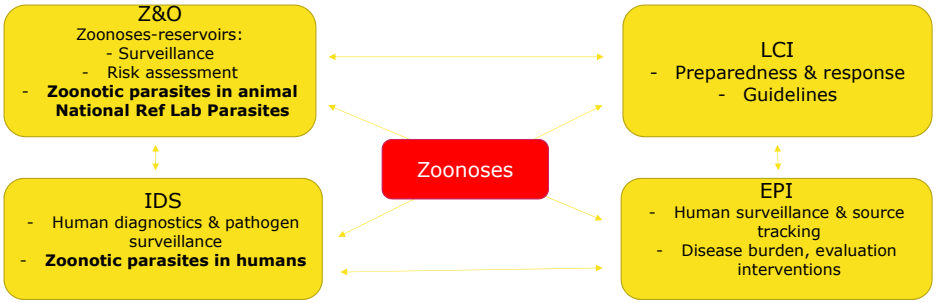
Rijksinstituut voor Volksgezondheid en Milieu
Ministerie van Volksgezondheid, Welzijn en Sport

One Health in parasitology at RIVM

Toxoplasma epidemiology and source attribution as an example

Titia Kortbeek, CIb-IDS
Marieke Opsteegh, CIb-Z&O

Center of Infectious Disease Control-RIVM
Different centers different tasks



Z&O Veterinary parasitology?

Preventive Veterinary Medicine 96 (2010) 232–240

Contents lists available at ScienceDirect

Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed

Evaluation of ELISA test characteristics and estimation of *Toxoplasma gondii* seroprevalence in Dutch sheep using mixture models

Marieke Opsteegh [a,b,*], Peter Teunis [a], Marieke Mensink [a], Lothar Züchner [c], Adriana Titilincu [d], Merel Langelaar [a], Joke van der Giessen [a]

[a] National Institute for Public Health and the Environment (RIVM), P.O. Box 1, 3720 BA Bilthoven, The Netherlands

Available online at www.sciencedirect.com
ScienceDirect
International Journal for Parasitology 38 (2008) 571–578
www.elsevier.com/locate/ijpara

Evidence for an increasing presence of *Echinococcus multilocularis* in foxes in The Netherlands

Katsuhisa Takumi [a,*], Ankje de Vries [a], Mei Ling Chu [a], Jaap Mulder [b], Peter Teunis [c], Joke van der Giessen [a]

[a] Laboratory for Zoonoses and Environmental Microbiology, Centre for Infectious Disease Control, National Institute for Public Health and Environment (RIVM), Antonie van Leeuwenhoeklaan 9, 3720 BA, Bilthoven, The Netherlands
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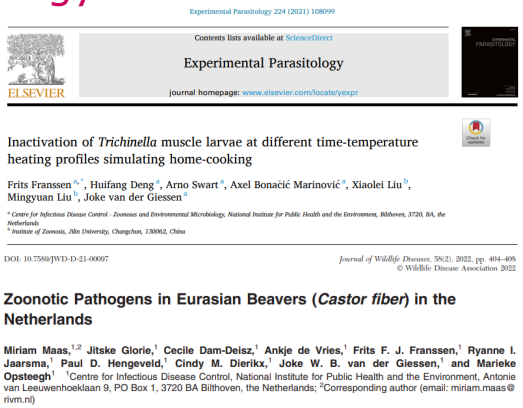

Experimental Parasitology 224 (2021) 108099

Contents lists available at ScienceDirect

Experimental Parasitology

journal homepage: www.elsevier.com/locate/yexpr

Inactivation of *Trichinella* muscle larvae at different time-temperature heating profiles simulating home-cooking

Frits Franssen [a,*], Huifang Deng [a], Arno Swart [a], Axel Bonačić Marinović [a], Xiaolei Liu [b], Mingyuan Liu [b], Joke van der Giessen [a]

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DOI: 10.7589/JWD-D-21-00097
Journal of Wildlife Diseases, 58(2), 2022, pp. 404–408

Zoonotic Pathogens in Eurasian Beavers (*Castor fiber*) in the Netherlands

Miriam Maas,[1,2] Jitske Glorie,[1] Cecile Dam-Deisz,[1] Ankje de Vries,[1] Frits F. J. Franssen,[1] Ryanne I. Jaarsma,[1] Paul D. Hengeveld,[1] Cindy M. Dierikx,[1] Joke W. B. van der Giessen,[1] and Marieke Opsteegh[1] [1]Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Antonie van Leeuwenhoeklaan 9, PO Box 1, 3720 BA Bilthoven, the Netherlands; [2]Corresponding author (email: miriam.maas@rivm.nl)

Animals as sources of zoonotic parasites

- Reservoirs
- Source attribution (example Toxoplasma)
- Intervention

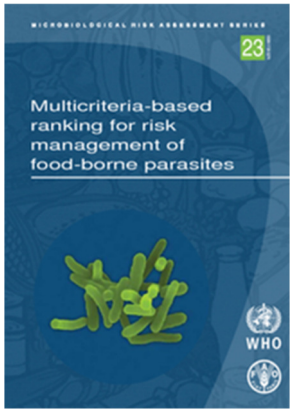
Methods to rank and prioritize infectious diseases

- Multicriteria decision analyses
  - Number of global foodborne illnesses
  - Global distribution (number of regions)
  - Acute morbidity severity (disability weight)
  - Chronic morbidity severity (disability weight)
  - Fraction of illness that is chronic (%)
  - Case-fatality ratio (%)
  - Likelihood of increased human burden (%)
  - How relevant is this parasite/food pathway for international trade?
  - What is the scope of impact to economically vulnerable communities?
- Disease burden estimation (DALY estimation)

Table 1. Ranking of foodborne parasites from a global perspective[a]

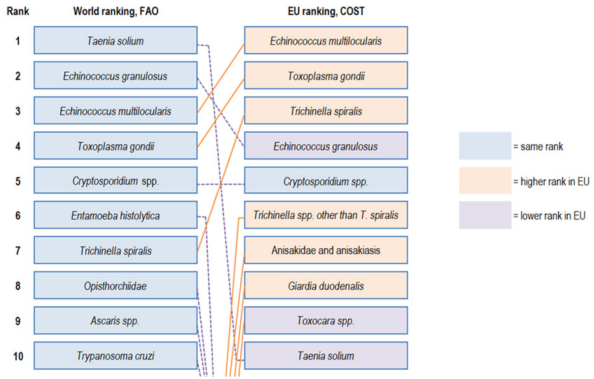
Ranking position	Parasite	Major food commodities associated with foodborne transmission
1	*Taenia solium*	Pork[b], fresh produce[c]
2	*Echinococcus granulosus*	Fresh produce
3	*Echinococcus multilocularis*	Fresh produce
4	*Toxoplasma gondii*	Meat from small ruminants, pork, beef, game meat (red meat and organs); also fresh produce
5	*Cryptosporidium* spp.	Fresh produce, fruit juice, milk
6	*Entamoeba histolytica*	Fresh produce
7	*Trichinella spiralis*	Pork
8	*Opisthorchiidae*	Freshwater fish
9	*Ascaris* spp.	Fresh produce
10	*Trypanosoma cruzi*	Fruit juices
11	*Giardia duodenalis*	Fresh produce
12	*Fasciola* spp.	Fresh produce (freshwater plants)
13	*Cyclospora cayetanensis*	Berries, fresh produce
14	*Paragonimus* spp.	Freshwater crustaceans
15	*Trichuris trichiura*	Fresh produce
16	*Trichinella* spp.[d]	Game meat
17	Anisakidae	Marine fish, crustaceans and cephalopods
18	*Balantidium coli*	Fresh produce
19	*Taenia saginata*	Beef
20	*Toxocara* spp.	Fresh produce
21	*Sarcocystis* spp.	Beef or pork depending on species
22	Heterophyidae	Freshwater/brackish water fish
23	Diphyllobothriidae	Fish (freshwater and marine)
24	*Spirometra* spp.	Frog, snake meat

[a]Table derived from data in report *Multicriteria-Based Ranking for Risk Management of Foodborne Parasites*, 24 October 2012 (http://www.fao.org/food/food-safety-quality/a-z-index/foodborne-parasites/en/ and http://www.who.int/foodsafety/micro/jemra/meetings/sep12/en/).



Report of a Joint FAO/WHO Expert Meeting, 3–7 September 2012, FAO Headquarters, Rome, Italy

Regional ranking Europe



Top 5 foodborne parasites in Europe

1. *Echinococcus multilocularis*
2. *Toxoplasma gondii*
3. *Trichinella spiralis*
4. *Echinococcus granulosus*
5. *Cryptosporidium* spp.

RESEARCH ARTICLE

Prioritisation of food-borne parasites in Europe, 2016

Martijn Bouwknegt[1], Brecht Devleesschauwer[2], Heather Graham[3], Lucy J Robertson[4], Joke WB van der Giessen[1], the Euro-FBP workshop participants[5]

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5. The Euro-FBP workshop participants are listed at the end of the article

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Bouwknegt Martijn, Devleesschauwer Brecht, Graham Heather, Robertson Lucy J, van der Giessen Joke WB, the Euro-FBP workshop participants. Prioritisation of food-borne parasites in Europe, 2016. Euro Surveill. 2018;23(9):pii=17-00161. https://doi.org/10.2807/1560-7917.ES.2018.23.9.17-00161

Article submitted on 03 Mar 2017 / accepted on 15 Aug 2017 / published on 01 Mar 2018

Recommendations

***Toxoplasma gondii* and toxoplasmosis**

- Make congenital toxoplasmosis reportable in all MS in humans
- Serosurveillance studies in human population (DALY estimations)
- **Risk based surveillance in meat producing animals**
- **Measures to control needed (meat producing animals/food) based on QMRA**

Parasite Epidemiology and Control 13 (2021) e00205

Contents lists available at ScienceDirect

Parasite Epidemiology and Control

journal homepage: www.elsevier.com/locate/parepi

Surveillance of foodborne parasitic diseases in Europe in a One Health approach

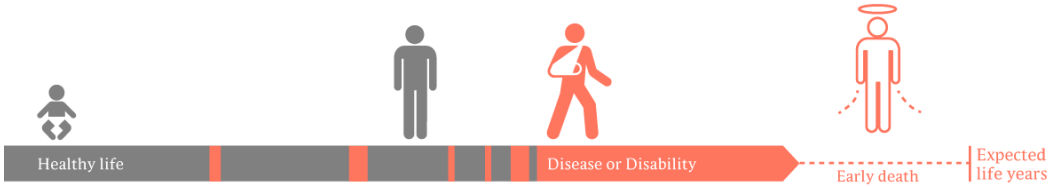
Joke van der Giessen [a,*], Gunita Deksne [b,c], Maria Angeles Gómez-Morales [d], Karin Troell [e], Jacinto Gomes [f], Smaragda Sotiraki [g], Miroslaw Rozycki [h], István Kucsera [i], Olgica Djurković-Djaković [j], Lucy J. Robertson [k]

Disease burden

DALY

Disability Adjusted Life Year is a measure of overall disease burden, expressed as the cumulative number of years lost due to ill-health, disability or early death

= YLD Years Lived with Disability + YLL Years of Life Lost

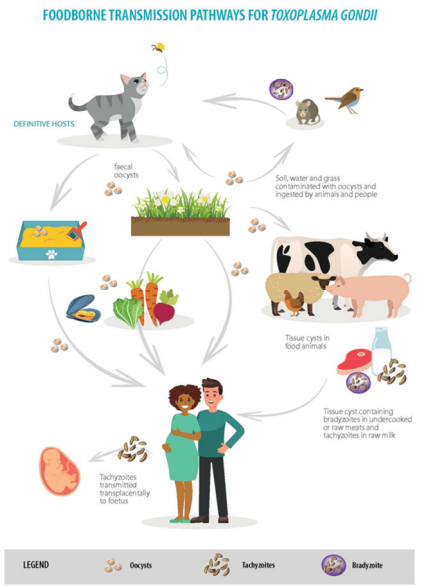


RIVM report 2021-0161

Source attribution

› Source attribution for *T. gondii* infection

- Epidemiological studies
  - Outbreak and case reports
- ★ – Risk factor analysis
- Subtyping
- Source specific diagnostics
- Expert elicitation
- ★ Comparative Risk Assessment



EFSA BIOHAZ Panel (2018)

Epidemiologische *Toxoplasma* seroprevalentie studies humaan in NL

- Peilstation onderzoeken 1980; 1985 : Toxoplasma IgG
- Toxoplasma interventie preventie (TIP) studie: 1986-1988
  Prevention of congenital toxoplasmosis; experience in The Netherlands.
  Conyn-van Spaendonck MA. International Ophthalmology 13: 403-406, 1989. doi: 10.1007/BF02306489.
- Pienter studies : 1996-1997; 2006-2007; 2016-2017.
  Decreased prevalence and age-specific risk factors for Toxoplasma gondii IgG antibodies in The Netherlands between 1995/1996 and 2006/2007. Hofhuis A, van Pelt W, van Duynhoven YT, Nijhuis CD, Mollema L, van der Klis FR, Havelaar AH, Kortbeek LM. Epidemiol Infect. 2011 Apr;139(4):530-8. doi: 10.1017/S0950268810001044
- Congenitale toxoplasmose studie (hielprik setjes 2006)
  Congenital toxoplasmosis and DALYs in the Netherlands. Kortbeek LM, Hofhuis A, Nijhuis CD, Havelaar AH. Mem Inst Oswaldo Cruz. 2009 Mar;104(2):370-3. doi: 10.1590/s0074-02762009000200034
- NESDA studie : Toxoplasmose en depressive en angststoornissen
  Toxoplasma gondii seropositivity in patients with depressive and anxiety disorders. de Bles NJ, van der Does JEH, Kortbeek LM, Hofhuis A, van Grootheest G, Vollaard AM, Schoevers RA, van Hemert AM, Penninx BWJH, Rius-Ottenheim N, Giltay EJ. Brain Behav Immun Health. 2020 Dec 31;11:100197. doi: 10.1016/j.bbih.2020.100197

Recente studie:

- Toxoplasma bron onderzoek
- Pienter 3

Toxoplasmose

- Congenitaal (overdracht moeder op kind ca. 29%)
  - Abortus/doodgeboorte (2%),
  - Chorioretinitis (14%), CZS afwijkingen (9%), aspecifieke symptomen,
  - Subklinisch (75%), evt later oogafwijkingen (2%/jaar)

- Verworven
  - Immuuncompetent
    - › Asymptomatisch of mild
    - › Chorioretinitis
    - › Gedragsveranderingen, schizophrenie?
  - Immuungecompromitteerd
    - › encephalitis, myocarditis, pneumonie, hepatitis

Meeste oculaire tox is verworven

- Oculaire toxoplasma door congenitale infecties :
  - Bij geboorte slechts een beperkt aantal kinderen met chorioretinitis (<10 %)
  - Regelmatig recidieven- gaat lang door
  - Risico op lesies: 6.8-80 / 100.000 personen

- Risico op oculaire lesies gedurende het leven door verworven infecties is hoger dan door CT:
  - 30-160 / 100.000 personen
- Vaak recidiverende opvlammingen

Petersen ea. Epidemiology of ocular toxoplasmosis Ocular immunology and Inflammation 2012 DOI: 10.3109/09273948.2012.661115

Arruda S. ea Clinical manifestations and visual outcomes associated with ocular toxoplasmosis in a Brazilian Population Scientific reports 2021 https://doi.org/10.1038/s41598-021-82830-z

Ferreira L.B., Furtado J.M., Charng J., Franchina M., Matthews J.M., MolanA.A.L., Hunter M., Mackey D.A. & Smith J.R., Prevalence of Toxoplasmic Retinochoroiditis in anAustralian Adult Population: a Community-Based Study, Ophthalmology Retina (2022), doi: https://doi.org/10.1016/j.oret.2022.04.022

Verschil in virulentie van stammen

- Moleculaire typering van stammen: drie clonal lineages
  - In Europa vooral type II, ook type III en soms type I
  - In Latijns Amerika : atypische stam: veel virulenter

- In Brazilie vaker oculaire problemen (50 % versus 10 %) bij congenital toxoplasmose en veel ernstiger oogproblemen dan in Europa.
  - Grotere lesies
  - Meer lesies
  - Meer visusstoornissen

Gilbert RE, Freeman K, Lago EG, Bahia-Oliveira LMG, Tan HK, et al. (2008) Ocular Sequelae of Congenital Toxoplasmosis in Brazil Compared with Europe. PLoS Negl Trop Dis 2(8): e277

Shwab, E.K., Zhu, X.Q., Majumdar, D., Pena, H.F., Gennari, S.M., Dubey, J.P., Su, C., 2014. Geographical patterns of Toxoplasma gondii genetic diversity revealed bymultilocus PCR-RFLP genotyping. Parasitology 141, 453–461. https://doi.org/10.1017/S0031182013001844.

Pienter 3 studie

- national cross-sectional serosurvey

- Toxoplasma IgG
  - In house ELISA
  - Same method as in P1 and P2
  - 6600 samples

Main questions:
- Changes in seroprevalence compared with P1 and P2 ?
- Riskfactors
  - If possible (limited material available) same in BES islands
  - Change in riskfactors?

Geselecteerde gemeenten

gemeenten in landelijke steekproef

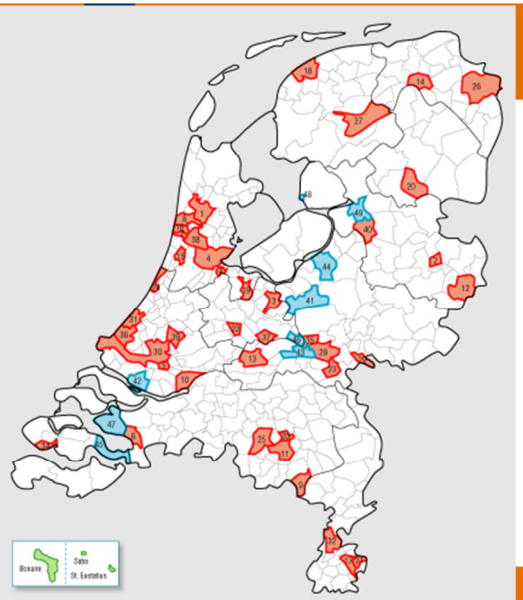
1	Alkmaar	21	Landgraaf
2	Almelo	22	Nieuwegein
3	Amersfoort	23	Nijmegen
4	Amsterdam	24	Noordwijk
5	Barendrecht	25	Oirschot
6	Bergen op Zoom	26	Oldambt
7	Beverwijk	27	Opsterland*
8	Castricum	28	Overbetuwe*
9	Cranendonck	29	Rijnwaarden
10	Dordrecht	30	Rotterdam*
11	Eindhoven*	31	's-Gravenhage
12	Enschede	32	Sittard-Geleen*
13	Geldermalsen	33	Son en Breugel
14	Groningen	34	Vlissingen
15	Haarlem	35	Wageningen
16	Heemskerk	36	Westland
17	Heerlen	37	Wijk bij Duurstede
18	het Bildt	38	Zaanstad
19	Hilversum	39	Zuidplas
20	Hoogeveen	40	Zwolle

*In deze gemeenten worden extra allochtonen uitgenodigd

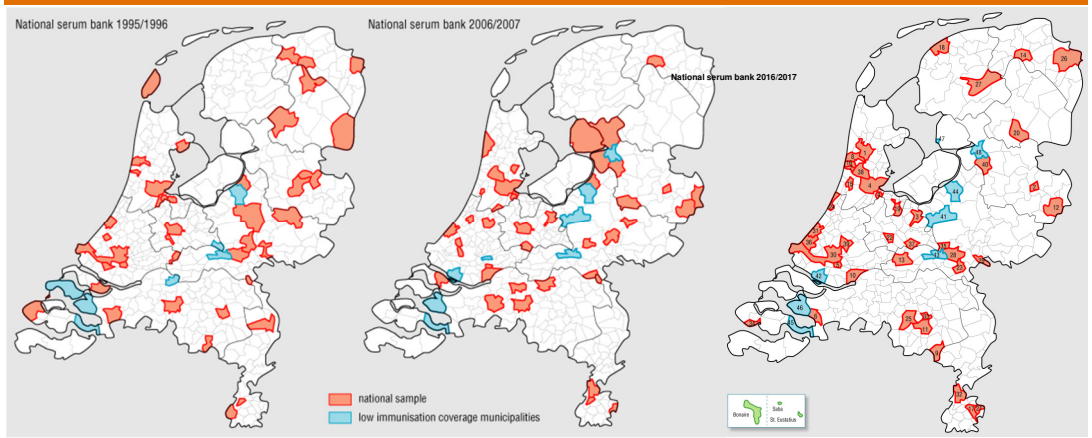
gemeenten met lage vaccinatiegraad

41	Barneveld	45	Reimerswaal
42	Korendijk	46	Rhenen
43	Neder-Betuwe	47	Tholen
44	Nunspeet	48	Urk
		49	Zwartewaterland

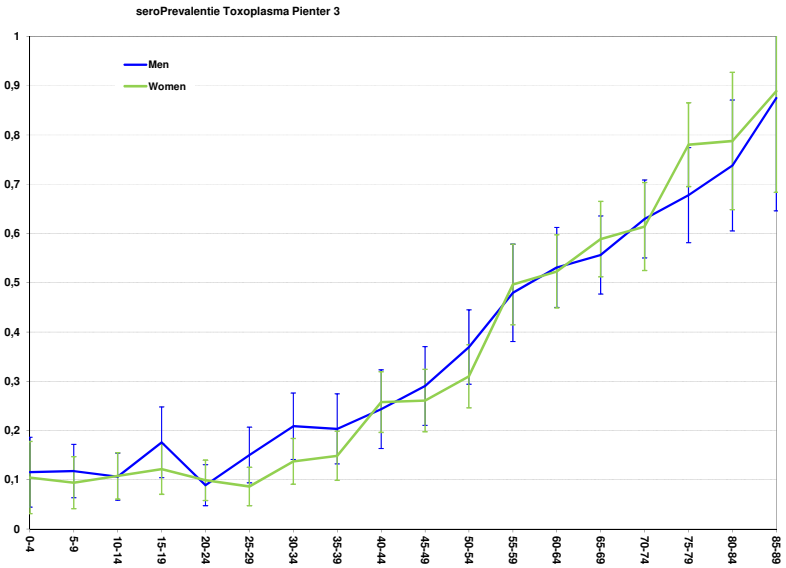
Caribisch Nederland



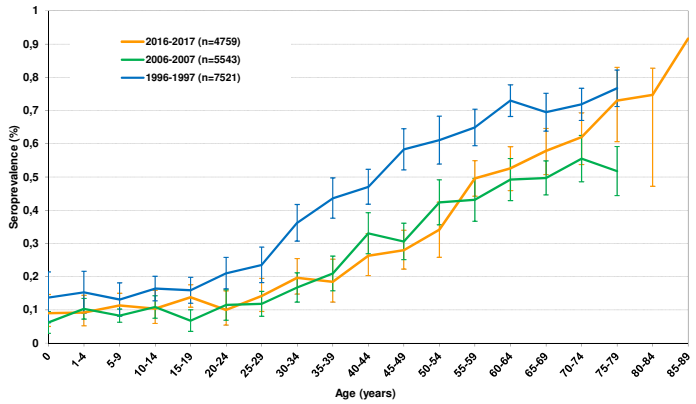
Serosurveillance in NL: PIENTER studies



*PIENTER='Peiling Immunisatie Effect Nederland ter Evaluatie van het Rijksvaccinatieprogramma'



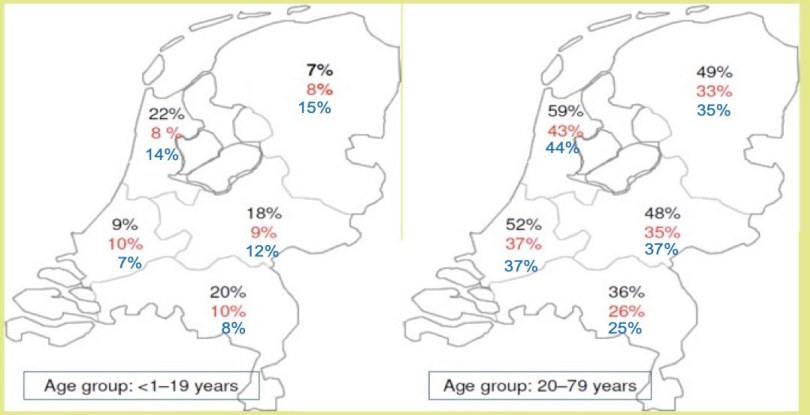
Age-specific weighed prevalence of *Toxoplasma gondii* IgG antibodies in the three Dutch serosurveys (PIENTER)



Seroprevalences

Study			
PIENTER 1		40.5%	(37.5%-38.6%)
PIENTER 2		26.0%	(24.0%-28.0%)
PIENTER 3	0-79	29.87%	(28.3%-31.4%)
	0-89	30.88%	(29.4%-32.4%)

Geographical distribution of Toxoplasma gondii IgG antibodies in the Netherlands:
Pienter 1996 (n=7521)
Pienter 2: 2007 (n= 7032)
Pienter 3: 2017 (n= 6190)



Risk factors

- Multivar, <20 years old
  - **P1**:
    - Country of birth,
    - geographical region (lowest: NE,SW),
    - Urbanization degree,
    - Gardening >5h /week
  - **P2**: only "Kept sheep or cattle in the past 5 years"
  - **P3**: only geographical region (highest: NE,NW)

    Region: NE & NW sign higher than SE (p=0.010, p=0.017)
    - NE: OR= 1.08 (1.02-1.15)
    - NW:OR= 1.06 (1.01-1.12)

Multivar, 20+ years old

- Age (continuous) → OR: 1.01 [1.01-1.01], p= <0.0001
- Regio (intercept = SE). All p= <0.0001
  - Central: OR: 1.09 [1.05-1.13]
  - NW: OR:1.17 [1.11-1.23]
  - SW: OR: 1.12 [1.07-1.17]
  - NE: OR: 1.11 [1.06-1.16]
- Country of birth (NL vs Other): OR: 1.08 [1.01-1.16], p= 0.02
- Education (intercept=high)
  - Middle: OR: 0.97 [0.94-1.01]. P =0.20
  - Low: OR: 1.06 [1.02-1.10], p=0.01

Multivar, 20+ years old (cont.)

- Eating meat (intercept = no meat)
  - Meat: OR: 1.25 [1.13-1.38], p=0.0002
  - Unknown: OR: 1.27 [1.16-1.39], p<0.0001
- Cattle (no vs yes) → 1.19 [1.08-1.29], p=0.0026
- Eat raw porkmeat (intercept = none)
  - <3 days a month: OR: 1.05[1.02-1.09], p=0.0027
  - >1 day a week: OR: 1.08 [1.00-1.17], p=0.044
  - Unknown: OR:1.1 [1.04-1.17], p=0.004
- Abroad Asia/Africa/America (no vs yes) → OR: 1.04 [1.01-1.07], p=0.038

Risk factors 20-79

P1	P2	P3
Divorced/Widowed		N/A
		Country of birth (not NL)
Low education [OR]	Low education [OR]	Low education [OR]
Region (SE=lowest) [OR]	Region (SE=lowest) [OR]	Region (SE=lowest) [OR]
Urbanization	Urbanization	
Gardening		
Professional contact with animals		
Kept a cat in the past 5 years	Kept a cat in the past 5 years	
Keeping a rabbit, hamster or guinea pig in the past 5 years (protective)		
N/A	Raw or undercooked pork	Raw or undercooked pork
	Occupational contact with clients or patients in the past 5 years (protective)	
N/A		Eating meat
		Having been abroad to Afrika/Asia/America

Conclusions

- Seroprevelance did not decrease in P3 compared to P2
- Riskfactors
  - It was not possible (due to limited material available) to examine the seroprevalence in BES islands
  - Change in riskfactors: yes

Tox bron onderzoek

Objective

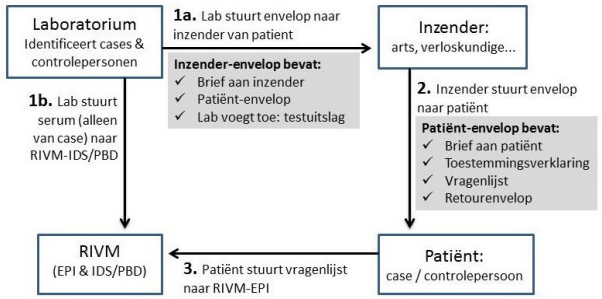
- Determine attribution of different transmission routes

- Risk factors for acute toxoplasmosis in the Netherlands:
  - Cases (recent infection) and controls via MMLs > RFs with OR
  - Recent case of toxoplasmosis
    - IgM anti-*Toxoplasma* positive with low to intermediate avidity of *Toxoplasma* IgG antibodies
  - min. 200 cases in 2 years
    - 1e serum binnen op 7-11-2016; laatste 18-5-2021;
    - Van veel cases geen vragenlijst (48 met vragenlijst)
    - Slechts 50 controle vragenlijsten.

Tox bron studie: prospectieve study

- Niet-WMO verklaring
- Logistics and materials

Logistiek *Toxoplasma* brononderzoek



Participating labs

1. **Streeklaboratorium voor de Volksgezondheid**, Haarlem
2. **Erasmus MC**, Rotterdam
3. **UMC Utrecht**, Utrecht
4. **Diakonessenhuis Utrecht**, Utrecht
5. **Antonius Ziekenhuis**, Nieuwegein
6. **Certe LvI**, Groningen*
7. **Izore**, Leeuwarden
8. **Alrijne Zorggroep**, Leiden
9. **Jeroen Bosch Ziekenhuis**, 's-Hertogenbosch
10. **Isala klinieken**, Zwolle
11. **LabMicta**, Hengelo
12. **Stichting PAMM**, Veldhoven**
13. **Laurentius ziekenhuis**, Roermond
14. **Maastricht UMC**, Maastricht

Resultaten: Univariate analyse

	Cases (%)	Controls (%)	OR (95% CI)
N	44	43	
Consumption of meat			
beef	43 (98)	34 (79)	11.38 (1.37-94.30)
veal	16 (36)	4 (9)	5.57 (1.68-18.47)
lamb	18 (41)	7 (16)	3.56 (1.30-9.76)
duck/goose (farm)	12 (27)	3 (7)	5.00 (1.30-19.25)
large game animals	14 (32)	3 (7)	6.22 (1.64-23.61)
Consumption of raw/undercooked meat			
any raw/undercooked beef	40 (91)	29 (67)	4.83 (1.44-16.18)
beef prepared undercooked	31 (70)	16 (37)	4.02 (1.64-9.85)
(steak) tartare	18 (41)	9 (21)	2.62 (1.01-6.76)
carpaccio	23 (52)	15 (35)	2.04 (0.86-4.84)
roast beef	19 (43)	9 (21)	2.87 (1.11-7.40)
smoked beef	16 (36)	9 (21)	2.16 (0.83-5.63)
any raw/undercooked pork	35 (80)	28 (65)	2.08 (0.79-5.46)
pork prepared undercooked	17 (39)	5 (12)	4.79 (1.57-14.56)
raw bacon	18 (41)	8 (19)	3.03 (1.14-8.03)
spreadable pork sausage	21 (48)	11 (26)	2.66 (1.07-6.57)
toppings of raw pork	9 (20)	2 (5)	5.27 (1.07-26.03)
dried/smoked sausage	26 (59)	18 (42)	2.01 (0.86-4.71)
Consumption of raw/undercooked crustaceans or shellfish	10 (23)	2 (5)	6.03 (1.24-29.41)
Consumption of fresh fruit or vegetable juice	23 (52)	15 (35)	2.04 (0.86-4.84)
Hand washing before preparing food			
always	15 (34)	28 (65)	1.00
sometimes	19 (43)	13 (30)	2.73 (1.06-7.01)
never/not applicable	10 (23)	2 (5)	9.33 (1.81-48.23)
Contact with sand/soil			
never	7 (16)	8 (19)	1.00
monthly	19 (43)	28 (65)	0.78 (0.24-2.50)
weekly	18 (41)	7 (16)	2.94 (0.77-11.21)
Animal contact (profession, volunteer work)	13 (30)	7 (16)	2.16 (0.77-6.08)
Recreation in wooded area	28 (64)	38 (88)	0.23 (0.08-0.70)

Multivariate analysis

- consumption of meat of large game animals OR: 8.23 (95%CI 1.62-41.87)
- sometimes or never washing hands before preparing food OR 4.06 (95%CI 1.08-15.30) and 15.87 (95%CI 2.18-115.45, respectively).
- Recreation in wooded areas: OR 0.13 :lower chance of being infected by *Toxoplasma* (95%CI 0.03-060).

Conclusie

- Het is heel lastig om voldoende patienten te includeren (met vragenlijst) en om controles te krijgen

- Klein aantal cases
  - significante resultaten zeggen wel wat (wild eten en handen wassen);
  - niet significante factoren zouden bij grotere aantallen wel risico kunnen zijn.