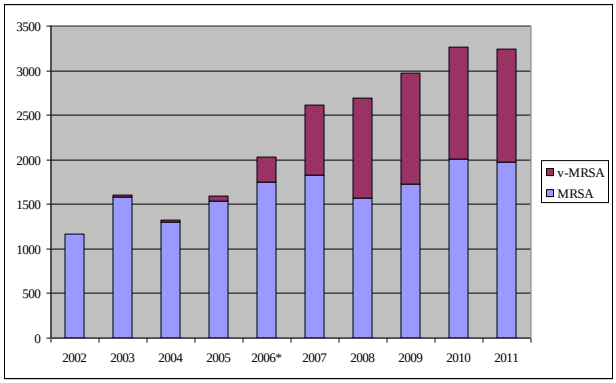
The first infection was puzzling, almost inexplicable. In July 2004, Andreas Voss of Radboud University Nijmegen Medical Center in the Netherlands admitted a 6-month-old girl for surgery to repair a congenital heart defect.

Because an infection with the common bacterium *Staphylococcus aureus* would pose a grave risk following heart surgery, Voss and his colleagues screened the baby girl for the microbe. They found not just *S. aureus* but also a menacing drug-resistant form known as methicillin-resistant *S. aureus* (MRSA). The physicians were flummoxed. Although MRSA has reached epidemic proportions in much of the developed world, MRSA infections are rare in the Netherlands, thanks to an aggressive "search and destroy" policy the country launched in the mid-1990s to screen for the superbug in health-care settings, where or other livestock harbored MRSA, and no MRSA strain had ever been known to jump from livestock to humans. If the Dutch doctors' fears were correct, a novel strain had just gained that ability, opening up a new route for a potentially dangerous superbug to spread among humans. "Initially, we were very much afraid that this would be a major problem that could spread to the entire population," says Jan Kluytmans, a microbiologist at VU University Medical Center in Amsterdam whom Voss recruited early on to help investigate.

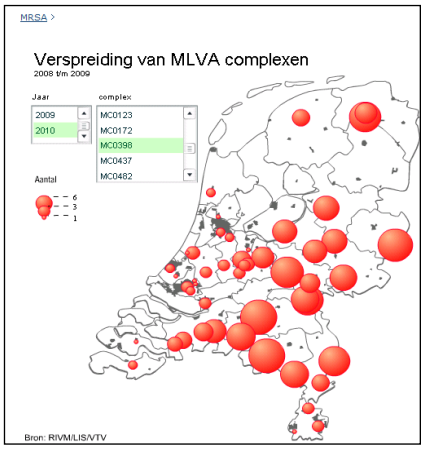
In recent months, the dangers of livestock-associated MRSA have been played up in controversial media missible, and harder to treat—and this newly

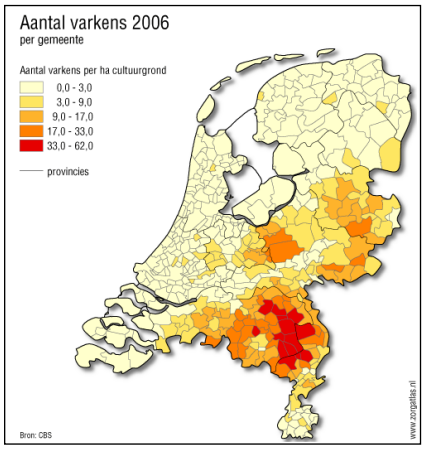
Index case. MRSA from pigs on Eric and Ine van den Heuvel's farm was detected in their daughter, Eveline, when she was an infant.

ccemag.org



LA-MRSA (3)





Staphylococcus aureus CC398: Host Adaptation and Emergence of Methicillin Resistance in Livestock

Lance B. Price et al.

ABSTRACT Since its discovery in the early 2000s, methicillin-resistant *Staphylococcus aureus* (MRSA) clonal complex 398 (CC398) has become a rapidly emerging cause of human infections, most often associated with livestock exposure. We applied whole-genome sequence typing to characterize a diverse collection of CC398 isolates ($n = 89$), including MRSA and methicillin-susceptible *S. aureus* (MSSA) from animals and humans spanning 19 countries and four continents. We identified 4,238 single nucleotide polymorphisms (SNPs) among the 89 core genomes. Minimal homoplasy (consistency index = 0.9591) was detected among parsimony-informative SNPs, allowing for the generation of a highly accurate phylogenetic reconstruction of the CC398 clonal lineage. Phylogenetic analyses revealed that MSSA from humans formed the most ancestral clades. The most derived lineages were composed predominantly of livestock-associated MRSA possessing three different staphylococcal cassette chromosome *mec* element (SCC*mec*) types (IV, V, and VII-like) including nine subtypes. The human-associated isolates from the basal clades carried phages encoding human innate immune modulators that were largely missing among the livestock-associated isolates. Our results strongly suggest that livestock-associated MRSA CC398 originated in humans as MSSA. The lineage appears to have undergone a rapid radiation in conjunction with the jump from humans to livestock, where it subsequently acquired tetracycline and methicillin resistance. Further analyses are required to estimate the number of independent genetic events leading to the methicillin-resistant sublineages, but the diversity of SCC*mec* subtypes is suggestive of strong and diverse antimicrobial selection associated with food animal production.

Mbio.asm.org Jan/Feb 2012
Vol.3;1 e00305-11

Publicatie in CMI

ORIGINAL ARTICLE 10.1111/j.1469-0691.2011.03497.x

2 Dutch patients, retail chicken meat and poultry share the same ESBL genes, plasmids and strains

M. A. Lever
Essen-Zandl
D. J. Mevius
1) Department o
Health and the E
4) SALTRO, Prim
3 6) Department o

Nieuwe aanwijzing: kip risico voor gezondheid

Kip eten lijkt toch niet zo veilig

Er wordt al jaren gewaarschuwd voor overmatig antibioticagebruik door boeren; concrete maatregelen blijven uit; infectieziektebestrijder Coutinho eet nog gewoon kip

Pluimveesector: we lossen het zelf wel op

'De bron moet aangepakt; dat is een politieke keuze'

Kippenbacteriën kunnen op termijn een ernstig gevaar voor de volksgezondheid vormen, zegt Roel Coutinho van het RIVM

Roel Coutinho

Institute for Public
IR, Lelystad,
e, Utrecht and

bla_{TEM-52} gene
94% contained
suggestive for

il meat samples,
ese findings are
food chain.

ESBL bij vleeskuikens en pluimveehouders/familie/werknemers

Vleeskuikens

- 50/50 bedrijven ESBL positief (100.0%)
- 482/500 gepoolde cloaca monsters ESBL positief (96.4%)

mensen

- Bij 27 bedrijven werden ESBL-positive personen gevonden: 57.5%

Pluimveehouders:	13/47	(28%)
Gezinsleden:	23/87	(27%)
Medewerkers:	3/8	(38%)

Antibiotic Usage in Animals in NL

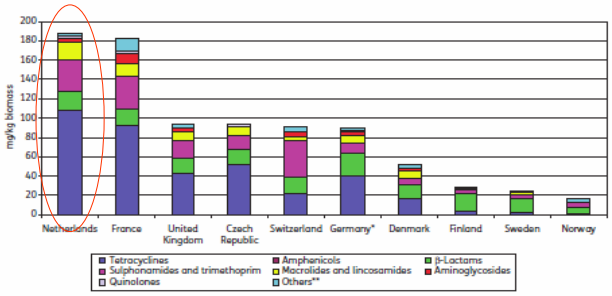


Figure 1. Amounts, in mg, of veterinary antibacterial agents sold in 2007 per kg biomass of pig meat, poultry meat and cattle meat produced plus estimated live weight of dairy cattle. *2005 data. **The substances included vary from country to country.

J Antimicrob Chemother 2010; **65**: 2037–2040
doi:10.1093/jac/dkq247 Advance Access publication 29 June 2010

Journal of Antimicrobial Chemotherapy

Comparison of the sales of veterinary antibacterial agents between 10 European countries

Kari Grave*, Jordi Torren-Edo and David Mackay

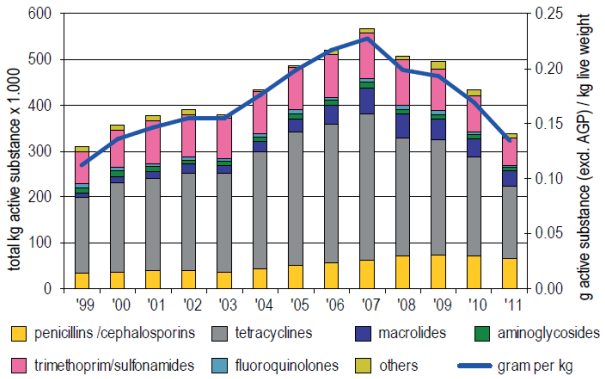


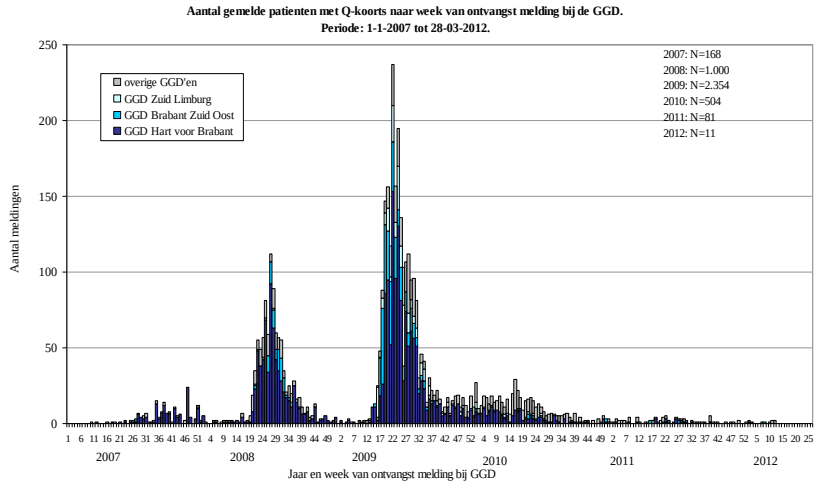
Figure ABuse01.Veterinary therapeutic sales from 1999-2011 (FIDIN, 2012, vertical bars). The line presents the trends in grams of active ingredients used per kg live weight

uit *MARAN 2012*
CVI, UU, Wageningen Univ.,RIVM, nVWA

Table 2. *Number of goats in The Netherlands*

YEAR	Total no. of goats
1983	7415
1995	76 063
2000	178 571
2009	374 184

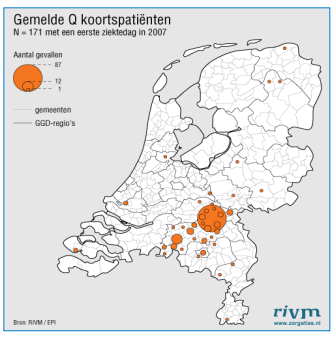
H.J. Roest et al., The Q fever epidemic in The Netherlands, Epidemiol.Infect. 2011,139,1-12

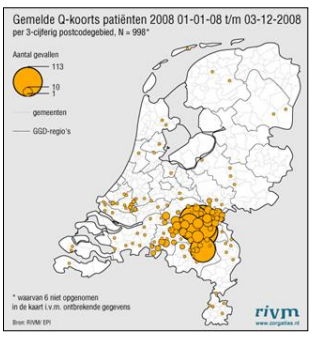


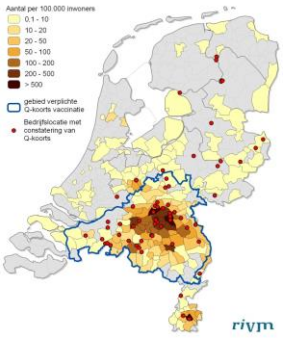
Q fever in the Netherlands

Q fever: a (re)emerging zoonosis in the Netherlands

2007 (n=171) **2008 (n=998)** **2009 (n =2363)**





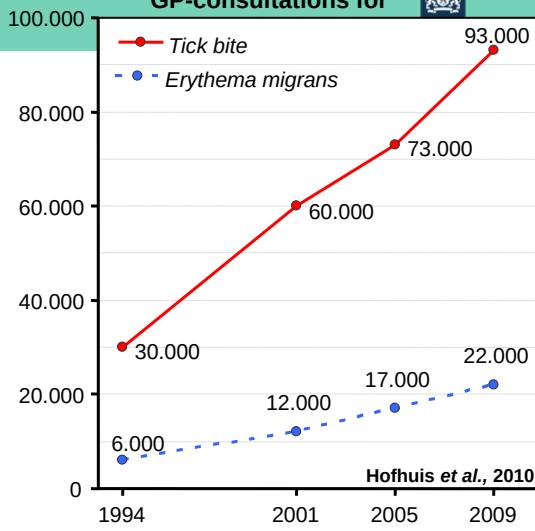


Veterinary interventions 2009

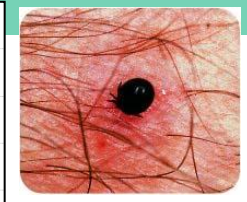
- Vaccination goats and sheep: at first voluntary, later mandatory
- Hygiene regulations
- Since October 2009 bulk milk monitoring with culling of pregnant goats on bulk milk positive farms

Incidence of Lyme disease is increasing in the Netherlands

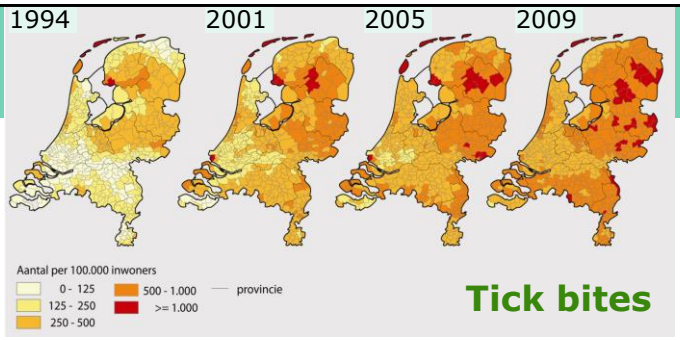
GP-consultations for



Tick bite

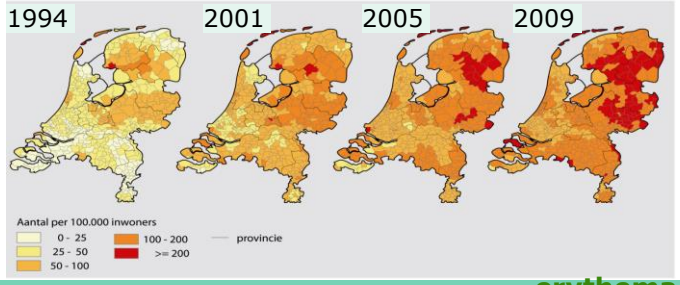


Erythema migrans



Tick bites

Based on consultations of general practitioners for…



erythema migrans

Tick-shelter: Increase in tick-suitable habitats

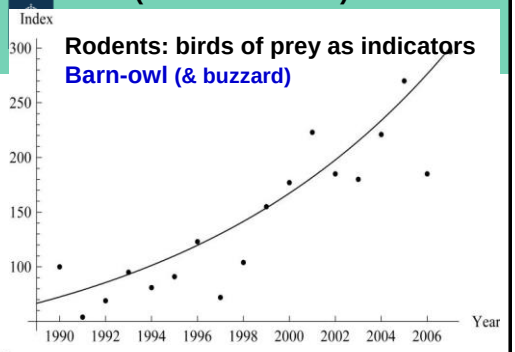
Land-usage in the Netherlands (in km^2)

Area	Teken	2001	2008	Difference
Forest/Dunes	Many	4598	5445	+ 18%
Heather/Grassland	Little	15402	15446	0%
Urban/Agriculture	Negligible	21527	20636	– 4%

***Future* of Ecological Main structure** (EHS: in km^2)

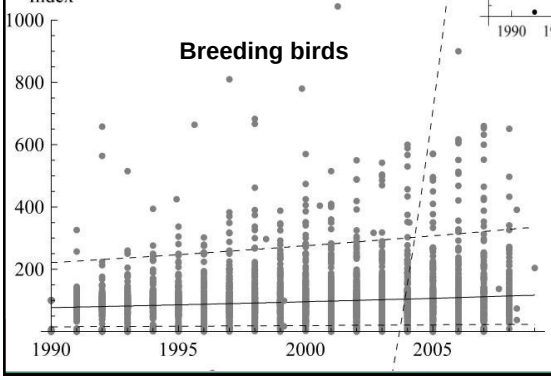
	1990	2008	2021
Nature-areas (Land)	4500	6000	7285

Blood meals: More intermediate hosts (rodents & birds)



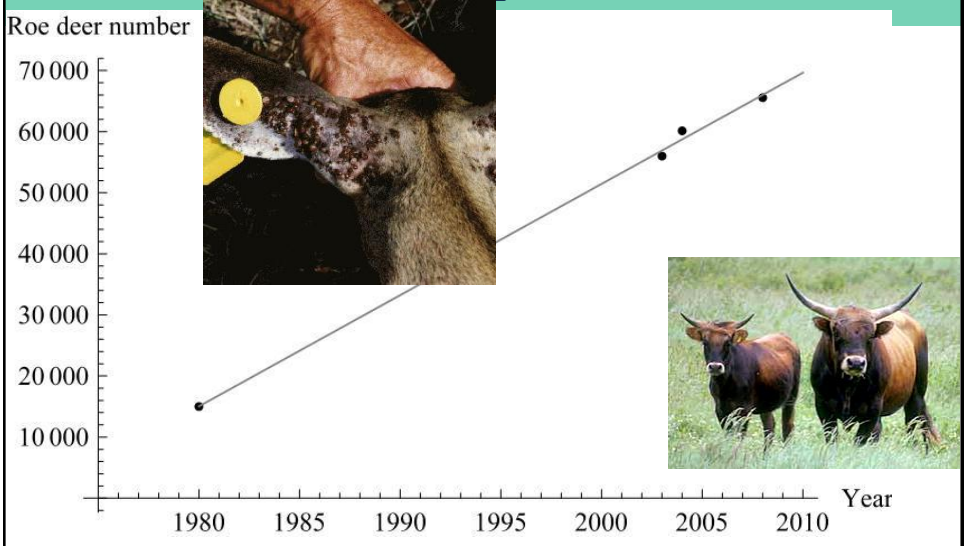
Rodents: birds of prey as indicators

Barn-owl (& buzzard)



Breeding birds

Propagation host: More deer



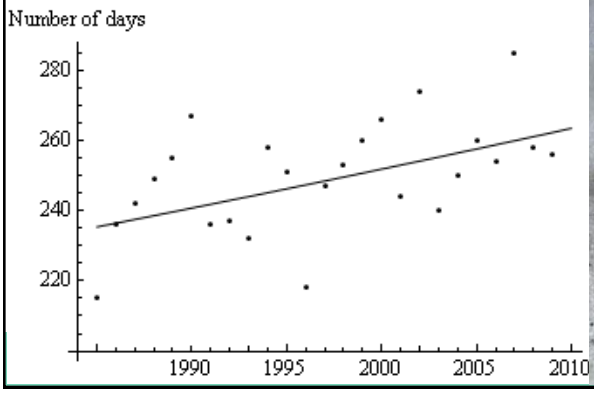
Also increase of (free ranging) cattle, sheep and horses in nature areas

Tick-activity: Long-term effect

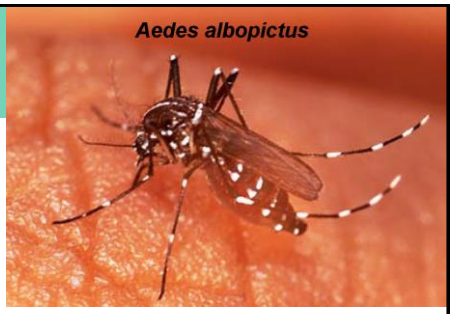
According to Natuurkalender (WUR)

Early spring starts 17 days earlier
Winter starts 9 days later (than centennial average)

Day/year >7°C (nymphal activity)



Risk of new vectors



Aedes albopictus (vector for flaviviruses, SE-Asia)

Since nineties in Southern Europe

2005 imports through "lucky-bamboo" in Holland
Can it survive, settle in Holland?

Day 7: **:** KAD informs surrounding area (mostly companies) and starts with removal potential breeding sites. One *albopictus* female is found close to company site (in BG sentinel trap) and one *Ae. aegypti* female (on human), also close to the company. Two French experts arrive, treatment starts late evening at company site in Heijningen with adulticiding (aqua-K-othrine). VROM inspection is present.

Conclusion I:

Two types of threats:

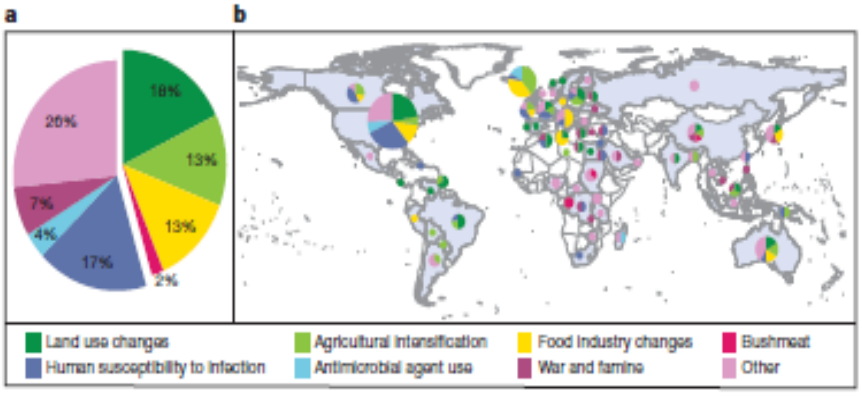
- predictable: influenza, vector borne infections, bioterrorism
- unpredictable: HIV, Creutzfeldt Jakob, SARS

We pay most attention to predictable threats

Conclusion II:

How to prepare for unpredictable threats:

- Strenghten structure of infectious disease control: national, local/regional, EU
- Strengthen public health in general
- Invest in knowledge and research
- Worldwide surveillance



Keesing et al. *Impacts of biodiversity on the emergence and transmission of infectious diseases* Nature 2010;468:647-652