Leptospirosis - a global disease but a local phenomenon

Jackie Benschop, Julie Collins-Emerson, Neville Haack, Shaan Mocke, Juan Sanhueza, Yuni Yupiana, Jenny Weston, Cord Heuer and Peter Wilson.

22 and 23 March 2016

One Health Aotearoa - A Symposium on Infectious Diseases

OIE Collaborating Centre for Veterinary Epidemiology and Public Health

mEpiLab: Molecular Epidemiology and Public Health Laboratory

- Food safety
- Public Health
- Surveillance
- Infectious disease

Leptospirosis

- Bacterial infection
- “Silent” urinary shedding
- Different serovars and hosts
- Environment important

Photo: Albert Ko

PLOS | NEGLECTED TROPICAL DISEASES

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RESEARCH ARTICLE

Global Morbidity and Mortality of Leptospirosis: A Systematic Review

Federico Costa[1,2,3☯], José E. Hagan[1,3☯], Juan Calcagno[1], Michael Kane[4], Paul Torgerson[5], Martha S. Martinez-Silveira[1], Claudia Stein[6], Bernadette Abela-Ridder[7], Albert I. Ko[1,3]*

PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

Global Burden of Leptospirosis: Estimated in Terms of Disability Adjusted Life Years

Paul R. Torgerson[1], José E. Hagan[2,3], Federico Costa[2,3,4], Juan Calcagno[2], Michael Kane[5], Martha S. Martinez-Silveira[2], Marga G. A. Goris[6], Claudia Stein[7], Albert I. Ko[2,3], Bernadette Abela-Ridder[8]*

PLOS | NEGLECTED TROPICAL DISEASES

RESEARCH ARTICLE

Environmental and Behavioural Determinants of Leptospirosis Transmission: A Systematic Review

Mwanajaa Abdalla Mwachui[1,2], Lisa Crump[1,2], Rudy Hartskeerl[3], Jakob Zinsstag[1,2], Jan Hattendorf[1,2]*

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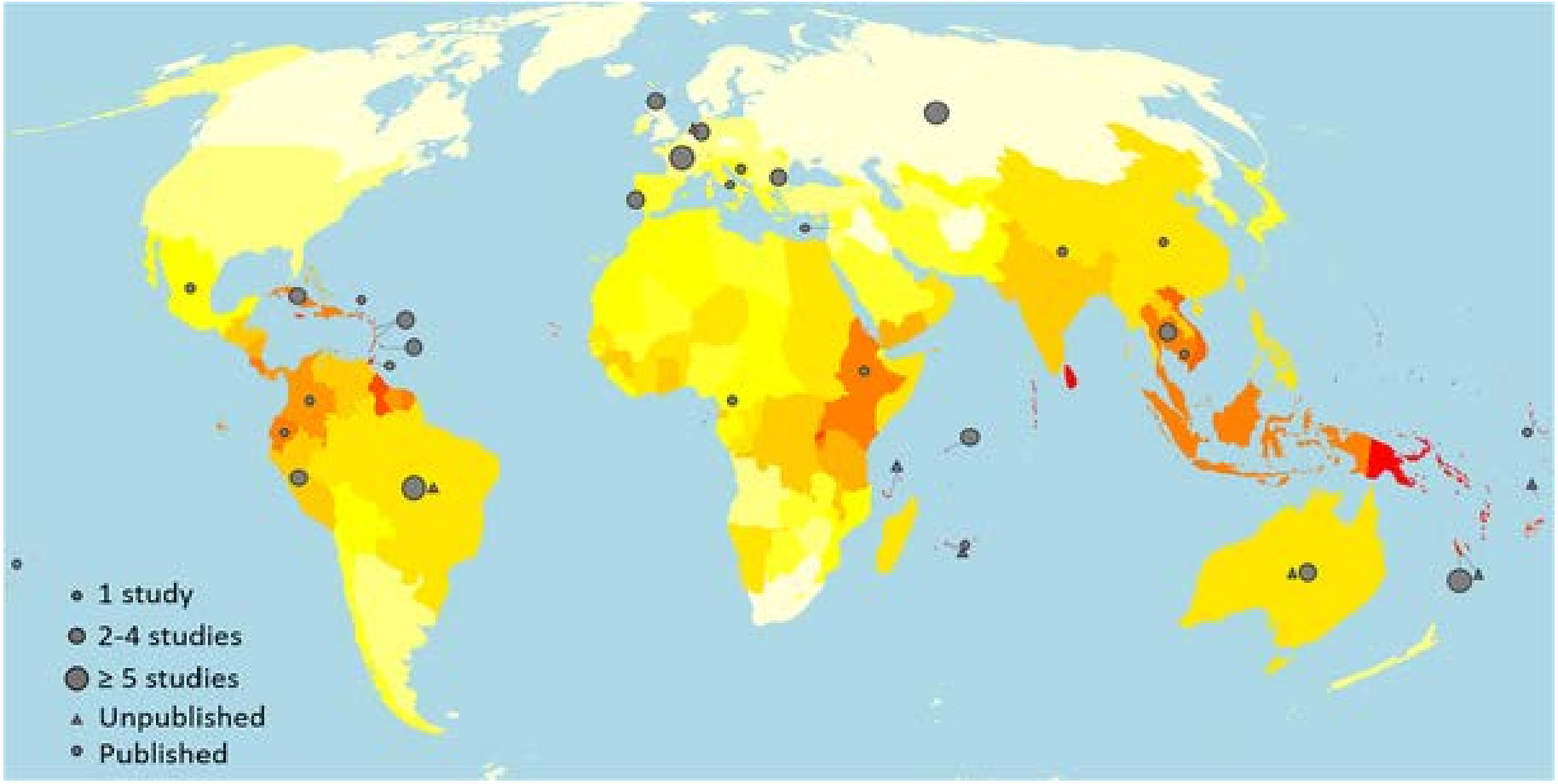
Fig 2. Estimated annual morbidity of leptospirosis by country or territory.



Costa F, Hagan JE, Calcagno J, Kane M, Torgerson P, et al. (2015) Global Morbidity and Mortality of Leptospirosis: A Systematic Review. PLoS Negl Trop Dis 9(9): e0003898. doi:10.1371/journal.pntd.0003898
http://journals.plos.org/plosntds/article?id=info:doi/10.1371/journal.pntd.0003898

Annual disease incidence is represented as an exponential colour gradient from white (0-3), yellow , orange to red (over 100), cases per 100 000 population.

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The global burden of leptospirosis and the top seven listed neglected tropical diseases

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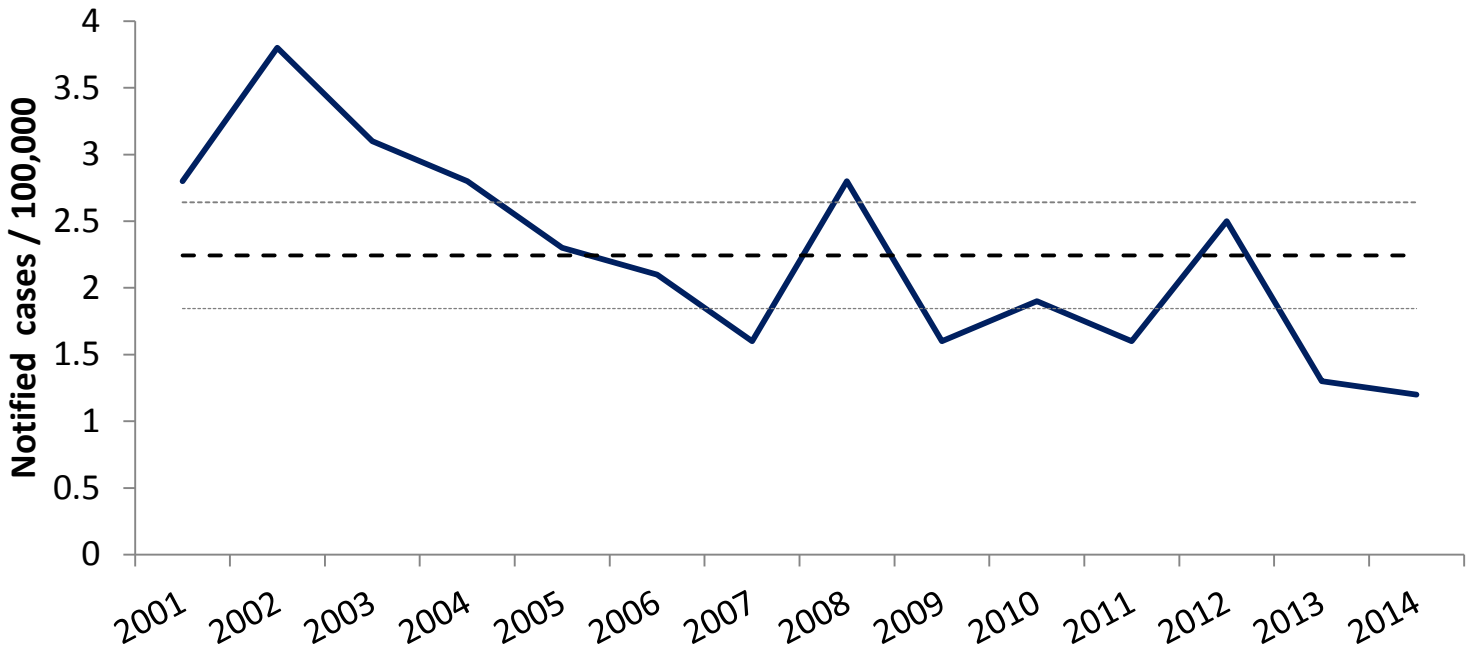
Diseases	Number of Cases	Deaths	DALYs (millions)
Intestinal nematodes	1,723 million	2,700	5.19
Leishmaniasis	10 million	51,600	3.32
Schistosomiasis	252 million	11,700	3.31
Leptospirosis*	1 million	**58,900**	2.90
Lymphatic filariasis	36 million	-	2.78
Food-borne trematodiasis	16 million	-	1.88
Rabies	1,100	26,400	1.46
Dengue	179,000**	14,700	0.83

*Is not a listed NTD (severe cases only)
** Incident (acute) symptomatic cases only

Source: Federico Costa with data from Hotez *et al.* 2014 and Togerson *et al.* 2015

Leptospirosis in NZ

- Human leptospirosis rate in New Zealand is among the highest in “developed” countries
- Average: 2.2 cases per 100,000 people



Data: ESR surveillance reports

Leptospirosis in NZ

- Highly prevalent: beef cattle, sheep and deer
  - Maybe associated with production loss (e.g. abortion, reduced growth)
- Human infection: influenza-like illness (most cases, not reported/notified) - severe disease (renal and hepatic failure)
  - Abattoir workers and farmers ~80%
  - Animal vaccination and PPE

Photos: RWNZ

Leptospirosis New Zealand

LARGELY UNKNOWN

Wild pig: ??

Wildlife

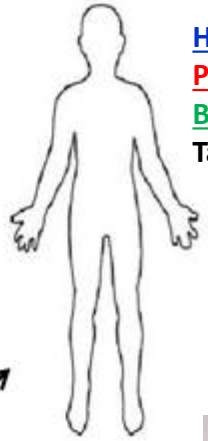
Possum: Balcanica

Rabbit: ??

Hedgehog: **Ballum**, **Pomona**

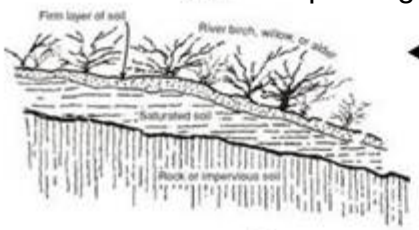
Rat/mouse: **Ballum**, Copenhageni

PARTIALLY KNOWN



Hardjobovis 46%
Pomona 23%,
Ballum 18%,
Tarassovi 8%

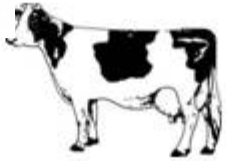
Soil and water



Hardjobovis, Bratislava, (Ballum, Pomona, **Tarassovi**, Copenhageni, Canicola)

Copenhageni, **Hardjobovis** (Pomona, Ballum, **Tarassovi**, Canicola)

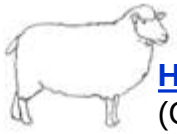
Hardjobovis, **Pomona**, (Copenhageni, Ballum, Arborea)



Hardjobovis, **Pomona**, (Copenhageni, Ballum)

Livestock

LARGELY KNOWN



Hardjobovis, **Pomona**, (Copenhageni, Ballum)

Three New Zealand studies

Outbreak in 3 dairy workers: Yuni Yupiana

Case series of persistent leptospirosis symptoms: Shaan Mocke

Estimation of economic cost: Juan Sanheuza

Background (1 March 2015)

Local dairy farm: two sheds

"One worker has been diagnosed with lepto, second worker now unwell

Both are hunters and pigs are on the farm which they both, I think, slaughter

The herd is not vaccinated …"

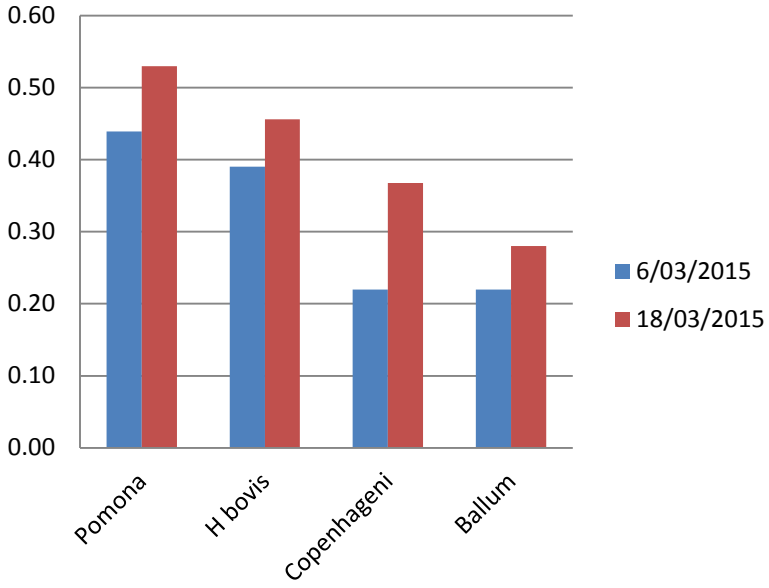
Human cases

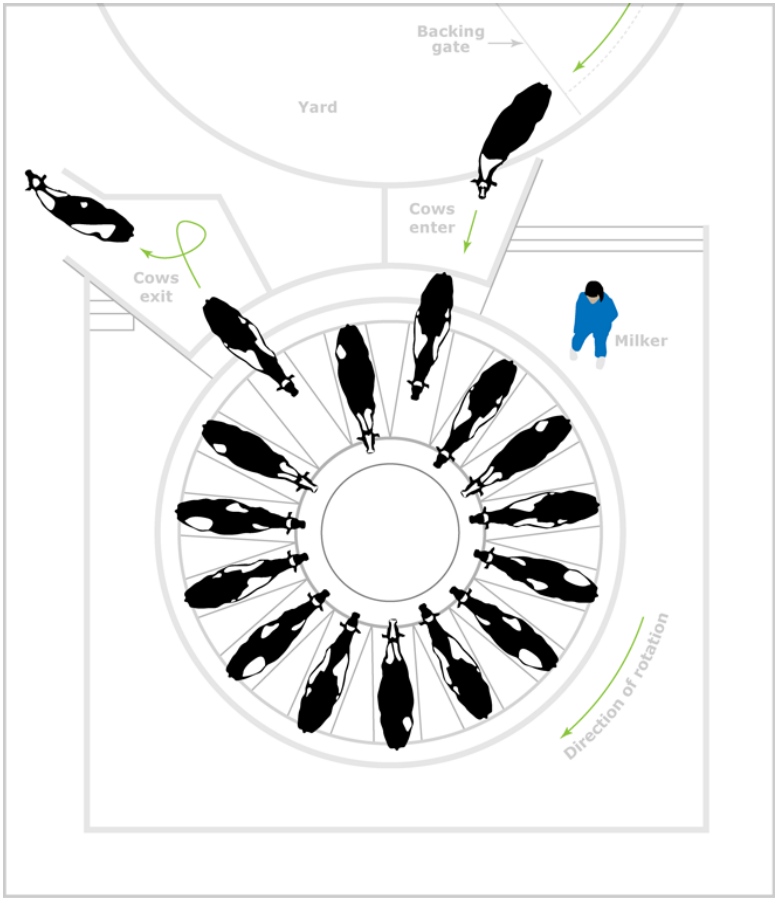
Case	Date of Symptom Onset	*Leptospira* IgM ELISA		*Leptospira* DNA		Serology MAT		serovar
		Sample 1	Sample 2	Sample	Result	Sample 1	Sample 2	
A	22 Jan 2015	neg	pos	urine	detected	400	200	Pomona
B	25 Feb 2015	neg	pos	urine	detected	<25	200	Hardjo
C	14 March 2015	neg	pos	plasma	detected	<25	400	Hardjo

Thanks to Patrick O'Connor and Margaret Tunbridge

MAT results 2015

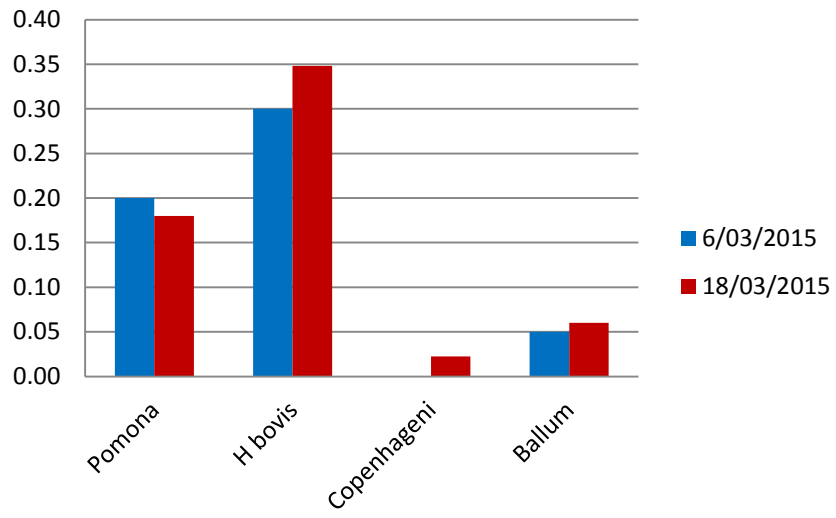
Titre	Pomona 6-Mar	Pomona 18-Mar	H bovis 6-Mar	H bovis 18-Mar	Copenhageni 6-Mar	Copenhageni 18-Mar	Ballum 6-Mar	Ballum 18-Mar
1\24	1	2	0	2	5	8	4	15
1\48	2	5	5	6	2	5	4	3
1\96	2	5	4	1	0	7	1	1
1\192	1	2	4	10	1	2	0	0
1\384	1	8	1	7	1	2	0	0
1\768	1	7	2	3	0	0	0	0
1\1536	4	4	0	1	0	0	0	0
1\3072	6	2	0	1	0	1	0	0
Total +ve	18	36	16	31	9	25	9	19
Sample size	41	68	41	68	41	68	41	68

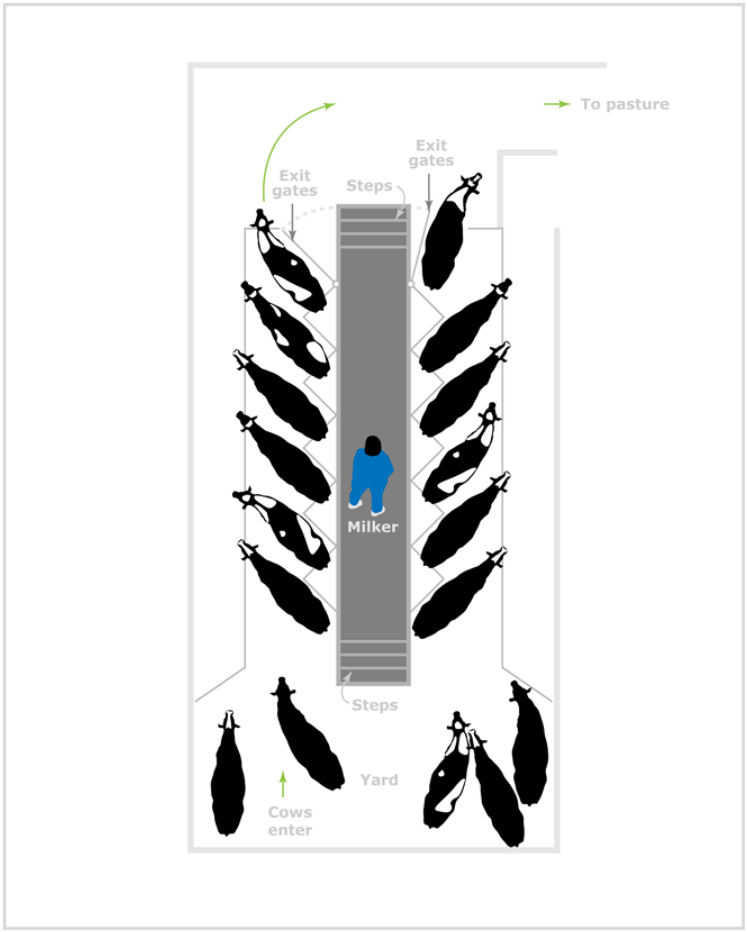




MAT results 2015

Titre	Pomona 6-Mar	Pomona 18-Mar	H bovis 6-Mar	H bovis 18-Mar	Copenhageni 6-Mar	Copenhageni 18-Mar	Ballum 6-Mar	Ballum 18-Mar
1\24	3	1	0	2	0	2	2	4
1\48	1	7	3	3	0	0	0	1
1\96	1	4	3	3	0	0	0	0
1\192	2	1	3	7	0	0	0	0
1\384	1	3	1	6	0	0	0	0
1\768	0	0	2	10	0	0	0	0
1\1536	0	0	0	0	0	0	0	0
1\3072	0	0	0	0	0	0	0	0
Total +ve	8	16	12	31	0	2	2	5
Sample size	40	89	40	89	40	89	40	89





Outbreak in 3 dairy workers

Adult cattle treated and vaccinated

Reduction in titres and urine PCR

Young stock vaccination programme underway

One of the three still not working (Oct 2015):

- “severe fatigue/lethargy, muscle aches, twitching”
- “unable to return to former function”
- “gait / stability affected especially with fatigue”
- “speech / language / concentration fatigability”

Three New Zealand studies

Outbreak in 3 dairy workers: Yuni Yupiana

Case series (persistent leptospirosis symptoms): Shaan Mocke

Estimation of economic cost: Juan Sanheuza

OPEN ACCESS Freely available online

PLOS ONE

Towards the Burden of Human Leptospirosis: Duration of Acute Illness and Occurrence of Post-Leptospirosis Symptoms of Patients in The Netherlands

Marga G. A. Goris[1*☯], Vanessa Kikken[2☯], Masja Straetemans[1], Sandra Alba[1], Marco Goeijenbier[3], Eric C. M. van Gorp[3], Kimberly R. Boer[1], Jiri F. P. Wagenaar[1,3], Rudy A. Hartskeerl[1]

1 WHO/FAO/OIE and National Leptospirosis Reference Center and section Epidemiology, Royal Tropical Institute, KIT Biomedical Research, Amsterdam, The Netherlands, **2** Athena Institute, Free University, Amsterdam, The Netherlands, **3** Department of Virology, Erasmus Medical Center, Rotterdam, The Netherlands

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New Year Honours 2014: John Kerr

By Patrick O'Sullivanpatrick osullivan@hbtoday co nz

10:11 AM Tuesday Dec 31, 2013

TONIC: John Kerr is pictured in his private cinema, which is used by community groups to raise money.
PHOTO/GLENN TAYLOR HBT134404-02

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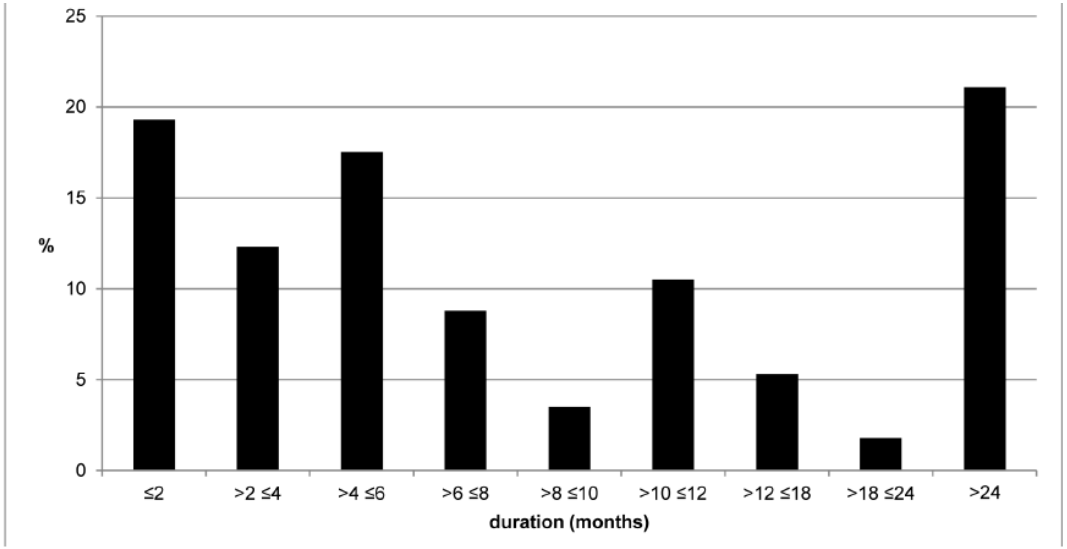
Netherlands: Post-lepto symptoms

1. active finding: 68/225 (30.2%)
   - extreme fatigue, headache, malaise, myalgia and joint pains
   - higher age (≥38 years) was positively associated with the occurrence of PS (OR 2.5, 95% CI 1.4-4.5),



Source Goris *et al* 2013

Figure 1. Persistent complaints by active case finding (PCAC) stratified according to months of duration. The bars represent the percentage of the total of reported post-leptospirosis complaints separated according to duration, expressed in periods of months as indicated on the X-axis.

Netherlands: Post-lepto symptoms

2. passive finding: 108/236 (45.8%)

   Hospitalised, data collected ~ 1 month after discharge

   - extreme fatigue, headaches, hair loss at young age, mild jaundice and disability to work
   - older age (≥ 38 years) were more likely to have PS compared to individuals of younger age (adj OR 2, 95% CI 1.2-3.5)
   - Sejroe group infections (OR 4.8, 95% CI 0.9-27.0) were more likely to result in PS compared to serogroup Grippotyphosa.

NZ Case series: Post-lepto symptoms

Exploratory study on the impact in 7 New Zealand men

Interpretative Phenomenological Analysis

Semi-structured face-to-face interviews conducted in January and February 2016

NZ Post-lepto symptoms: interim findings 1

5 out of 7 were hospitalised.

Delay in diagnosis/treatment of initial infection.

Generally diagnosed as having a virus.

Active hard working men with few previous/ concurrent health issues.

Limited support from employers.

Generally good family support in most cases.

NZ Post-lepto symptoms: interim findings 2

2 out of 7 have returned to full time employment in the career they had prior.

Chronic fatigue most common complaint. Back pain, headaches, kidney infections, neurological problems, reduced immunity, light intolerance, muscle pain and mood swings.

Many found positives in their circumstances, for example spending more time with the family or in careers they wouldn't have considered before.

Three New Zealand studies

Outbreak in 3 dairy workers: Yuni Yupiana

Case series of persistent leptospirosis symptoms: Shaan Mocke

Estimation of economic cost: Juan Sanheuza

Objectives

- A combined estimate of the burden of leptospirosis in humans (Disability-Adjusted Life Years and cost due to work absenteeism and treatment) and in livestock due to production loss and vaccination

Infection in New Zealand Workers

Occupation	Seroprevalence# (%)	Clinical Disease Population Attributable Risk*
Abattoir workers	10.9	2.8 (0.9 – 5.0)
Farmers	6.6	1.3 (0.0 - 3.1)
Veterinarians	5.1	0.52 (0.0 - 1.68)
Vet Students	0	NA

#MAT titre cut-point ≥ 48 to Hardjobovis and /or Pomona (abattoir workers) and /or Ballum, Copenhageni , Tarassovi (other occupations)
*number of cases of influenza like illness per 100 persons per year attributed to seroconversion

Source: Sanhueza *et al.* ILS meeting 2015 and Epi & Inf 2015; Dreyfus *et al*. Int. J. Environ. Res. Public Health 2014 and Epi & Inf 2015; Fang *et al.* NZ Vet J 2012.

Disease severity, duration and cost

Disease severity and duration

- Exposed cases (incidence)
  - Severe vs Mild: 13% severe 87% mild (Dreyfus et al., 2015)
  - Persistent: 30% of severe cases (>0.3 – 2 years) (Goris et al., 2013 and expert opinion)

  - Different disease weights (Salomon et al., 2012)

Cost:

- **Human**: Work absence + treatment cost
- **Livestock**: Production loss cost + vaccination

Livestock production loss data

Deer [Ayanegui-Alcerreca 2006, Subharat et al., 2012]

- 3.7kg lower slaughter weights in infected vs non-infected
- 6% lower calf mortality in vaccinated vs control hinds
- ~**5%** affected | infection

Sheep [Vallée et al., 2014]

- 0.75kg lower weights in control vs vaccinated lambs

Beef [Vallée et al., 2014, Sanhueza et al., 2013]

- 14kg weight loss in control vs vaccinated animals
- 8.2% abortions due to *Leptospira* and 3% abortion rate in population

Annual livestock production loss

Sheep: 1.65 (0.41–5.19) million or ($0.09/ewe)

Beef: 1.32 (0.43–3.47) million or ($1.36/cow)

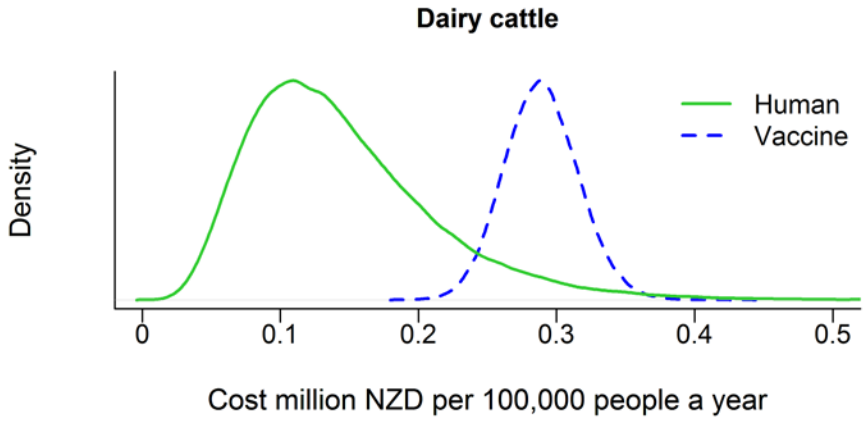
Deer: 3.11 (1.26–6.08) million or ($6.79/hind)

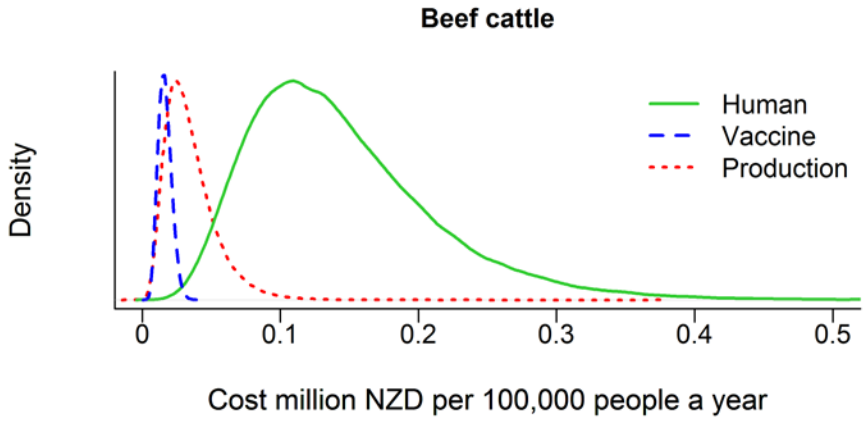
Total: 6.46 (3.55–11.12) million

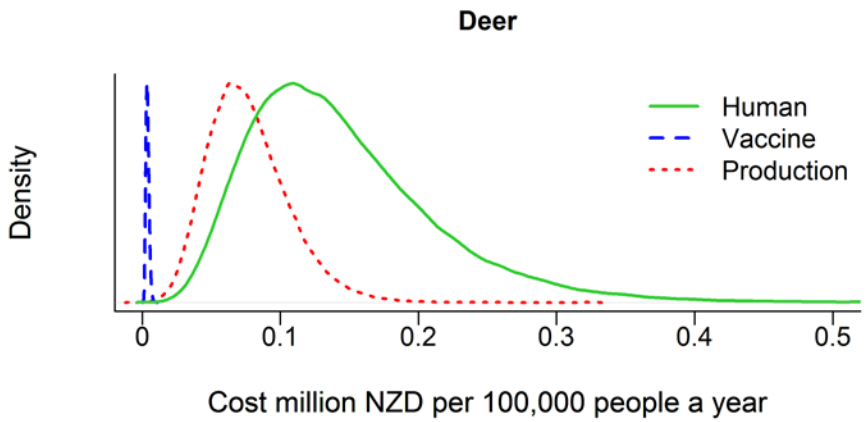
<u>Current vaccination cost:</u>

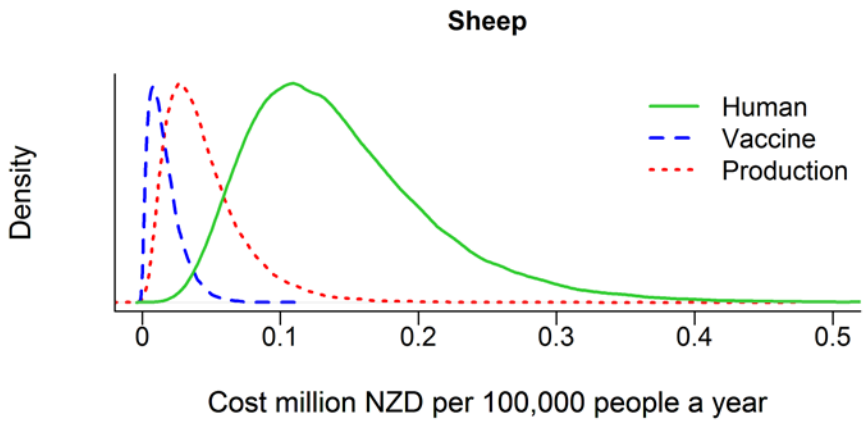
13.77 million (dairy cattle, beef cattle, sheep and deer)

Annual Burden of leptospirosis









Total NZ$ 26.3 million (0.62 million per 100,000 people)

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Acknowledgments

Study participants: PLS men, farmers, vets, meat workers.

John Kerr - Occupational Physician
Jane Lennan - Clinical Psychologist
Ron Janes, Allie Maskill - Rural GPs

Hawkes Bay Medical Research Foundation
Wairarapa Veterinary Association
Sustainable Farming Fund

New Zealand Aid
Massey University Doctoral Scholarship
IVABS Summer Scholarship

10th International Leptospirosis Society Meeting
November 27 - December 01, 2017
Palmerston North, New Zealand

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http://www.leptospirosis.org.nz/News/VideoSeries.aspx

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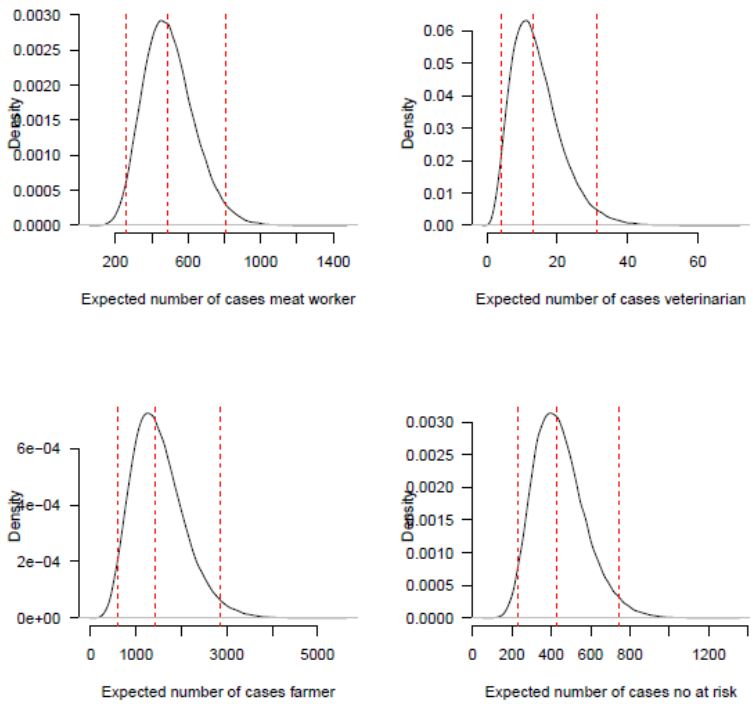
Results

Estimated annual number of human cases:

- Exposed cases
  - 356 Severe
    - **UR** = 3.9
  - 2,372 Total
    - **UR** = 26



Burden: Annual DALYs and Cost

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At risk occupations:

DALY = 27.23 (7.86–83.57) per 100,000 people

Cholera 65 - Rabies 21 - Dengue 12

Not at risk occupations:

DALY = 0.16 (0.05–0.50) per 100,000 people

Absence and treatment:

Cost: $5.61 (2.1–13.2) million/year

0.13 (0.05–0.31) million per 100,000 people