Diagnostic performance estimates for diagnosis of animal Tuberculosis obtained using BLCMs

Time to move away from the Golden calf?

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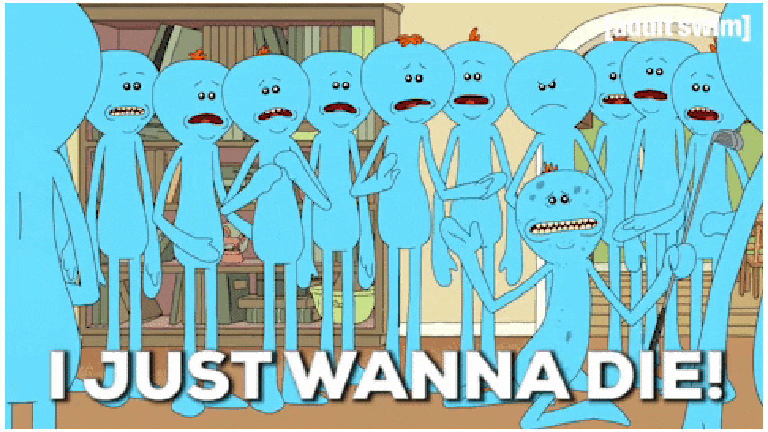
Outline

- Brief recap on animal (bovine) tuberculosis and why it is so difficult to eradicate
- Diagnostic tests available for bTB diagnosis
  - Estimates on their performance
  - Problems associated with their assessment
- Review of the use of BLCMs in the context of bTB diagnosis
- Take home messages

Mycobacterial (animal) diseases

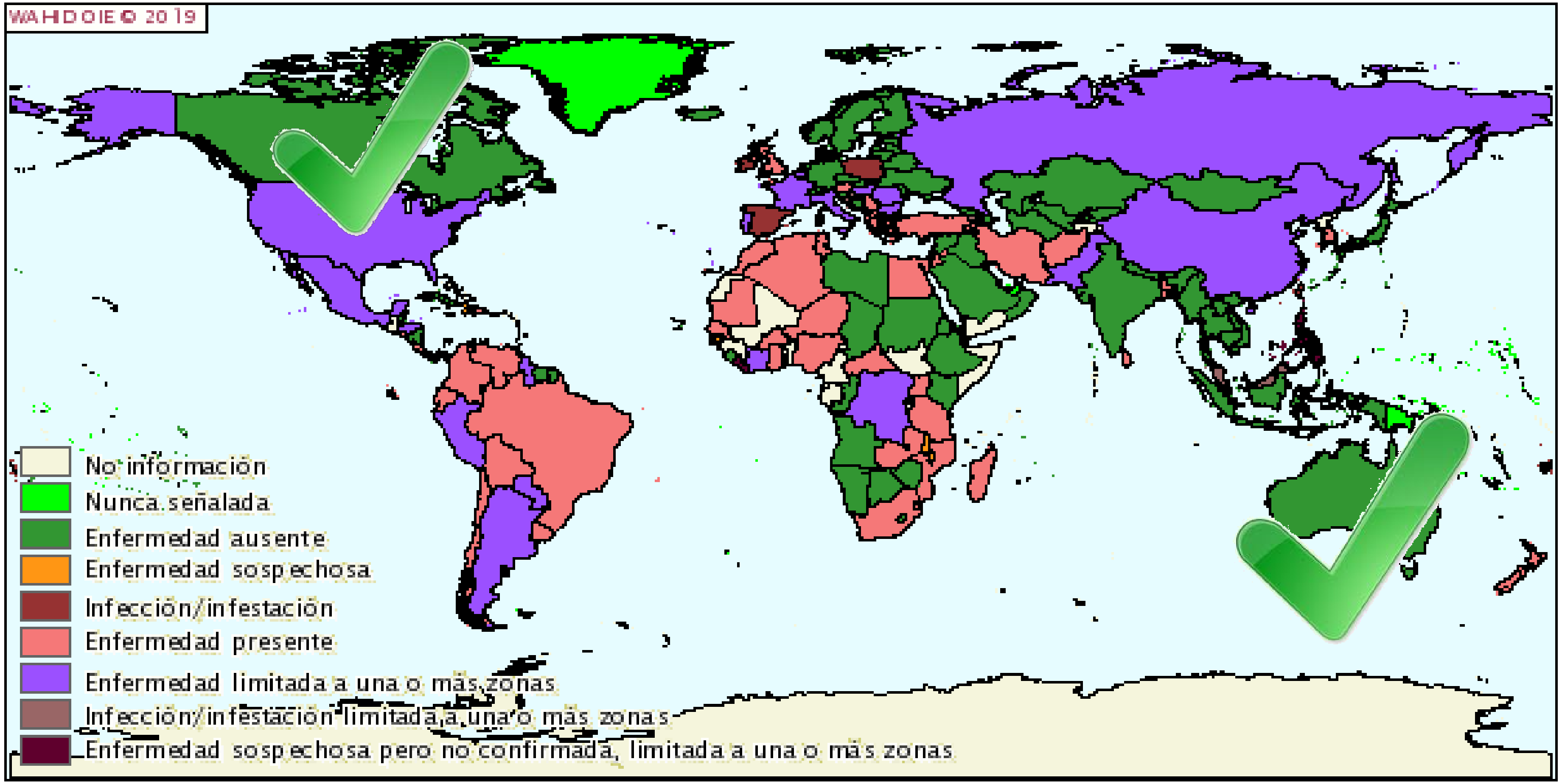
- Most famous ones:
  - animal (and human!) tuberculosis (*Mycobacterium bovis, M. caprae, M. tuberculosis*)
  - Johne's disease (*M. avium* subsp. *paratuberculosis*)
  - Others → Non tuberculous micobacteria (avian tuberculosis due to *M. avium*, marine mycobacteria, etc.)
  - Zoonotic impact (tuberculosis… *Map*?)

- The dream of the diagnostician ☹
  - Chronic and slow clinical course
  - Delayed (non-protective) immune response



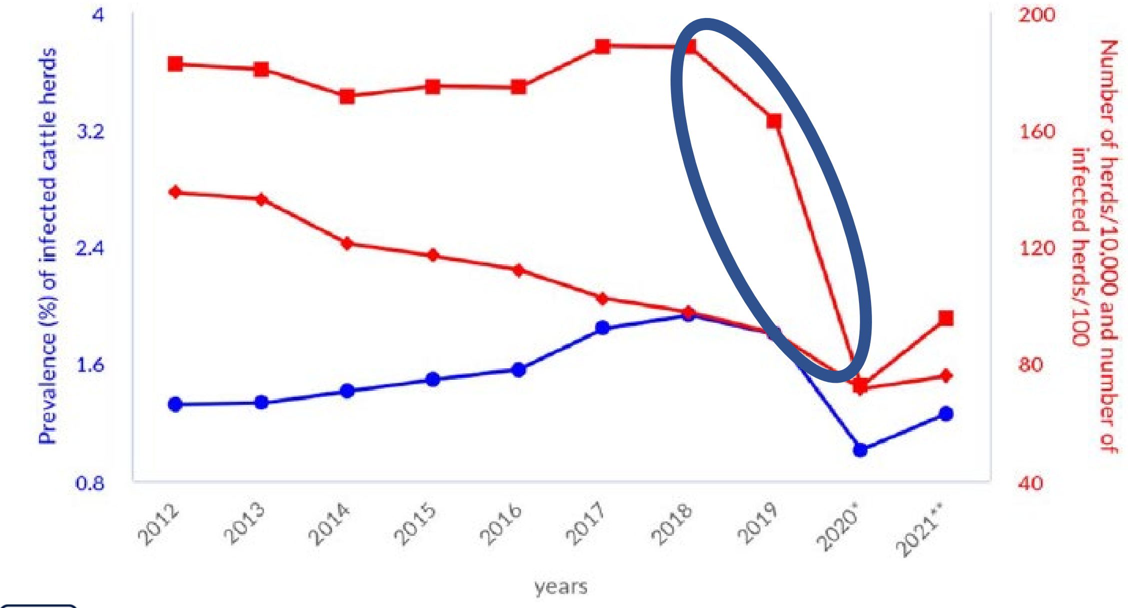
Bovine tuberculosis

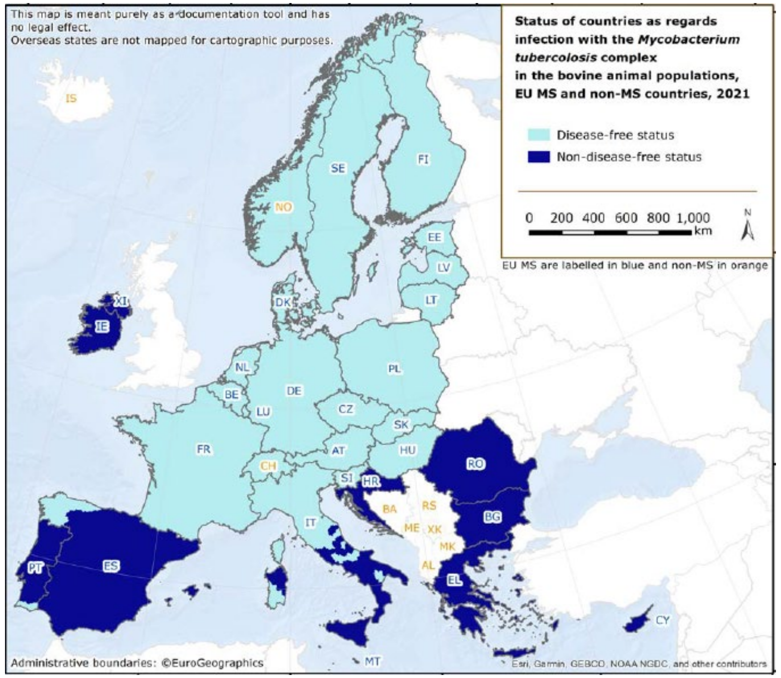
- Worldwide distribution, few success stories



Bovine tuberculosis in the EU

- EU definition (SANCO/7059/2013): “*Infection in cattle with any of the disease-causing mycobacterial species within the M. tuberculosis complex*” (≠ from “infection with *M. bovis* in any animal species!)
- Still a very relevant disease: limited progress





Why is it so challenging to eradicate bTB?

- “Eradication of bovine tuberculosis is achievable at farm level […] provided the integrity of the farm, i.e. the epidemiological unit, is maintained” (J. Collins, 2006)

- ¿Program failures? → All (successful or not) programs are based on test-and-cull strategies

Lack of success related with (combination of factors)

- Wildlife reservoirs (badger, wild boar, possum)
- Management factors (extensive, dairies, stress, movements)
- **Diagnostic failures**

Available tools for controlling bTB

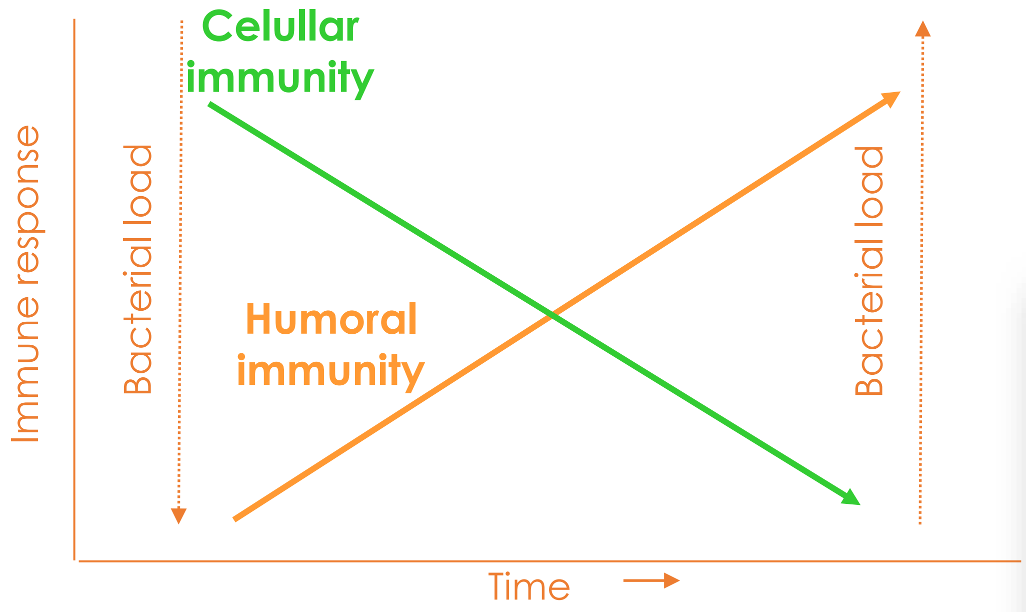
TB free status

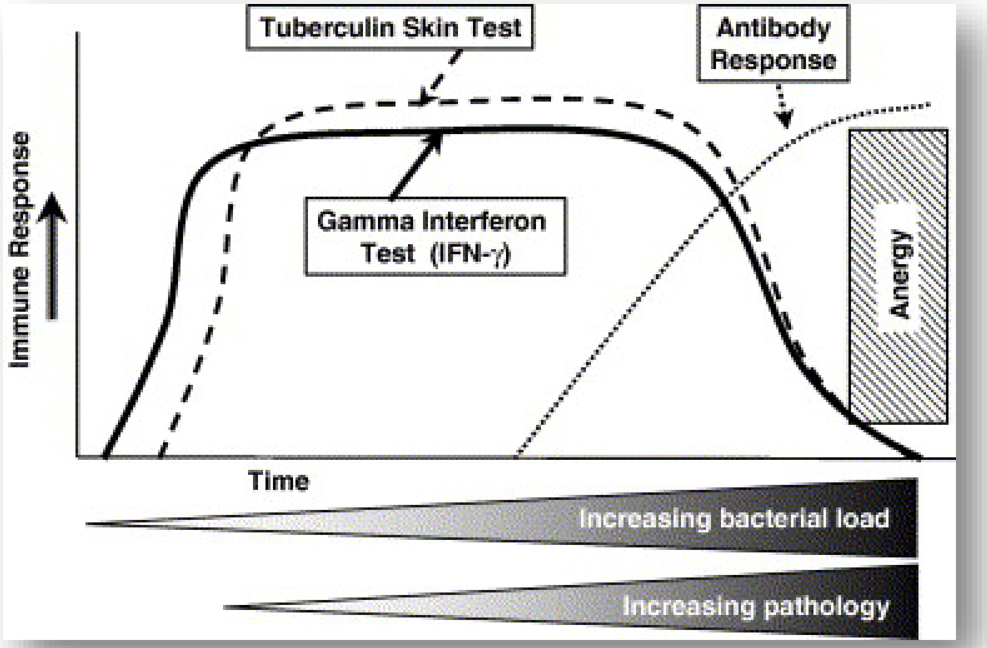
Vaccination

Biosecurity

Detection

Diagnosis of bovine TB

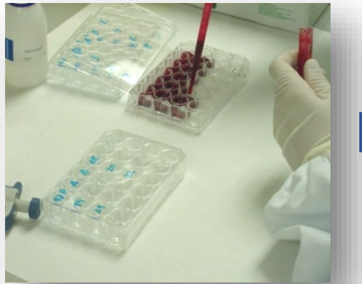




Main diagnostic test for bTB

- Skin tests: based on the cellular immune response → inoculation of TB-related antigen and measurement of the increase in skin fold thickness 72 hours later (>2 or 4 mm)
  - **Single** intradermal **cervical** tuberculin **test**: inoculation of bovine PPD (bPPD) in cervical region
  - **Caudal fold test**: inoculation of bPPD in caudal region (not used in the EU)
  - **Comparative tuberculin test**: inoculation of bovine and avian PPD in cervical region → comparison of skin fold thickness increase (if avian > bovine = "false positive")

Alternative tests




- Interferon-gamma release assay (IFN-γ): *"in-vitro version of skin tests"*
  - Collection of blood sample and in-vitro stimulation with aPPD and bPPD
  - Measurement of the level of IFN-γ produced in response to antigen in an ELISA (if level is high and bPPD>aPPD animal is likely positive)
- Serological test
  - Detection of "specific" antibodies (multiple antigens used)
  - Current paradigm: limited usefulness in cattle (late stage of infection)
- Post-mortem: confirmation
  - Bacteriology (gold standard)
  - Detection of visible lesions, histopathology (uncommon)
  - Direct PCR (increasing)

Typical way of assessing test performance (for bTB)

- Select a cohort of known infected animals and of known not-infected animals
- Run the test on these populations and estimate Se and Sp
- Known infected TB animals?
  - Experimentally infected
  - Positive in a reference test (bacteriology)
- Known not-infected animals?
  - Animals from officially free populations (countries, regions)
  - Negative in a reference test (bacteriology, other ante-mortem)

	Infection +	Infection -	**Total**
Test +	TP	FP	T+
Test -	FN	TN	T-
Total	Infected	Not-infected	**N**

$$Se = \frac{TP}{Infected} \qquad Sp = \frac{TN}{Not-infected}$$

Performance of these tests

- (very) Heated debate!!
  - Extremely wide ranges published
    - Skin tests: Se 30-100%, Sp 70-100%
    - IFN-γ: Se 50-100%, Sp 50-100%
    - Serology: Se 20-100%, Sp 80-100%
- Sources of variability?
  - Different populations (reactors to a previous tests, age, breed, management…)
  - Variations in test protocols
  - Lack of a reliable gold standard!
    - **Bacteriology** has a particularly limited Se in the animals in which tests are typically assayed (recently infected cattle): systematic overestimation of the Se!!
    - Large part of the literature reports optimistic (>80%) values for the skin test
    - Use of post-mortem as confirmation of in-vivo diagnosis leads to the wrong belief of the common occurrence of false positive reactors (even with CCT).

Ante mortem diagnosis of tuberculosis in cattle: A review of the tuberculin tests, γ-interferon assay and other ancillary diagnostic techniques

R. de la Rua-Domenech [a,*], A.T. Goodchild [b], H.M. Vordermeier [c], R.G. Hewinson [c], K.H. Christiansen [b], R.S. Clifton-Hadley [d]

Current *ante-mortem* techniques for diagnosis of bovine tuberculosis

Javier Bezos [a,b,*], Carmen Casal [b], Beatriz Romero [b], Bjoern Schroeder [c], Roland Hardegger [c], Alex J. Raeber [c], Lissette López [d], Paloma Rueda [d], Lucas Domínguez [b,e]

Bovine Tuberculosis: A Review of Current and Emerging Diagnostic Techniques in View of their Relevance for Disease Control and Eradication

I. Schiller[1], B. Oesch[2], H. M. Vordermeier[3], M. V. Palmer[4], B. N. Harris[5], K. A. Orloski[6], B. M. Buddle[7], T. C. Thacker[4], K. P. Lyashchenko[8] and W. R. Waters[4]

Meta-analyses of the sensitivity and specificity of ante-mortem and post-mortem diagnostic tests for bovine tuberculosis in the UK and Ireland

Javier Nuñez-Garcia [a,1], Sara H. Downs [a,*,1], Jessica E. Parry [a], Darrell A. Abernethy [b,c], Jennifer M. Broughan [a], Angus R. Cameron [d], Alasdair J. Cook [a,e], Ricardo de la Rua-Domenech [f], Anthony V. Goodchild [a], Jane Gunn [a], Simon J. More [g], Shelley Rhodes [a], Simon Rolfe [h], Michael Sharp [a], Paul A. Upton [a], H. Martin Vordermeier [a], Eamon Watson [a,i], Michael Welsh [j,k], Adam O. Whelan [a,l], John A. Woolliams [m], Richard S. Clifton-Hadley [a], Matthias Greiner [n]

Advances in ante-mortem diagnosis of tuberculosis in cattle

BM Buddle[*§], PG Livingstone[†] and GW de Lisle[‡]

Known facts… that get often “lost in translation”

- Se often assessed in highly biased (heavily infected) populations
- Sp often assessed in epidemiologically unrelated populations

Highly Accurate Antibody Assays for Early and Rapid Detection of Tuberculosis in African and Asian Elephants[∇]

Rena Greenwald,[1] Olena Lyashchenko,[1] Javan Esfandiari,[1] Michele Miller,[2] Susan Mikota,[3] John H. Olsen,[4] Ray Ball,[4] Genevieve Dumonceaux,[4] Dennis Schmitt,[5] Torsten Moller,[6] Janet B. Payeur,[7] Beth Harris,[7] Denise Sofranko,[8] W. Ray Waters,[9] and Konstantin P. Lyashchenko[1*]

recognized by elephant antibodies during disease. The serologic assays demonstrated 100% sensitivity and 95 to 100% specificity. Rapid and accurate antibody tests to identify infected elephants will likely allow

on disease status and history of exposure (Table 1). The TB-infected group included 26 animals from 17 herds with culture-confirmed TB due to *M. tuberculosis* (n = 25) or *M. bovis* (n = 1). Of the 26 elephants, 7 died and 11 were humanely euthanized. TB was not necessarily the cause of death or the reason for euthanasia. Disease was diagnosed antemortem by trunk wash culture (n = 15; 58%) or only postmortem by isolating *M. tuberculosis* or *M. bovis* from various tissues (n = 11; 42%). Ten elephants were treated with first-line anti-TB drugs

Development and Evaluation of an Enzyme-Linked Immunosorbent Assay for Use in the Detection of Bovine Tuberculosis in Cattle[∇†]

W. R. Waters,[1*] B. M. Buddle,[2] H. M. Vordermeier,[3] E. Gormley,[4] M. V. Palmer,[1] T. C. Thacker,[1] J. P. Bannantine,[1] J. R. Stabel,[1] R. Linscott,[5] E. Martel,[5] F. Milian,[6] W. Foshaug,[7] and J. C. Lawrence[5]

TABLE 1. Sensitivity of IDEXX *M. bovis* antibody ELISA with sera collected from naturally infected cattle

M. bovis-infected serum type		n[d]	No. of herds	Sensitivity (%)		
Source	ID or characterization[c]			Lot 1	Lot 2	Lot 3
Great Britain	AHVLA-2[a]	134	31	74.6	72.4	73.1
	AHVLA-1[b]	50	>5	86	88	86
Ireland	No visible lesions[b]	50	>5	48	44	46
	With visible lesions[b]	50	>5	72	70	70
	Skin test positive, Bovigam positive, with visible lesions[b]	30	22	96.7	86.7	90.0
New Zealand	AgResearch[b]	42	7	42.9	40.5	35.7
USA	Colorado[a]	81	1	44.4	45.7	49.4
	NVSL serum bank[a]	31	12	48.4	48.4	48.4
	Michigan[a]	10	1	30	30	30
Overall value		478	>89	63.6	61.9	62.6

[a] Infection status determined by histopathology with IS*6110* PCR and/or culture.
[b] Infection status determined by culture or presence of gross lesions and/or from a tuberculosis-affected herd.
[c] ID, identification. NVSL, National Veterinary Service Laboratory.
[d] n, number of animals.

TABLE 2. Specificity of IDEXX *M. bovis* antibody ELISA with sera collected from noninfected cattle from various geographic regions

Source of noninfected sera[a]	n[b]	No. of herds	Specificity (%)		
			Lot 1	Lot 2	Lot 3
Maine	126	2	99.2	98.4	99.2
Maine	126	2	99	98.4	99.2
Pennsylvania	79	1	88.6	92.4	98.7
Arkansas	39	1	100	100	97.4
New York	84	1	98.8	100	98.8
North Dakota	110	1	96.3	97.2	99.1
Washington	84	2	98.8	98.8	98.8
South Dakota	84	1	98.8	100	100
Missouri	92	>2	94.5	95.7	98.9
Texas	96	>2	93.7	93.8	95.8
Michigan	92	2	100	100	100
Iowa	8	1	100	100	100
Colorado	121	11	99.2	100	99.2
Great Britain (AHVLA)	50	>5	94	98	96
Ireland (UCD/DAFF)	92	16	100	100	95.7
Austria	316	>10	97.5	99.1	98.1
Overall value	1,473	>58	97.4	98.2	98.4

[a] Samples obtained from cattle from tuberculosis-free herds. AHVLA, Animal Health and Veterinary Laboratories Agency; UCD, University College Dublin; DAFF, Department of Agriculture, Fisheries and Food.
[b] n, number of animals.

An example on how this matters…

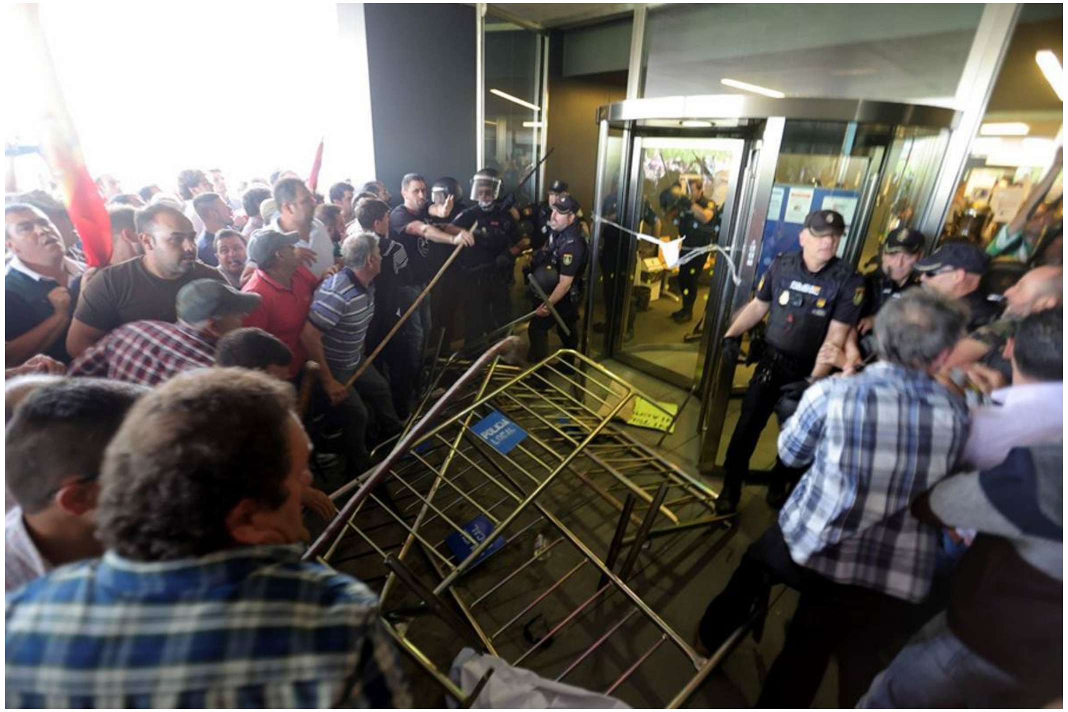
25-05-2023

Castilla y León pide a la Comisión Europea flexibilizar los controles veterinarios en saneamientos ganaderos

24-05-2023

Sindicatos veterinarios de Castilla y León advierten de las consecuencias de la flexibilización de los saneamientos ganaderos

Asimismo, el vicepresidente ha denunciado que "no hay derecho" a que, como se sigue haciendo hasta ahora, "por un **falso positivo** haya que detener los movimientos de toda una cabaña ganadera"



(Exodus 32-34)


A GOLD
WHAT?
BACTERIOLOGICAL CULTURE
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GOLD
STANDARD!

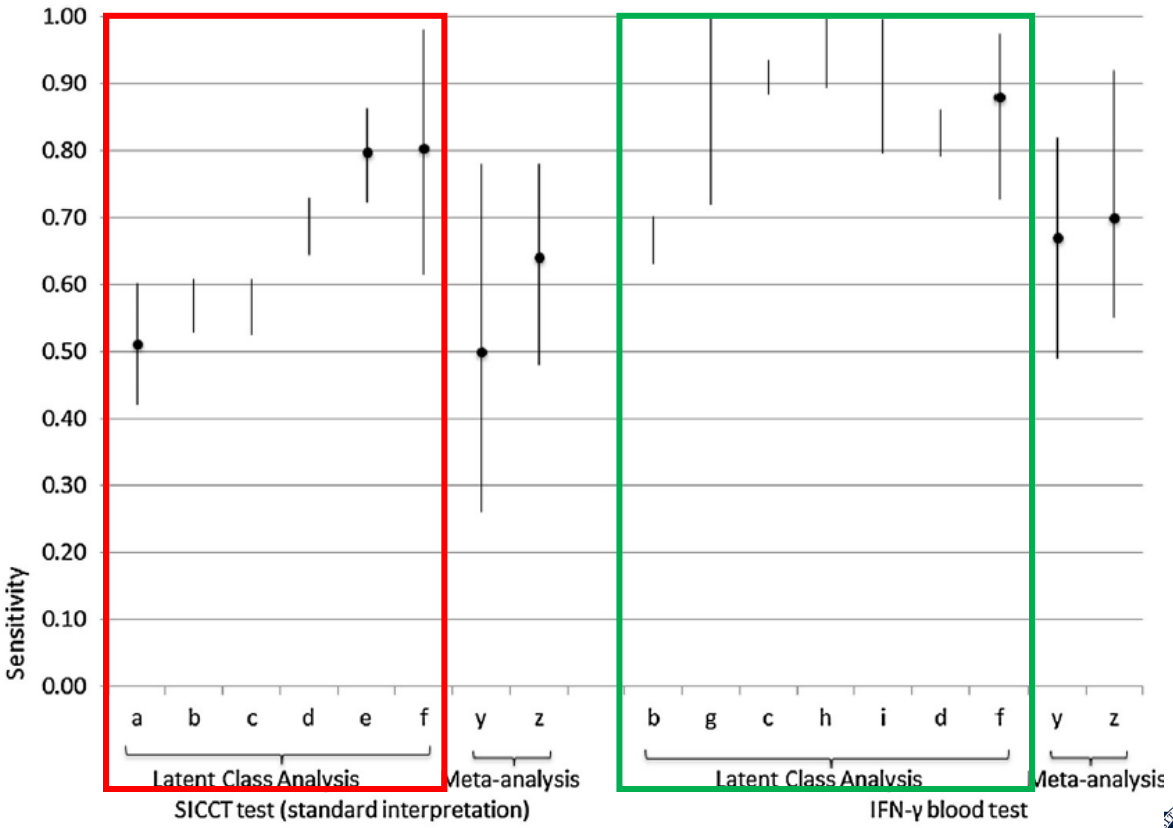
Is there a way out?

Meta-analyses of the sensitivity and specificity of ante-mortem and post-mortem diagnostic tests for bovine tuberculosis in the UK and Ireland

Javier Nuñez-Garcia[a,1], Sara H. Downs[a,*,1], Jessica E. Parry[a], Darrell A. Abernethy[b,c], Jennifer M. Broughan[a], Angus R. Cameron[d], Alasdair J. Cook[a,e], Ricardo de la Rua-Domenech[f], Anthony V. Goodchild[a], Jane Gunn[a], Simon J. More[g], Shelley Rhodes[a], Simon Rolfe[h], Michael Sharp[a], Paul A. Upton[a], H. Martin Vordermeier[a], Eamon Watson[a,i], Michael Welsh[j,k], Adam O. Whelan[a,l], John A. Woolliams[m], Richard S. Clifton-Hadley[a], Matthias Greiner[n]

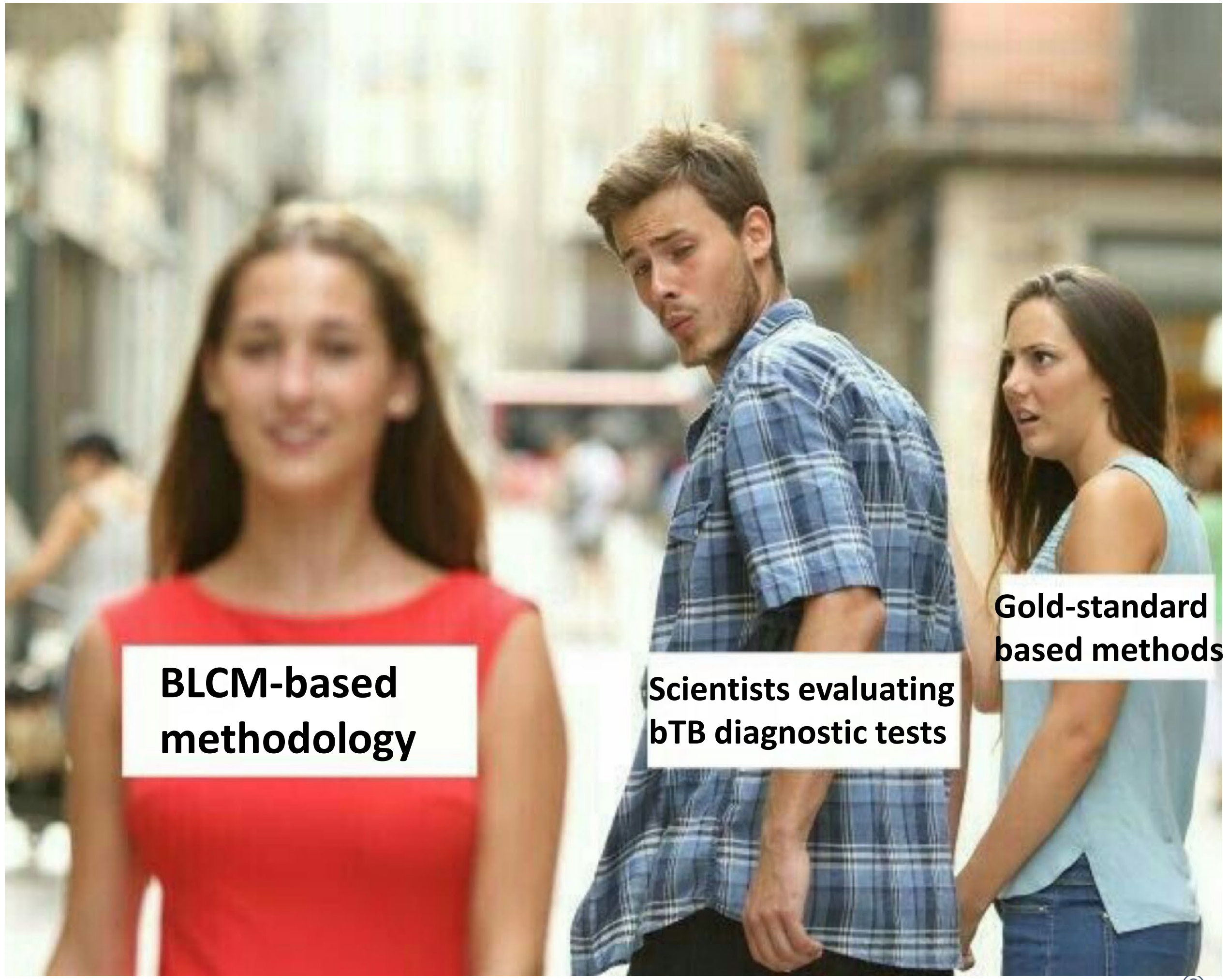
- Recent metaanalysis of performance of bTB diagnostic tests
  - Comparison of "classical vs. Bayesian estimates for Se of CCT and IGRA

Test Name	References n	Sensitivity Estimates N	Pooled Sensitivity Estimate
Skin tests with PPD			
Single intradermal skin test	7	16	0.92
SICCT test standard interpretation	14	38	0.78
SICCT test severe interpretation	14	38	0.84
Caudal fold	15	69	0.92
IFN-γ blood tests			
IFN-γ Bovine	27	166	0.84
IFN-γ Bovine PPD- Avian PPD	27	166	0.83
IFN-γ ESAT6/CFP10	27	166	0.84
IFN-γ MPB70	27	166	0.42



Time for a change in the "default" method?

- Use of BLCMs could overcome the (major!) limitations associated with the gold-standard based approach in the case of TB



Hindawi
Transboundary and Emerging Diseases
Volume 2023, Article ID 7615716, 18 pages
https://doi.org/10.1155/2023/7615716

WILEY | Hindawi

Review of the use of BLCMs in the assessment of TB diagnostic tests

Review Article

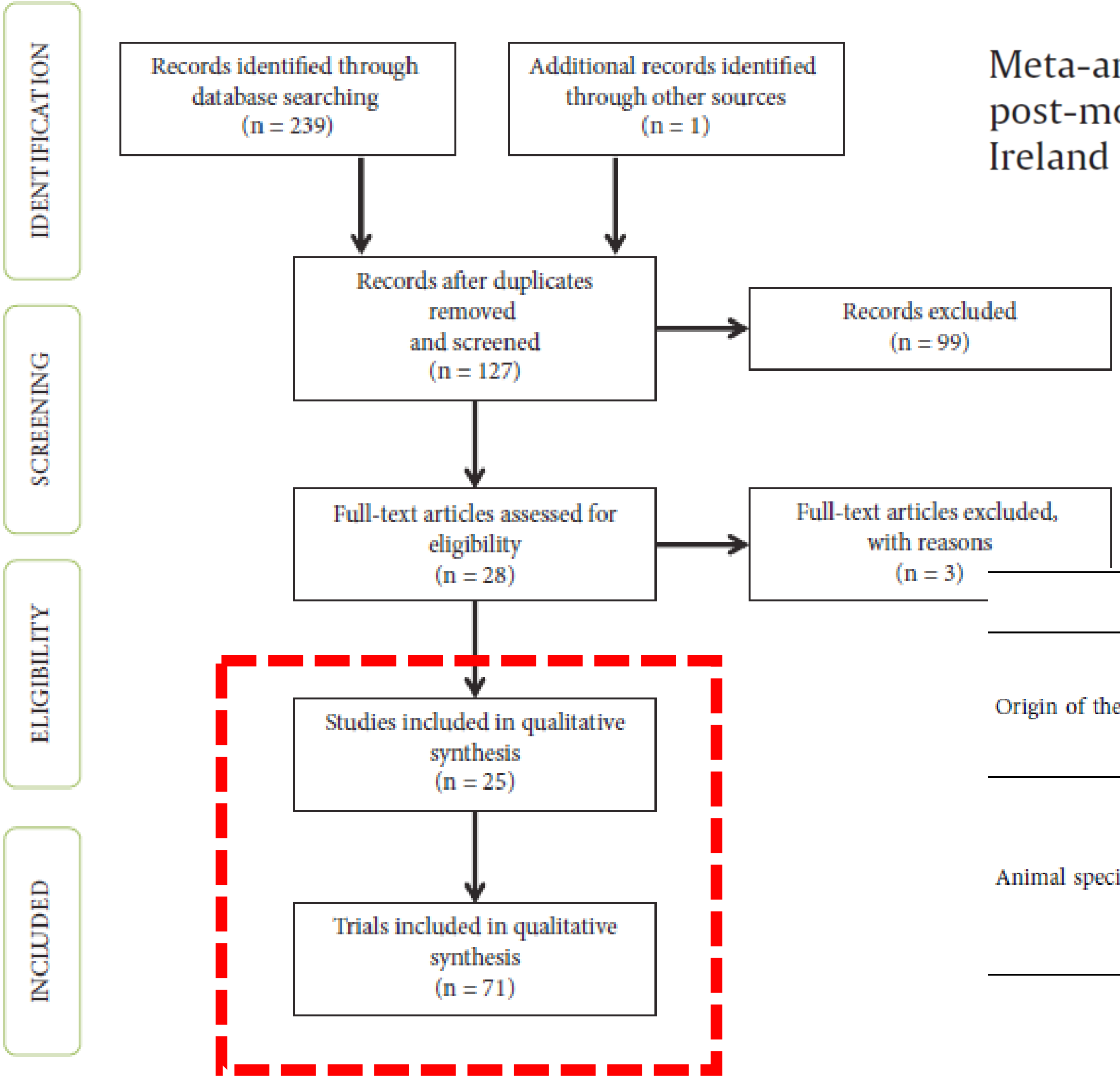
Accuracy of Tests for Diagnosis of Animal Tuberculosis: Moving Away from the Golden Calf (and towards Bayesian Models)

Alberto Gomez-Buendia,[1] Pilar Pozo,[1] Catalina Picasso-Risso,[2,3] Adam Branscum,[4] Andres Perez,[2] and Julio Alvarez[1,5]

- Systematic review with the aim of describing the application of BLCMS in the field of diagnosis of TB in animals with a focus on:
  - Models and methodologies used (use of priors!)
  - Quality of reporting (STARD-BLCM)
  - Posterior estimates for Se and Sp of tests under evaluation
- PRISMA and MOOSE guidelines for systematic reviews
  - Literature search in PubMed, WoS and Scopus using predefined/tested search strings (also grey literature: EFSA SciOp)
  - Step 1: screening of titles and abstracts of non-duplicates by two authors
  - Step 2: screening of full texts, data extraction
  - Comparison of prior and posterior estimates

Inclusion and exclusión criteria

- **Inclusion**
  - Language: EN or ES
  - Use of at least on test for TB diagnosis on samples collected from domestic or wild terrestrial animals
  - Use of at least on BLCM to estimate Se and/or Sp
- **Exclusion**
  - Use of diagnostic tests for the detection of infection due to other (non-tuberculous) mycobacteria



All articles published after January 2009

Meta-analyses of the sensitivity and specificity of ante-mortem and post-mortem diagnostic tests for bovine tuberculosis in the UK and Ireland

119 articles included in Nuñez-Garcia et al. 2018

	Category	Number of articles (25)	Number of trials (71)
Origin of the study	Europe	11	44
	South America	4	13
	North America	2	3
	Africa	4	5
	Asia	4	6
Animal species	Bovine	19	63
	Wild boar	1	2
	Elk/deer	1	2
	Swine	1	1
	Bison	1	1
	Meerkat	1	1
	Badger	1	1
Diagnostic test	Antemortem	20	61
	(i) Skin test	13	49
	(ii) IFN-γ	12	44
	(iii) Serology	13	39
	Postmortem	13	30
	(i) Culture	9	17
	(ii) Direct PCR	10	21
	(iii) Pathology	2	10
	(iv) Meat inspection	5	9
	(v) Culture + Meat inspection	1	3

12 only ante-mortem
5 only post-mortem
8 ante and post-mortem

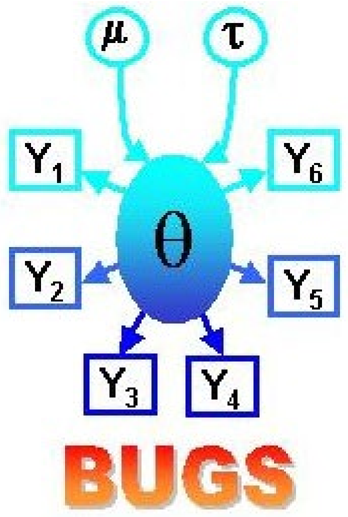
BLCMs characteristics

384 estimates of Se y Sp

Conditional dependence (70% of models)

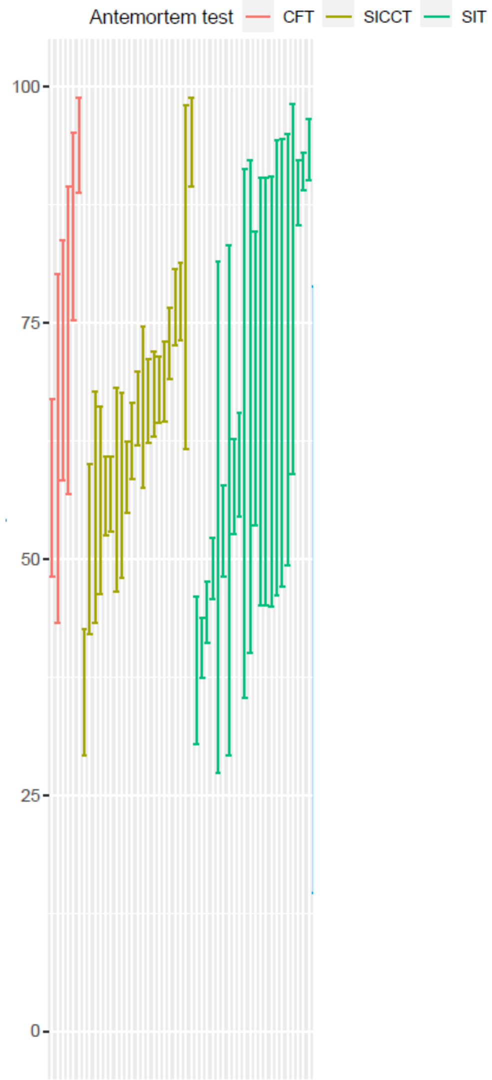
Diffuse priors (49% of the estimates)

	Category	Number of articles (25)	Number of trials (71)
Conditional dependence	Yes	20	49
	No	11	22
Number of populations	1	15	42
	2	5	19
	Multiple	5	10
Number of tests	1	2	6
	2	5	17
	Multiple	18	48
Source of priors	Unspecified	0	0
	Literature	13	26
	Expert knowledge and literature	7	26
	Weakly-informative	5	19
Software	Win BUGS	13	33
	Open BUGS	7	17
	JAGS	5	21
Test dependence	Skin test-IFN-γ	7	26
	Skin test-serology	1	1
	Serology-serology	5	6
	PCR-culture	5	7
	PCR-meat inspection	2	3
	PCR-pathology	1	2



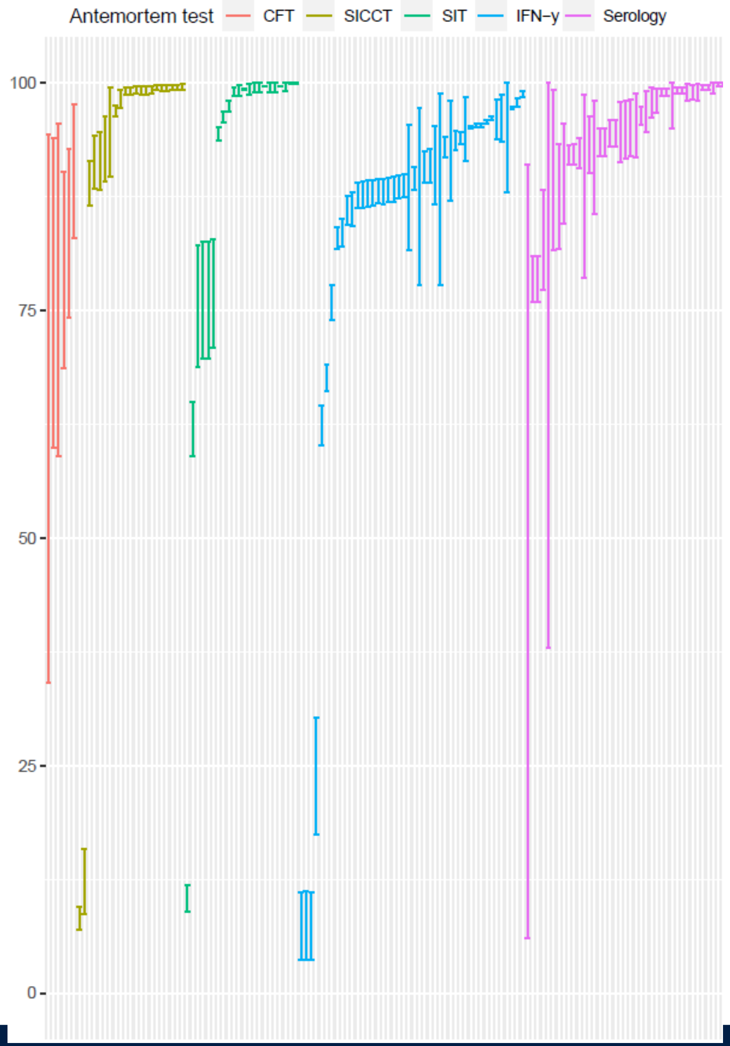
Posterior estimates: Se ante-mortem tests

Test	N†	Se estimates‡	APM and 95% APPI Se estimates (%)§	Species
Skin test (PPD-based)	13	49	66.3 (52.5–74.6)	
Cervical	10	43	66.1 (49.3–72.0)	Cattle
SIT standard interpretation	6	12	63.9 (46.6–84.0)	Cattle
SIT severe interpretation	6	10	69.8 (46.0–91.8)	Cattle
SICCT standard interpretation	5	13	57.5 (52.5–66.6)	Cattle
SICCT severe interpretation	4	8	70.4 (66.8–75.6)	Cattle
Caudal fold	3	6	72.9 (57.6–86.6)	Cattle, bison



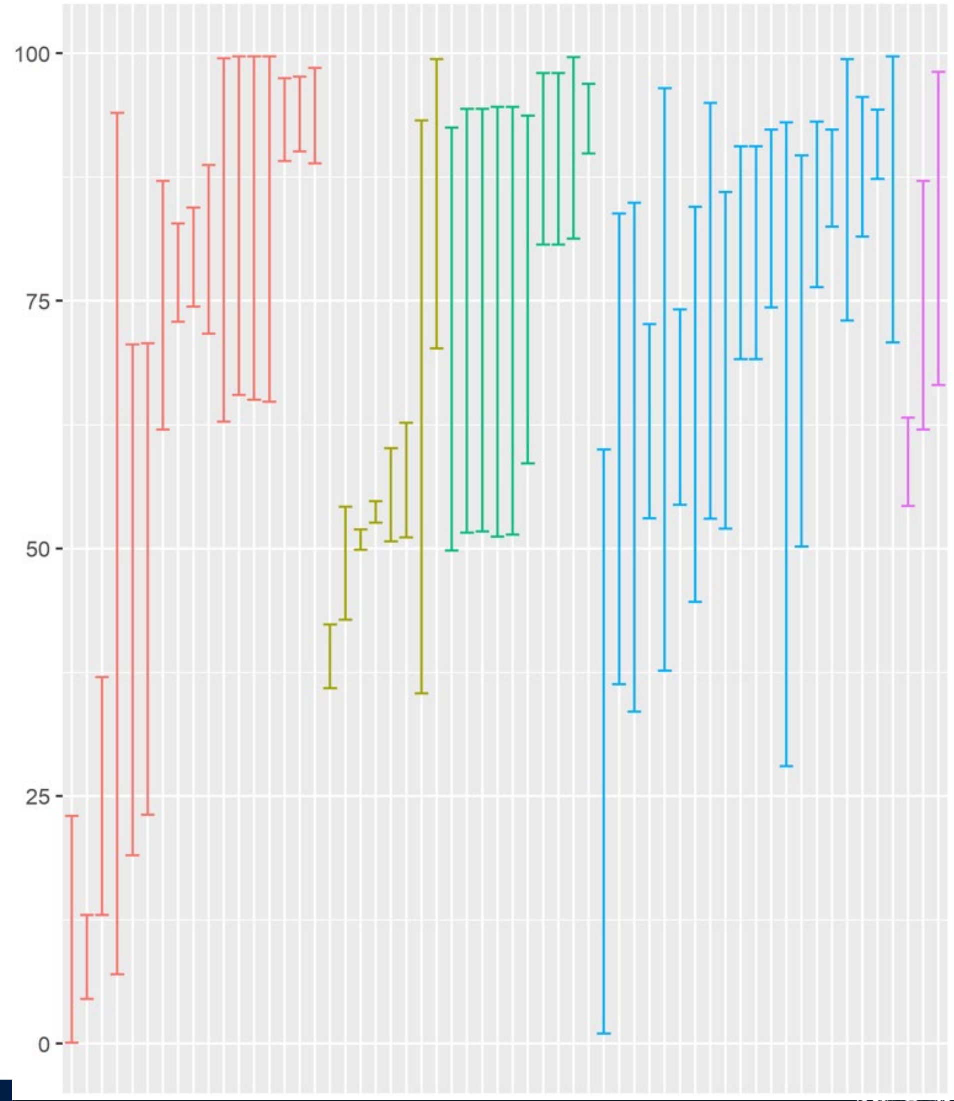
Posterior estimates: Sp ante-mortem tests

Test	N†	Sp estimates‡	APM and 95% APPI Sp estimates (%)$	Species
Skin test (PPD-based)	13	49	99.1 (98.6–99.5)	
Cervical	10	43	99.2 (98.7–99.5)	Cattle
SIT standard interpretation	6	12	96.9 (96.3–97.4)	Cattle
SIT severe interpretation	6	10	99.4 (98.8–99.9)	Cattle
SICCT standard interpretation	5	13	99.1 (98.2–99.7)	Cattle
SICCT severe interpretation	4	8	99.2 (98.7–99.6)	Cattle
Caudal fold	3	6	78.7 (64.3–94.1)	Cattle, bison
IFN- γ blood test	12	44	89.3 (86.9–91.7)	
BOVIGAM (OD 0.05)	5	10	88.1 (85.6–91.1)	Cattle
BOVIGAM (OD 0.1)	7	23	88.2 (86.6–89.6)	Cattle
BOVIGAM (OD 0.2)	1	1	23.5 (17.4–30.3)	Cattle
IDvet	1	3	97.9 (97.4–98.4)	Cattle
Antigen TB-feron (OD 0.1)	1	1	97.0 (91.4–98.5)	Cattle
ESAT6/CFP10	2	5	95.3 (95.0–95.5)	Cattle
In-house	1	1	95.0 (91.4–98.5)	Badger
Serology test	13	39	95.5 (92.0–98.8)	
ELISA	6	15	95.5 (91.7–98.8)	Cattle, wild boar
Multiplex immunoassay	5	16	98.7 (97.4–99.5)	Cattle, elk, badger, meerkat, bison
FPA	3	5	94.0 (92.0–95.0)	Cattle, bison, elk
LST	1	2	79.0 (76.0–81.0)	Elk
Rapid lateral flow	1	1	99.0 (95.0–100)	Cattle



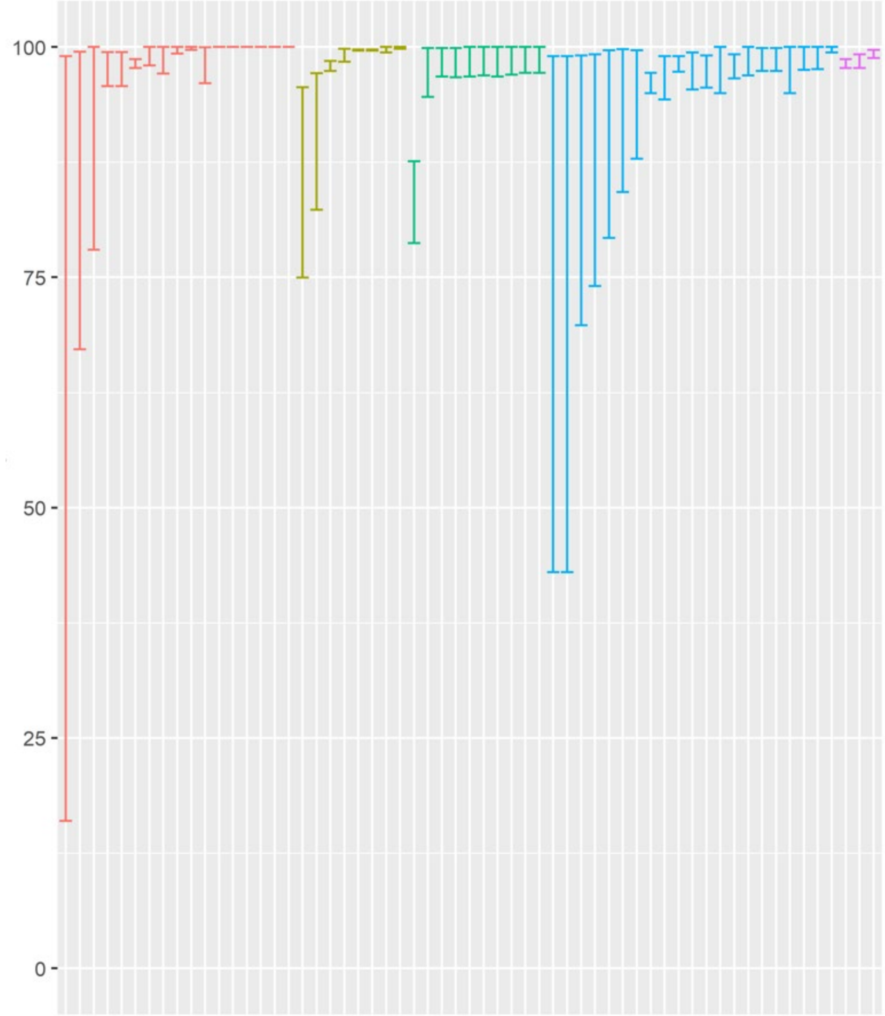
Posterior estimates: Se post-mortem tests

Test	N[†]	Se estimates[‡]	APM and 95% APPI Se estimates (%)[§]	Species
Culture	9	17	79.2 (64.8–88.7)	
Tissue	8	15	79.9 (65.0–94.0)	Cattle, wild boar, swine, meerkat, badger
Milk and blood	1	2	15.0 (6.6–30.0)	Cattle
Direct PCR	10	21	80.6 (54.4–92.3)	
Tissue	9	19	82.9 (69.1–92.3)	Cattle, wild boar, swine,
Milk and blood	1	2	48.5 (27.0–77.5)	Cattle
Meat inspection	5	9	53.7 (49.9–54.8)	Cattle
Histopathology	2	10	77.8 (55.2–94.6)	Cattle
Culture + meat inspection	1	3	74.6 (62.0–87.1)	Cattle

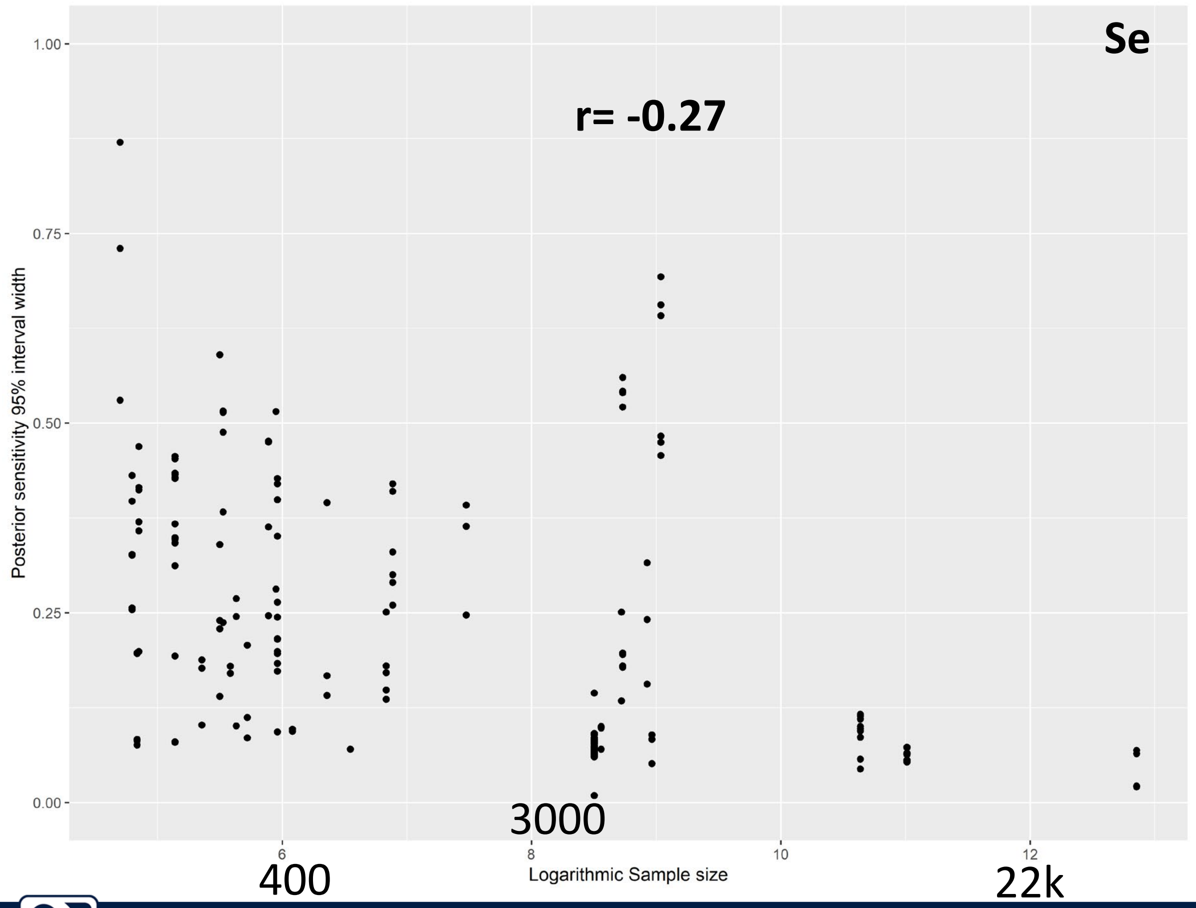


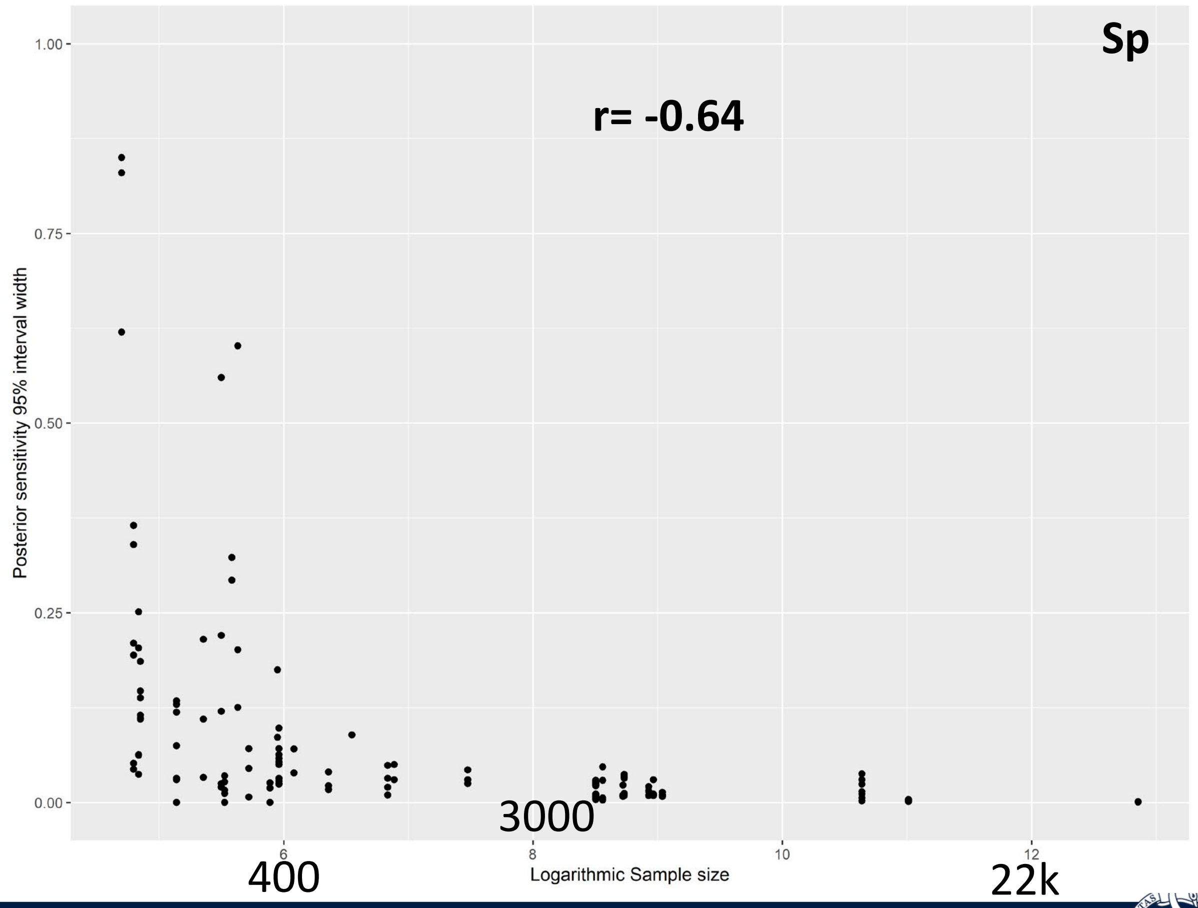
Posterior estimates: Sp post-mortem tests

Test	$N^{\dagger}$	Sp estimates‡	APM and 95% APPI Sp estimates (%)§	Species
Culture	9	17	99.8 (98.0–100)	
Tissue	8	15	99.9 (99.3–100)	Cattle, wild boar, swine, meerkat, badger
Milk and blood	1	2	97.5 (88.0–100)	Cattle
Direct PCR	10	21	97.6 (95.0–99.7)	
Tissue	9	19	97.6 (95.4–99.7)	Cattle, wild boar, swine,
Milk and blood	1	2	93.0 (69.0–99.5)	Cattle
Meat inspection	5	9	99.1 (98.4–99.7)	Cattle
Histopathology	2	10	99.0 (96.8–100)	Cattle
Culture + meat inspection	1	3	98.5 (97.7–99.2)	Cattle



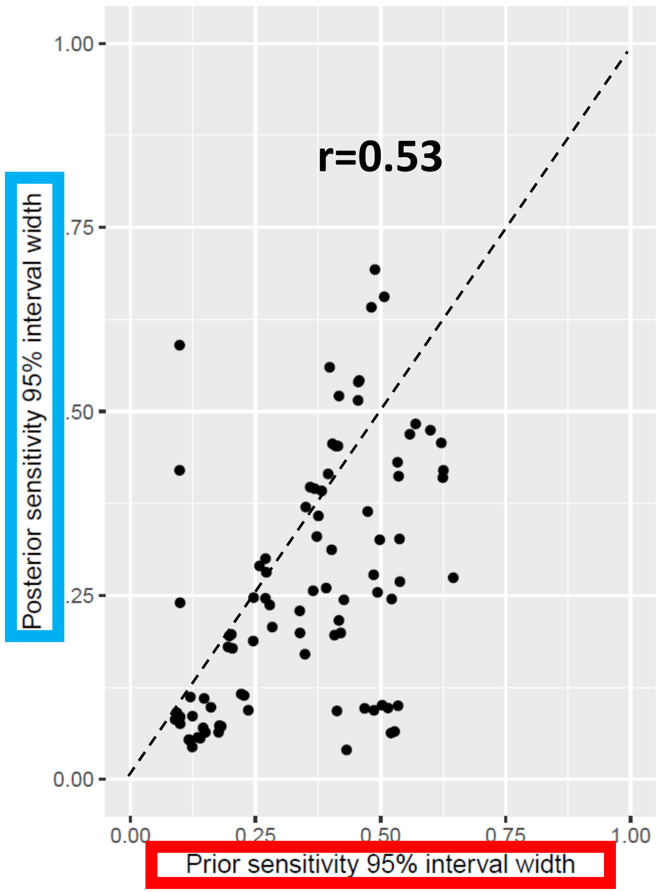
Impact of sample size on (precision) of posteriors

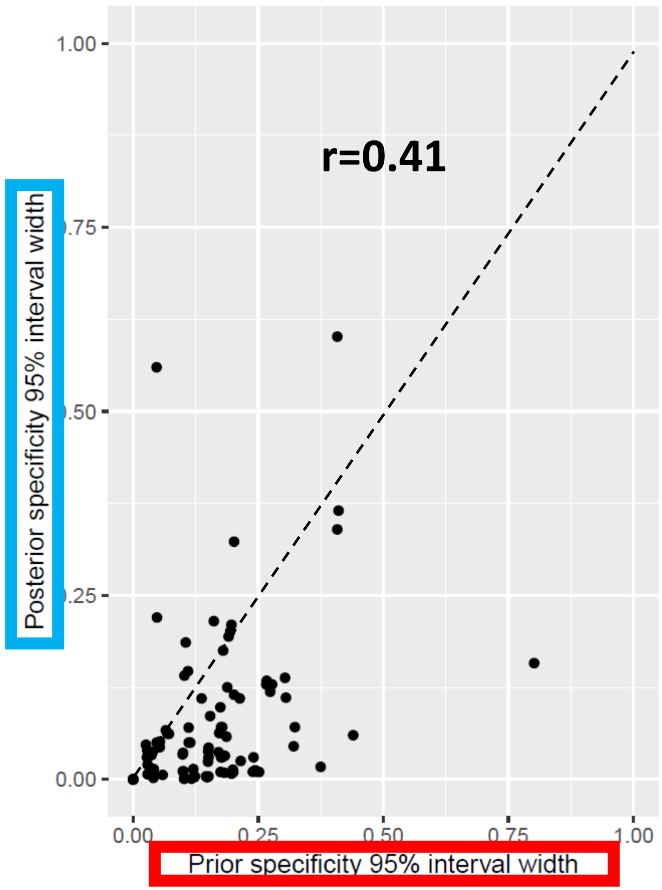




Impact of priors on (precision) of posteriors

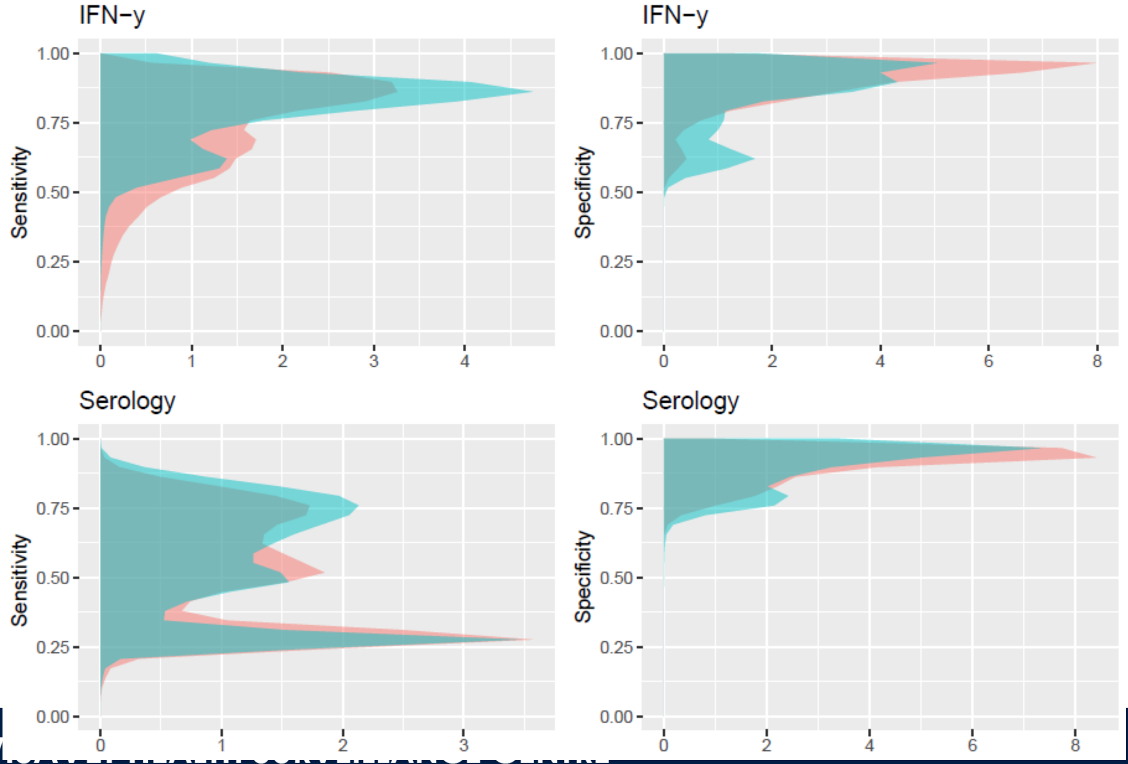
- Width more correlated for Se
- Wider prior than posterior intervals
  - Prior Se: Median PIW=0.37 (IQR 0.18-0.47)
  - Prior Sp: Median PIW=0.15 (0.06-0.20)
  - Post Se: Median PIW=0.24 (0.10-0.40)
  - Post Sp: Median PIW=0.04 (0.01-0.10)

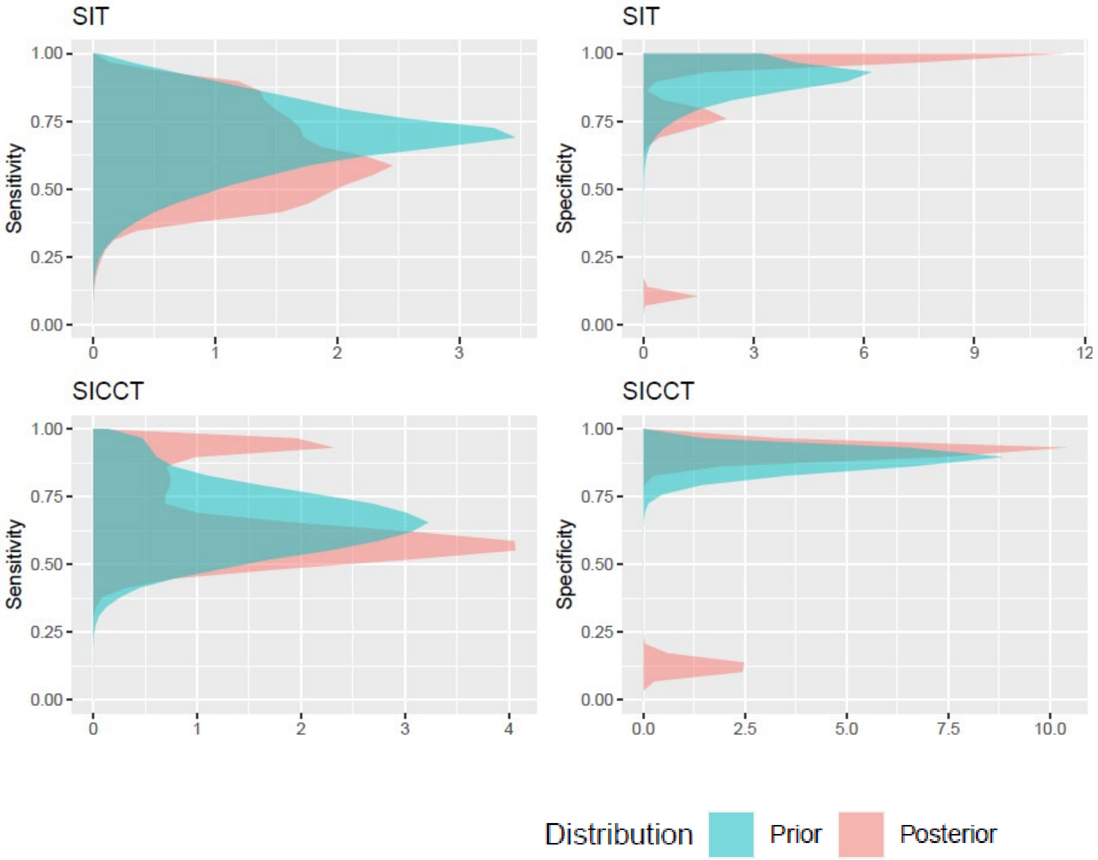




Agreement between prior and posteriors?

- Overlap of prior vs. posterior distributions
  - Se: 61.0% (95% range: 55.3-66.7)
  - Sp: 29.9% (95% range: 23.6-36.2)
- “optimistic” prior distributions? (SIT-IFN)





Quality of reporting

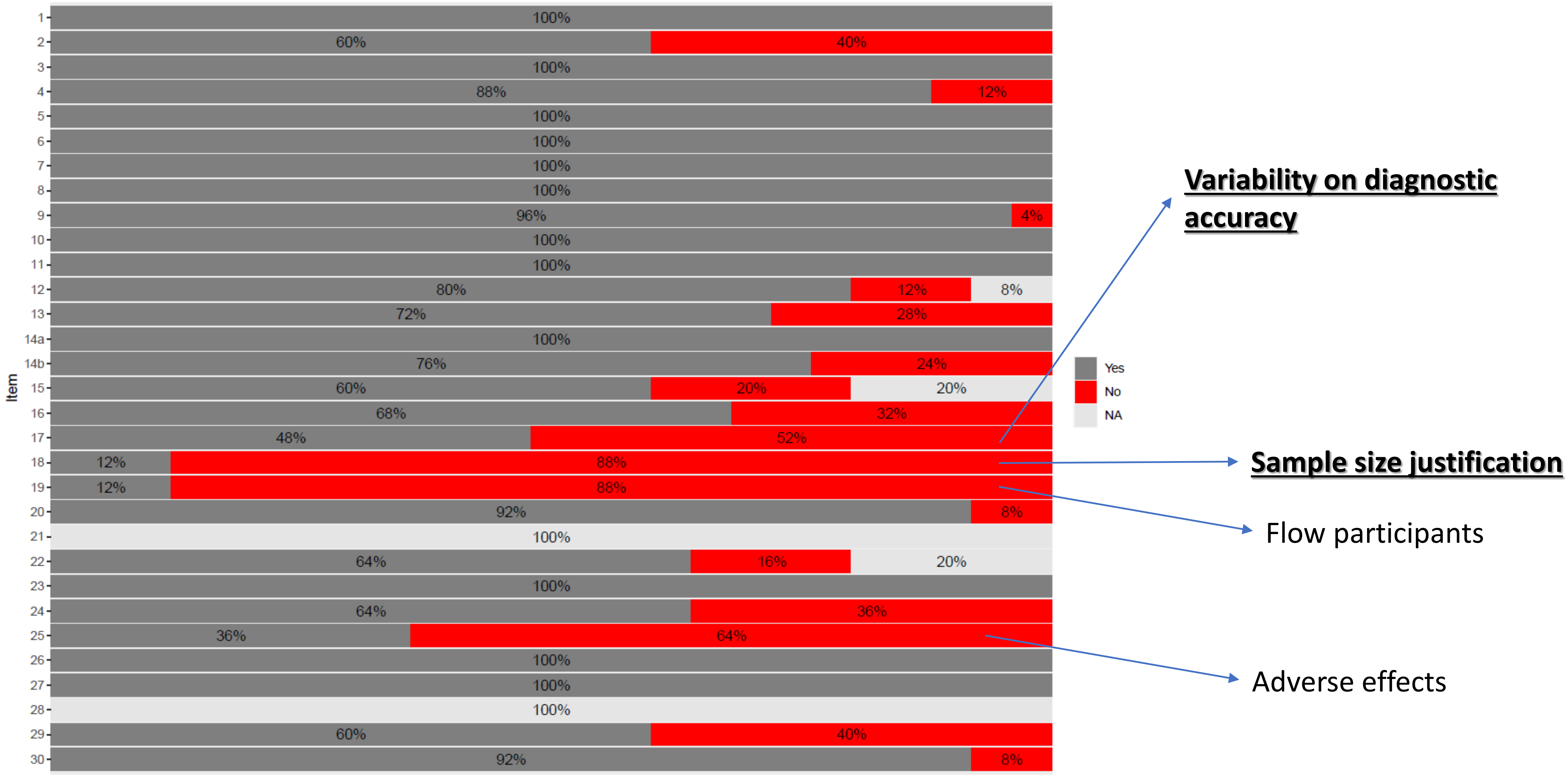
Contents lists available at ScienceDirect
Preventive Veterinary Medicine
journal homepage: www.elsevier.com/locate/prevetmed

STARD-BLCM: Standards for the Reporting of Diagnostic accuracy studies that use Bayesian Latent Class Models

Polychronis Kostoulas[a,*], Søren S. Nielsen[b], Adam J. Branscum[c], Wesley O. Johnson[d], Nandini Dendukuri[e], Navneet K. Dhand[f], Nils Toft[g], Ian A. Gardner[h]

- 14/25 articles published after the release of STARD-BLCM guidelines (2017)
  - 3 provided checklist and 4 reported following guidelines
- Screening of all papers to assess fulfillment of conditions
  - 81.4% of all posible evaluations (28 items evaluated in 25 articles) satisfactorily fulfilled

NA: 21 (distribution of targeted condition), 28 (registration number)



Conclusions on use of BLCMs for aTB diagnosis

- BLCMs increasingly used for analysis of bTB diagnostic tests (14/25 papers published after 2019)
- “Typical”subject
  - **Bovine** (but most (wild) species included to some extent – ~~goat)~~
  - **Cellular immune response** (but also new serological tests – wildlife)
  - **WinBUGS**, OpenBUGS, JAGS (~~Stan~~)
  - Informative priors
    - 4 studies based non-informative priors for well established tests?
    - Sensitivity analysis not conducted in 7/25 studies

Conclusions on test performance

- Overall picture agrees with gold-standard based results
  - Specificity typically very high (>90%; exception: CFT, IFN-g)
  - Sensitivity estimates very variable
- Still… consistent differences in Se based on BLCMs
  - **Skin test**: Median Se<70% (except CFT)
    - SIT: 64-70% vs. with 81% or 94% estimates in metaanalysis (Nuñez-Garcia et al., 2018).
    - SICCT: fairly consistent (BLCMs APPI 52-66% for standard and 67-76% for severe interpretation) vs. with 50-100% based on gold-standard
  - **IFN-g**: more consistent (APPI BLCMs 71-90% vs. 49-82% based on gold-standard… often in OTF herds)
    - Temporal bias: more standardized techniques in recent studies?

Conclusions on test performance

- Variability on estimates for **serology-based** tests likely related with heterogeneity of populations tested… but:
  - BLCM estimates less optimistic (~50%) compared with gold-standard (>63-75%)
- Variability in **post-mortem** (culture, PCR) related with heterogeneity of populations… but:
  - Both tests had similar performance (in agreement with current belief that PCR can perform as well as culture)
  - High values mostly related with reasons for culture (“suspected” animals) as opposed to ante-mortem tests… and still values were not so high! (~80%)

Overall conclusions on test performance

- **There is no single answer to “how well do TB diagnostic tests perform”** even when removing the “gold-standard factor”… since there are multiple others that are known to affect test performance
  - Presence of cross-reacting (myco)bacteria
  - Host-related factors (immune response, other diseases, age…)

There is potential for further studies that account formally for these factors

- Results show consistent biases associated with relying on gold standard based techniques, and support the use of BLCMs in the future

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Review Article

Accuracy of Tests for Diagnosis of Animal Tuberculosis: Moving Away from the Golden Calf (and towards Bayesian Models)

Alberto Gomez-Buendia,[1] Pilar Pozo,[1] Catalina Picasso-Risso,[2,3] Adam Branscum,[4] Andres Perez,[2] and Julio Alvarez[1,5]

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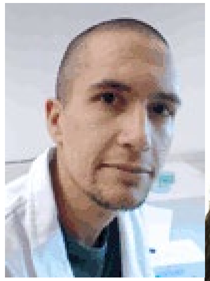



- Mycobacteria unit at VISAVET

- Funding: Epi-TUB Project

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AGENCIA ESTATAL DE INVESTIGACIÓN

Take home message: the time has come to consider new approaches!

Thanks for your attention

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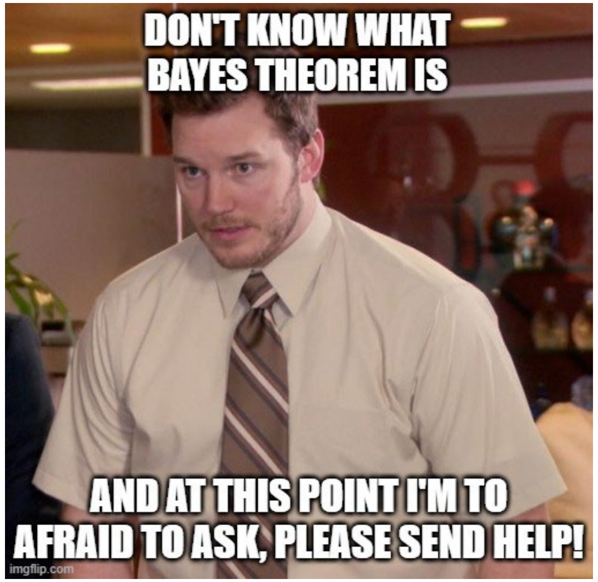

Frequentist

Bayesian