Module 1

Taking epidemiology into account – what to sequence and how much?

SEQAFRICA

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15 February 2021 (10:30 – 11:00)

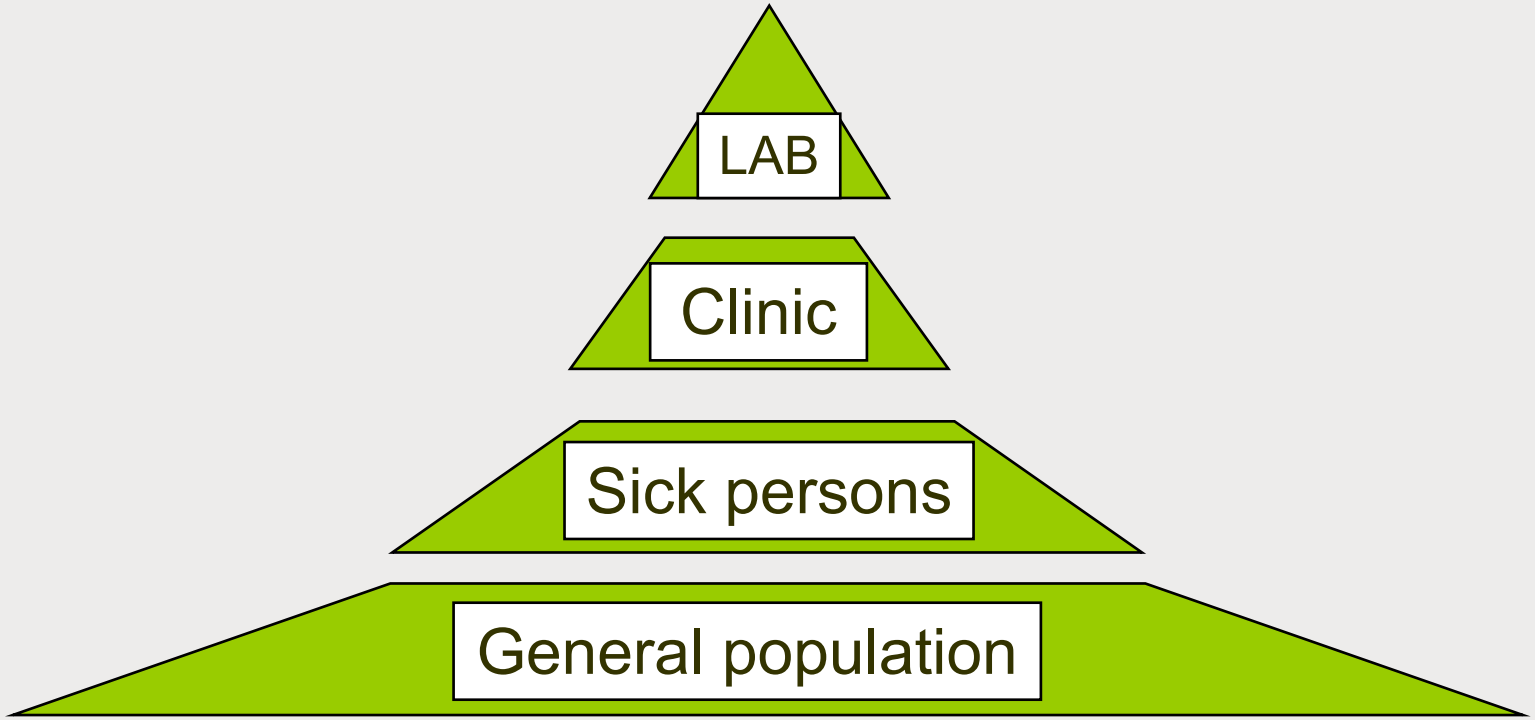
Dr. Alessandro Foddai (DVM, MSc, PhD, epidemiologist)

Aim of the lecture

- Basic sampling design to test stored specimens, while keeping track of the main limitations

- Estimate confidence in absence or eventual prevalence of pathogen AMR “P1” in a “population” of lab stored specimens “Np”

General principle behind the lecture…. NUMERATOR DATA (cases) pros and cons



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What to test and how much?

- Not always possible to use the most sophisticated test on big populations. Consider:
    - Testing capacity
    - Feasibility
    - Logistics
    - Limitations

Test/s performance:

- **Sensitivity (Se)**: % of “truly positive” units correctly identified pos
- **Specificity (Sp)**: % of “truly negative” units correctly identified neg

Testing strategy:

Parallel testing to increase sensitivity (but can ↑ false **+**ves)

Serial testing to increase specificity (but can ↑ false **-**ves)

Surveillance type combines:

Objective, way of sampling, test performance, testing strategy e.g:

- Passive surveillance
  - Observer/patient initiated, could be part of early warning or monitoring
- Active surveillance
  - specific questions about a defined disease/pathogen
  - investigator initiated and defined

The context of the lecture

- Samples collected from passive surveillance available at the labs
- Investigating some of them with special test (e.g WGS for AMR)
- WGS on all available samples could be time consuming and expensive
- Results and limitations of the study are both important….

Practical example of the lecture for a basic protocol

Background

- Authorities of country “C” know that pathogen “P” is endemic
- Wondering if AMR subtype “P1” is present in a region
- 3/100 “P1” cases (travel related) detected in a previous study
- This is our “Prior” knowledge available (before our study is made)

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Example context

- Authorities do not exclude a random survey later on in the resident population

- But before.. a pilot study is commissioned for addressing two research questions (“a” and “b”), using samples already available (≈ 3000 specimens stored at regional lab).

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Example context

- Specimens uniquely indentified e.g. by: patient passport, name, etc
- Suppose the WGS used to detect P1 has Se 98% and Sp 100%

Research questions from authorities

a) Is P1 absent? Confidence in freedom?

b) If P1 is present, what is the prevalence?

Aim

From all available specimens we would like to test “enough” for:

Detecting P1 with 95% confidence IF PRESENT in the population of stored specimens, at the expected prior design prevalence 3%

IF NOT FOUND → reach confidence in freedom PFree ≥ 95%

IF DETECTED → estimate its “true” prevalence TP with 95% confidence and precision 2%, considering “prior” prevalence 3%

How many to test randomly between those stored?

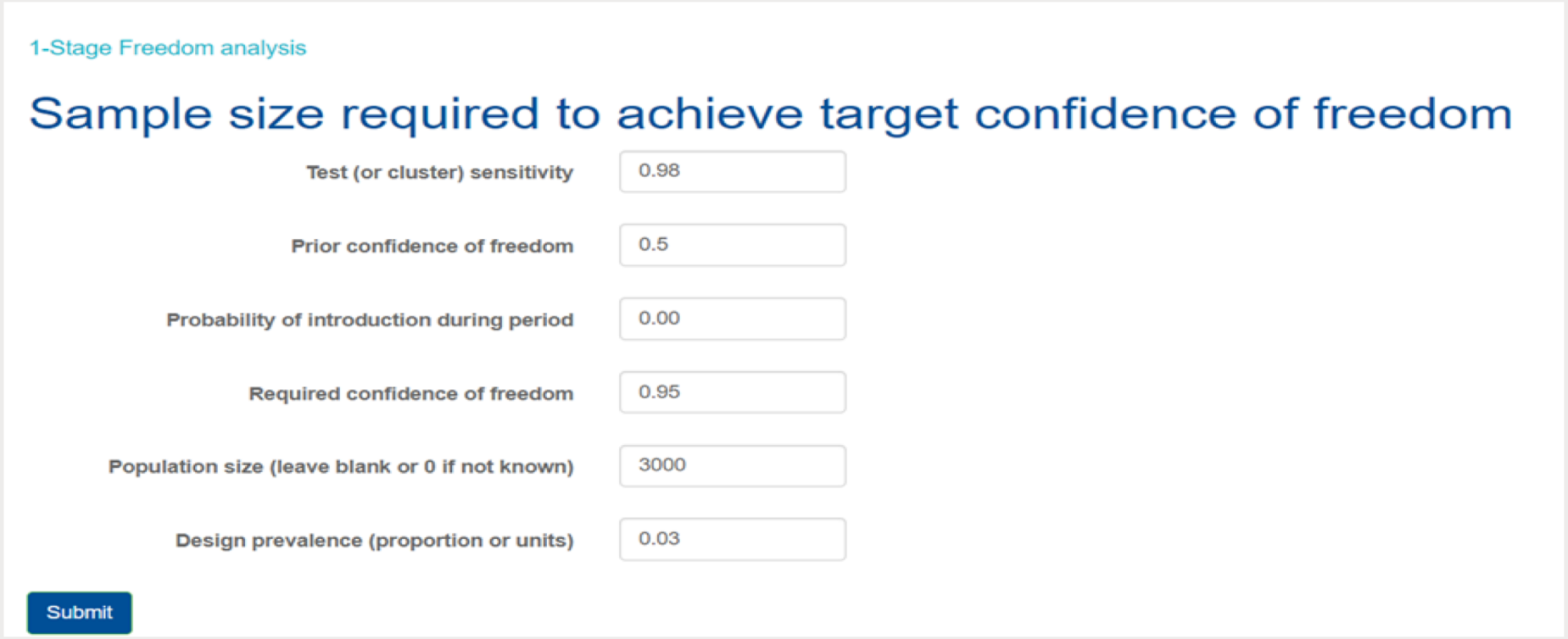
Two steps:

1) Calculate sample sizes ”n1” and ”n2” to address ”a” and ”b”

2) Randomize list of stored specimens from which sampling ”n1” & ”n2”

1) Calculate ”n1” to estimate ”PFree”

https://epitools.ausvet.com.au/freedomssthree



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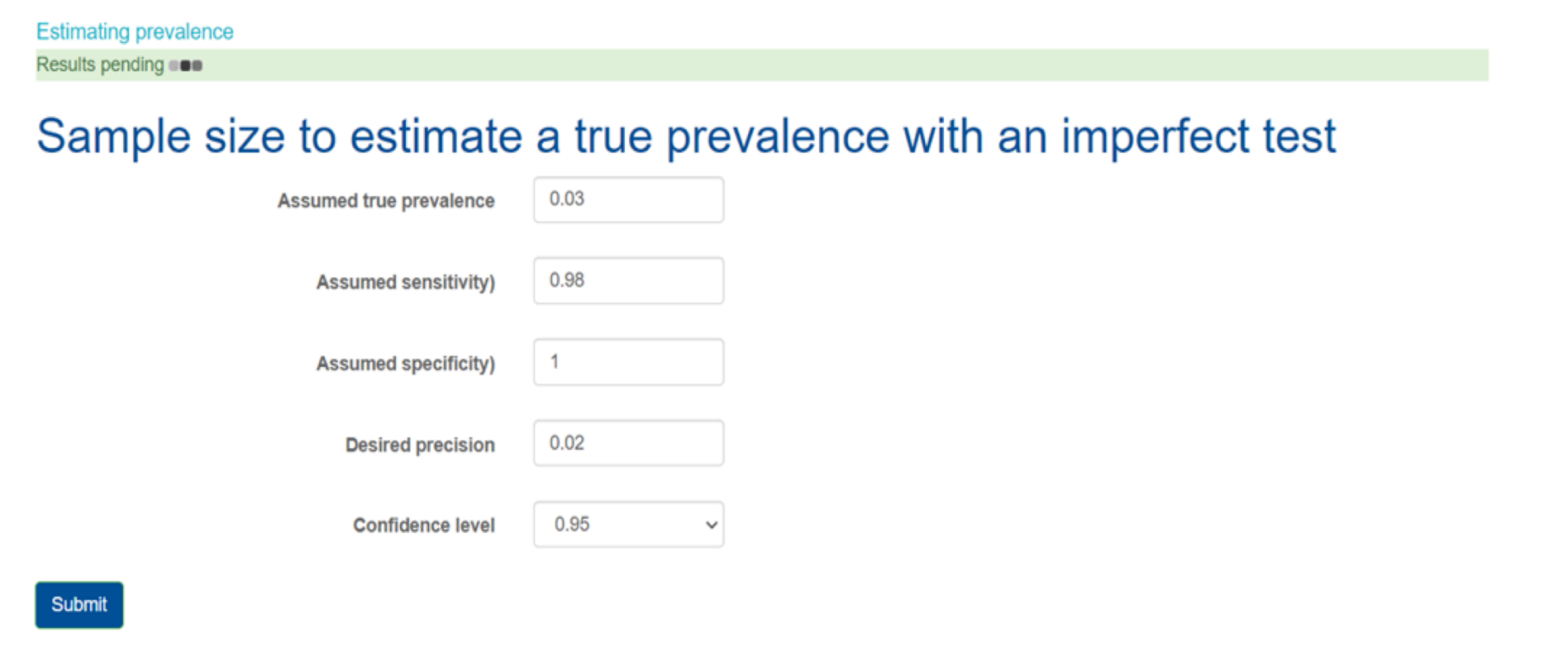
1) Calculated ”n1”

Results

Adjusted prior	0.5
Population sensitivity required	0.947
Sample size required	99 units

1) Calculate ”n2” to estimate ”TP”

https://epitools.ausvet.com.au/prevalencess



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1) Calculated ”n2”

https://epitools.ausvet.com.au/prevalencess

Results

Sample size required for specified inputs

Sample size	286

Sample sizes for varying prevalence and precision values

Samples sizes required for sensitivity = **0.98**, specificity = **1** and a range of true prevalence and precision values are shown below:

	TP = 0.01	TP = 0.02	TP = 0.05	TP = 0.1	TP = 0.2	TP = 0.5
Precision = 0.01	389	769	1864	3536	6304	9996
Precision = 0.02	98	193	466	884	1576	2499
Precision = 0.05	16	31	75	142	253	400
Precision = 0.1	4	8	19	36	64	100
Precision = 0.2	1	2	5	9	16	25

2) Ramdomize list of all stored specimens

Can be made in different programs: excel, R, SAS etc.

e.g. in excel: https://www.youtube.com/watch?v=CxSwNyVT1C8

Test the first 286 of the randomized list, for both aims (“a” and “b”)

Discussion on advantages

The obtained PFree or TP will be corrected for:

1. The error of the test (Se e Sp)
2. The assumptions on PriorTP or PriorPFree
3. The sample size
4. The number of stored specimens

PFree and/or TP become MORE comparable between laboratories

Discussion on assumptions and limitations

- Calculation of n2 assumed n2/Np < 10%
- The surveillance unit was at individual level
- PriorPFree set at 50% conservatively → large n1
- Initial passive collection bias of the 3,000 specimens/lab remains

Discussion on limitations

- The example is a basic approach
- Improvements possible (e.g stratified random sampling for age cat.)
- If 2 tests (1 & 2) serially on each chosen unit, consider serial Se & Sp

Appendix: for two tests in series or parallel

https://epitools.ausvet.com.au/twoteststwo

Diagnostic test evaluation and comparison

Sensitivity and specificity of two tests used in parallel or series

Test sensitivities and specificities

Test Number	Test Name	Sensitivity (Se)	Specificity (Sp)
1	Test1	0.80	1
2	Test2	0.98	1

Submit

Appendix: for two tests in series or parallel

Sensitivity and specificity for two tests interpreted in parallel or series

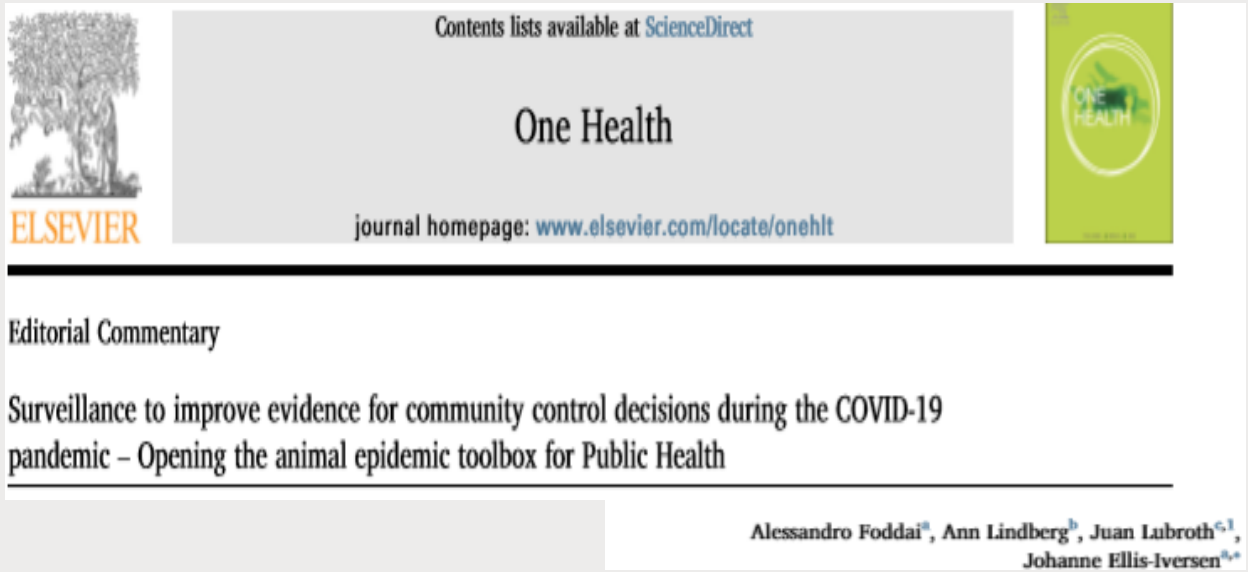
Analysed: Tue Feb 09, 2021 @ 11:37 UTC

Results

The table below summarises the sensitivities and specificities of two tests used in parallel or series. These results assume that the two tests are independent, conditional on disease status.

	Test1	Test2	Series	Parallel
Sensitivity	0.8	0.98	0.784	0.996
Specificity	1	1	1	1

Example references:



Contents lists available at ScienceDirect

One Health

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

Editorial Commentary

Surveillance to improve evidence for community control decisions during the COVID-19 pandemic – Opening the animal epidemic toolbox for Public Health

Alessandro Foddai[a], Ann Lindberg[b], Juan Lubroth[c,1], Johanne Ellis-Iversen[a,*]

Contents lists available at ScienceDirect

One Health

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

Base protocol for real time active random surveillance of coronavirus disease (COVID-19) – Adapting veterinary methodology to public health

Alessandro Foddai[a,*], Juan Lubroth[b], Johanne Ellis-Iversen[a]

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Example references:

ELSEVIER

Available online at www.sciencedirect.com
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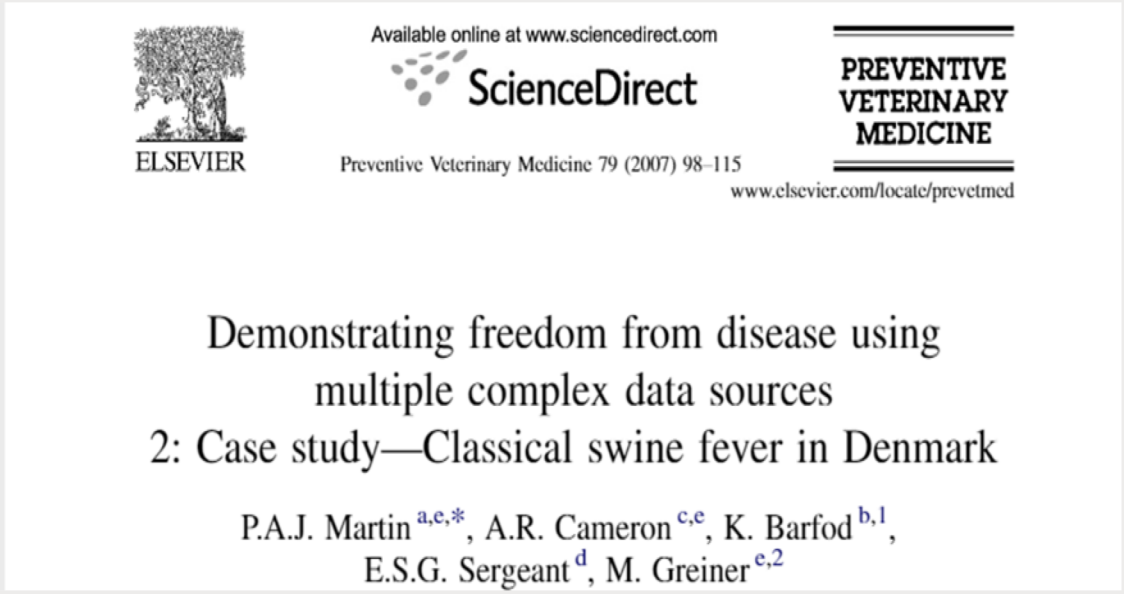
Preventive Veterinary Medicine 79 (2007) 71–97
www.elsevier.com/locate/prevetmed

PREVENTIVE VETERINARY MEDICINE

Demonstrating freedom from disease using multiple complex data sources
1: A new methodology based on scenario trees

P.A.J. Martin [a,c,*], A.R. Cameron [b,c], M. Greiner [c,1]



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Available online at www.sciencedirect.com
ScienceDirect
Preventive Veterinary Medicine 79 (2007) 98–115
www.elsevier.com/locate/prevetmed

PREVENTIVE VETERINARY MEDICINE

Demonstrating freedom from disease using multiple complex data sources
2: Case study—Classical swine fever in Denmark

P.A.J. Martin [a,e,*], A.R. Cameron [c,e], K. Barfod [b,1], E.S.G. Sergeant [d], M. Greiner [e,2]

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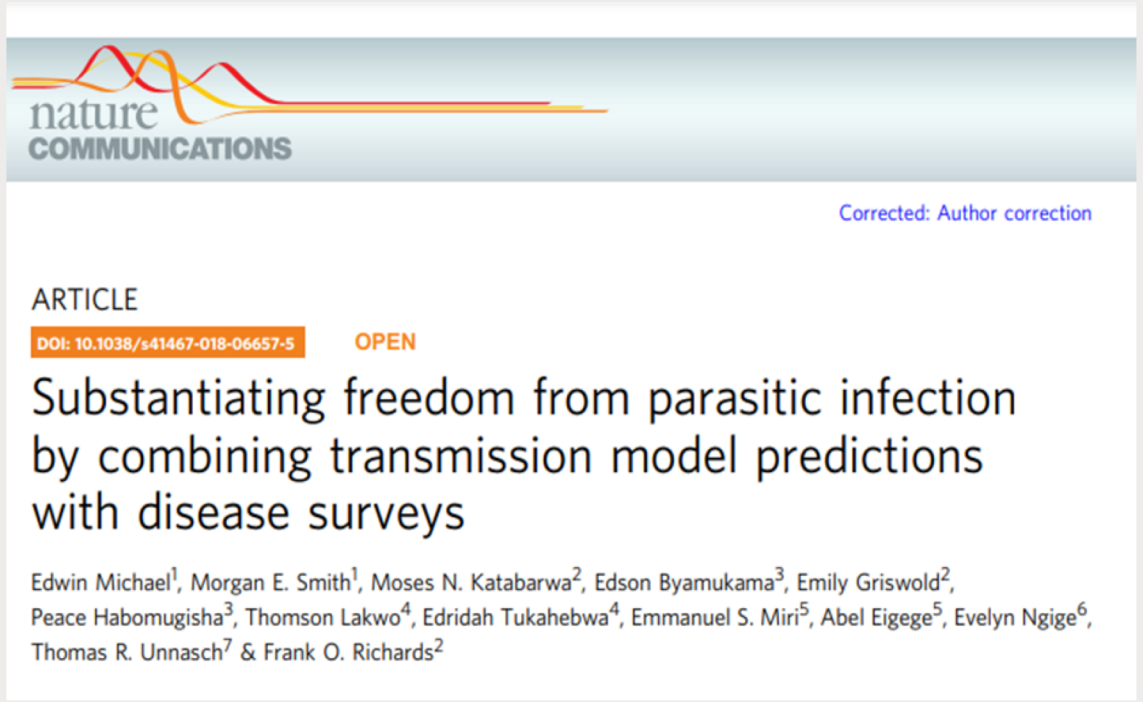
Example references:



nature COMMUNICATIONS

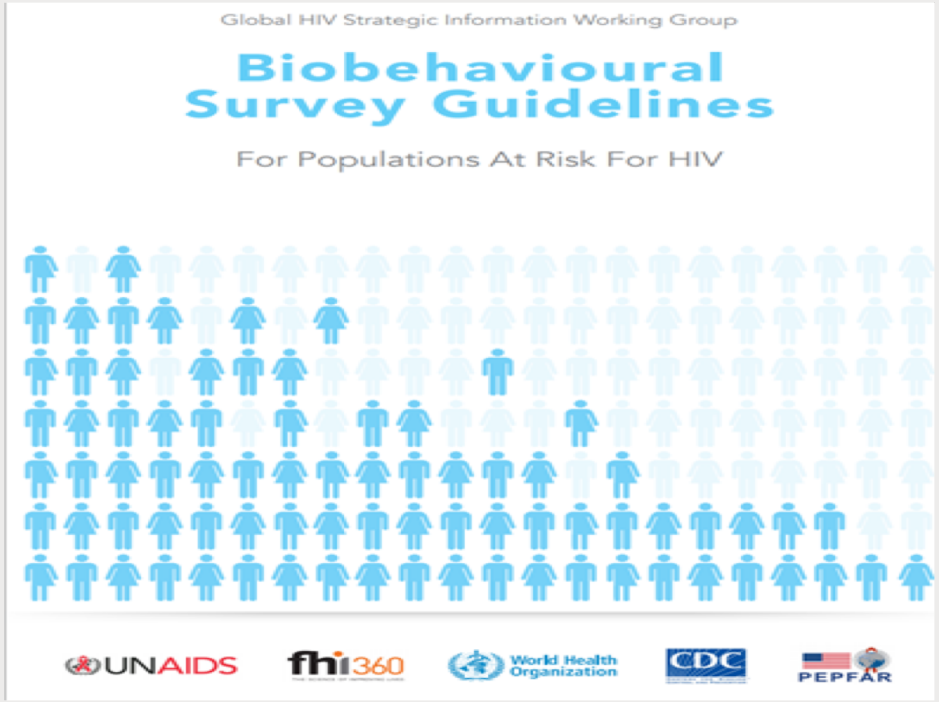
Corrected: Author correction

ARTICLE

DOI: 10.1038/s41467-018-06657-5 OPEN

Substantiating freedom from parasitic infection by combining transmission model predictions with disease surveys

Edwin Michael[1], Morgan E. Smith[1], Moses N. Katabarwa[2], Edson Byamukama[3], Emily Griswold[2], Peace Habomugisha[3], Thomson Lakwo[4], Edridah Tukahebwa[4], Emmanuel S. Miri[5], Abel Eigege[5], Evelyn Ngige[6], Thomas R. Unnasch[7] & Frank O. Richards[2]



Global HIV Strategic Information Working Group

Biobehavioural Survey Guidelines

For Populations At Risk For HIV

UNAIDS fhi360 World Health Organization CDC PEPFAR

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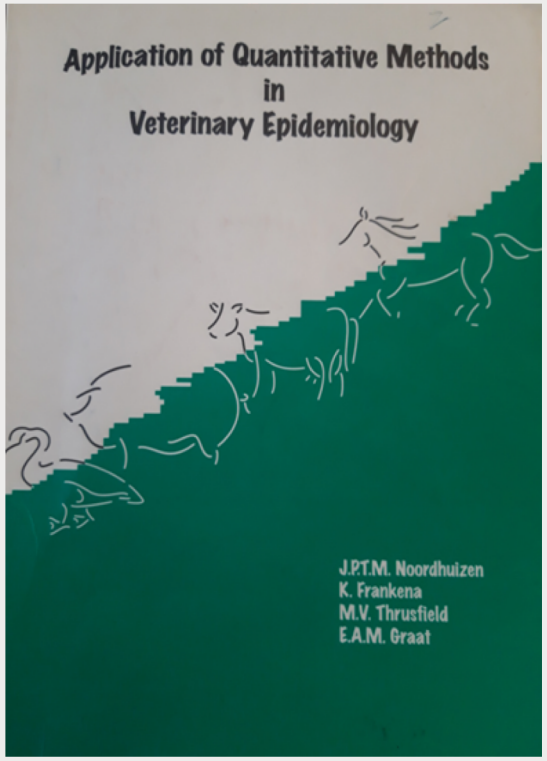
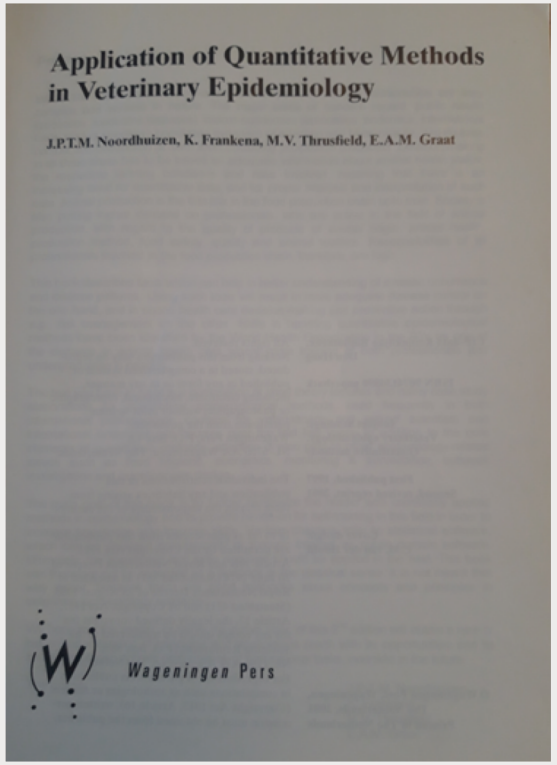
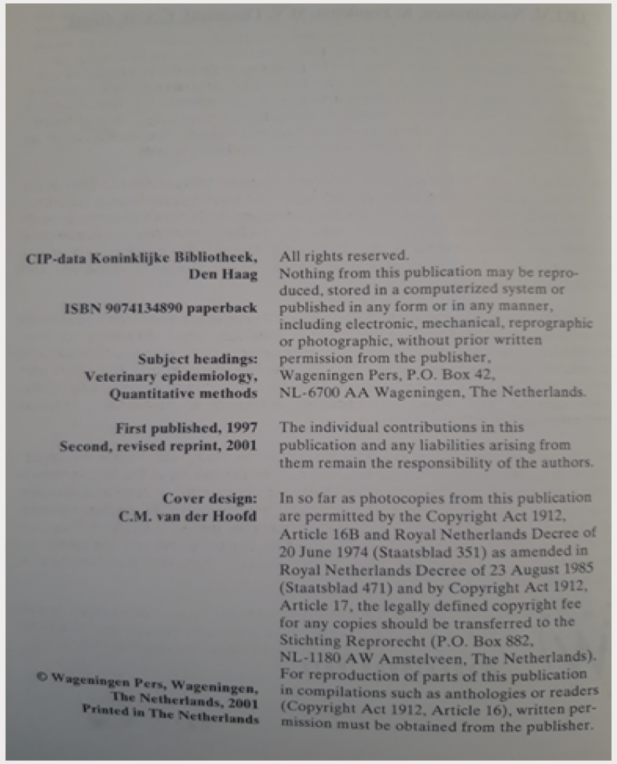
Example references:







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Useful links

- https://epitools.ausvet.com.au/freedomssthree
- https://epitools.ausvet.com.au/prevalencess
- https://epitools.ausvet.com.au/twoteststwo
- https://epitools.ausvet.com.au/
- https://www.who.int/ncds/surveillance/steps/resources/EpiInfo/en/
- https://www.surveysystem.com/sscalc.htm
- https://epitools.fp7-risksur.eu/tools/index?toolId=46

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