JVDI: Supplementary material

Jia B, et al. Diagnostic sensitivity and specificity of tests for infectious diseases in wild mammals: review of published validation studies and recommendations for design, analysis, and reporting improvements

**Supplementary Data 1.** Methodologic review: literature search, appraisal, and review

**Literature search: search strategy and compilation of references**

We searched journal publications reporting laboratory test validation studies for OIE-listed diseases in wild mammals published between 2008 and 2017. The starting date of 2008 was chosen to allow authors adequate time to incorporate epidemiologic approaches into the design and reporting of validation studies. Test validation terms in the title, abstract, or keywords, such as sensitivity, specificity, validation, diagnostic, and performance either were necessary but not exclusively used for a paper to be considered as a candidate for further evaluation.

Two parallel approaches were applied by using 3 search engines with combinations of search terms and Boolean operators. For PubMed and EBSCO (method 1), we used a combination of the OIE disease list of wild mammals (Suppl. Table 1), common and scientific names of wild mammal species (Suppl. Table 1), and test validation terms (diagnosis, validation, performance, sensitivity, specificity). All search terms were connected with "OR." For method 2, we used wildcard characters, validation terms with "AND/OR," and nesting parentheses to search the CABI Veterinary Medicine Resources (CABVMR, see Suppl. Data 2); the study species were limited to only captive or free-ranging wild mammals.

## Literature appraisal: paper selection, full-text review, and synthesis

Following the literature search, study relevance was evaluated by the primary reviewer based on the title, and then the abstract was read by all 3 reviewers to decide which papers should be included for full-text review. The 3 reviewers had a range of experience and were assigned different roles: 1) primary reviewer: an early-career researcher (B. Jia) with formal training in veterinary epidemiology was solely responsible for literature searches; 2) 2 experts assisted with paper selection and compilation of references. One (A. Colling) had 15 y of experience in an OIE reference laboratory and the second (I.A. Gardner) had authored or co-authored >50 test-validation studies.

Based on titles, the primary reviewer grouped the papers identified by the search engines into “most relevant,” “less relevant,” and “not relevant.” Papers were designated as “most relevant” if there were at least 2 different tests, test performance data, and a description of sampling methods and specimen types. The most relevant papers were then combined into a single group of 635: PubMed (*n* = 136), EBSCO (*n* = 184), and CABVMR (*n* = 315; Fig. 1). Sixty-one papers had duplicate records and were excluded. The remaining 574 papers were filtered by their titles, based on whether they contained any of the following terms: diagnostic sensitivity, diagnostic specificity, comparison, validate, evaluate, performance. This resulted in 89 papers.

The 3 reviewers independently evaluated the titles and abstracts of these papers in terms of their reporting completeness and quality. Three categories were used for their assessments: “yes,” “no,” and “undecided.” The abstract appraisal of the 89 papers was as follows: 3 “yes” (*n* = 35), 1 or 2 “yes” (*n* = 40), and no “yes” (*n* = 14). Based on the agreement from all reviewers’ assessments, 45 studies were included for the full-text reading and information synthesis, including 3 “yes” (*n* = 33) and non–*Mycobacterium*

*bovis* papers with 1 or 2 "yes" ($n$ = 12) with the potential omission of some papers if there was disagreement among reviewers (Fig. 1).

***Synthesis and analysis.*** In order to summarize reporting characteristics of the 45 references, we developed a 17-item template (Table 1) to capture and quantify the most relevant factors: 1) sampling (diseases/pathogen, studied species, study purpose, source population, internal/external validity, specimen types), 2) test performance (specimen, index test, reference test, diagnostic sensitivity, diagnostic specificity, percentages of positive and negative results, statistical methods, overall quality of reporting), and 3) publication information (author, publication year). Major reporting gaps were also identified and accounted for, such as whether the source population matched the study purpose, availability and quality of reference standards to which the tests under evaluation were compared, and overall reporting quality based on guidance provided by the Standards for Reporting of Diagnostic Accuracy Studies (STARD) initiative.

***Results of literature appraisal.*** Among the 33 papers with 3 "yes" for full-text reading, we identified 15 papers with 3 "yes" reporting the performance of tests for detection of *M. bovis* infection in wildlife distributed in South Africa, Great Britain, United States, Canada, Spain, and Ireland between 2008 and 2017. Wild mammals studied included wild meerkat (*Suricata suricatta*), fallow deer (*Dama dama*), roe deer (*Capreolus capreolus*), red deer (*Cervus elaphus*), white-tailed deer (*Odocoileus virginianus*), wood bison (*Bison bison athabascae*), reindeer (*Rangifer tarandus*), elk (*Cervus canadensis*), various species of furbearers, warthog (*Phacochoerus africanus*), African buffalo (*Syncerus caffer*), and European badger (*Meles meles*). A summary of sampling design, sample types, diagnostic test methods, statistical methods, and validation results for diagnostic tests is listed in Table 1, and Supplementary Figures 1 and 2.

The remaining 18 papers with 3 “yes” reported the following infectious agents and diseases in the corresponding wildlife species: African swine fever virus in wild boar (*Sus scrofa*); *Anaplasma* spp. in wild ungulates; bovine spongiform encephalopathies in macaques, *Brucella abortus* in elk (*Cervus elaphus*) and African buffalo (*Syncerus caffer*); chronic wasting disease virus in white-tailed deer; (*Odocoileus virginianus*), classical swine fever virus in wild boar (*Sus scrofa*); epizootic hemorrhagic disease in impala and dromedary camel; foot-and-mouth disease virus in African buffalo (*Syncerus caffer*); hemorrhagic septicemia in Asian elephants (*Elephas maximus*); henipavirus in fruit bats; *M. avium* subsp. *paratuberculosis* in fallow deer (*Dama dama*); *Notoedres cati* in bobcats (*Lynx rufus*); *Leishmania infantum* in rabbits; multiple pathogens (canine parvovirus and *Anaplasma phagocytophilum*) in fishers (*Martes pennanti*) and gray foxes (*Urocyon cinereoargenteus*); *Sarcoptes scabiei* in wild boar (*Cervus elaphus*), wild rabbits (*Oryctolagus cuniculus*), and Iberian ibex (*Capra pyrenaica*); tick-borne encephalitis virus in wild rodents (*Myodes rufocanus bedfordiae*, *Apodemus speciosus*, and *Apodemus argenteus*); *Toxoplasma gondii* in wild boar (*Sus scrofa*); *Trichinella* in wild boar (*Sus scrofa*); *Trypanosoma* spp. in raccoons (*Procyon lotor*) and buffalo; rabies virus in foxes and raccoon dogs.

**Supplementary Data 2. S**earch terms in CABI Veterinary Medicine Resources (limited to selected species: Exotics, Zoo & Wild animals).

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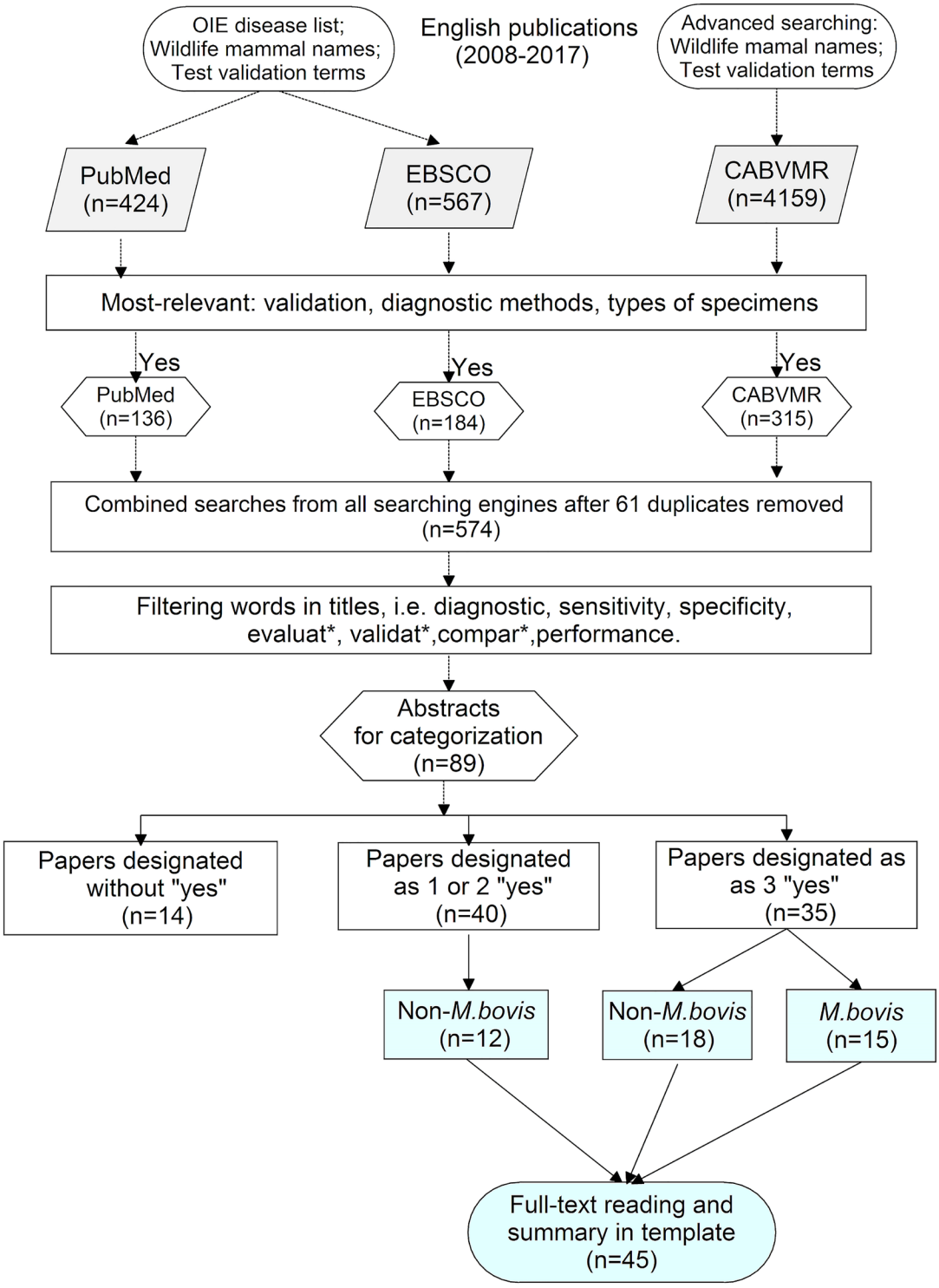
| (Diagnos* OR Validate* OR test* OR Evaluate* OR Performance OR test OR sensitivity OR specificity) AND (Wild* OR Wildlife OR Wild animals OR Captive OR Feral OR Free-ranging OR Zoo*) AND la:(English) AND it:("Abstract only" OR "Journal article") NOT od:("Human*" OR "man" OR "birds" OR "fowls" OR "plants" OR "Fish") NOT up:("aquatic organisms" OR "aquatic species" OR "aquatic*") NOT ("non-infectious" OR "nutritional" OR "toxicities") |

Field tags associated with index searching fields: Language (la); Publication type (it); Organism descriptor (od); Broader term (up). CABI training materials, user guide: https://www.cabi.org/Uploads/CABI/publishing/training-materials/vet-med-resource-user-guide-low-res.pdf

**Supplementary Table 1.** Search strategies in PubMed and EBSCO.

| Item | Searching terms and Boolean connectors |
|---|---|
| OIE-listed diseases | Anthrax OR Bluetongue OR Crimean Congo haemorrhagic fever OR Epizootic haemorrhagic disease OR Equine encephalomyelitis OR Heartwater OR Infection with Aujeszky's disease virus OR Infection with *Brucella abortus*, *Brucella melitensis* and *Brucella suis* OR Infection with *Echinococcus granulosus* OR Infection with *Echinococcus multilocularis* OR Infection with foot and mouth disease virus OR Infection with rabies virus OR Infection with Rift Valley fever virus OR Infection with rinderpest virus OR Infection with *Trichinella* OR Japanese encephalitis OR New world screwworm OR Old world screwworm OR Paratuberculosis OR Q fever OR Surra OR Tularemia OR West Nile fever OR *Bovine anaplasmosis* OR *Bovine babesiosis* OR Bovine genital campylobacteriosis OR Bovine spongiform encephalopathy OR Bovine tuberculosis OR Bovine viral diarrhoea OR Enzootic bovine leucosis OR Haemorrhagic septicaemia OR Infectious bovine rhinotracheitis OR infectious pustular vulvovaginitis OR Infection with *Mycoplasma mycoides* OR contagious bovine pleuropneumonia OR Lumpy skin disease OR Theileriosis OR Tritrichomonas OR Trypanosomosis OR tsetse-transmitted OR Caprine arthritis/encephalitis OR Contagious agalactia OR Contagious caprine pleuropneumonia OR Infection with *Chlamydophila abortus* OR Enzootic abortion OR ovine chlamydiosis OR Infection with peste des petits ruminants virus OR *Maedi visna* OR Nairobi sheep disease OR Ovine epididymitis (*Brucella ovis*) OR Salmonellosis OR Scrapie OR Sheep pox OR goat pox OR Contagious equine metritis OR Dourine OR Equine encephalomyelitis OR Equine infectious anaemia OR Equine influenza OR Equine piroplasmosis OR Glanders OR Infection with African horse sickness virus OR Infection with equid herpesvirus-1 OR Infection with equine arteritis virus OR Venezuelan equine encephalomyelitis OR African swine fever OR Infection with classical swine fever virus OR Infection with *Taenia solium* OR Porcine cysticercosis OR Nipah virus encephalitis OR Porcine reproductive and respiratory syndrome OR Transmissible gastroenteritis OR Camelpox OR Leishmaniosis |

| | |
|---|---|
| Names of wild mammal species | Antelope OR prong-horned OR *Antilocapra americana* OR badger OR *Taxidea taxus* OR bats OR *free-tailed* OR *Tadarida* OR *mastif* OR *Eumops* spp OR plain-nosed OR *Myotis** OR bear OR *black* OR *Euarctos americanus* OR beaver OR *Castor canadensis Kuhle* OR bobcat OR *Lynx rufus* OR *chipmunk* OR *Eutamias* spp OR coati OR *coatimundi* OR *Nasua narica* OR *Linnaeus* OR coyote OR *Canis latrans* OR deer OR mule OR black-tailed OR *Odocoileus hemionus* OR *Rafinesque* OR white-tailed deer OR eastern OR *O. virginianus* OR *Zimmermann* OR *elk* OR *Cervus Canadensis* OR *Erxleben* OR fox OR gray fox OR *Urocyon cinereoargenteus* OR *Shreber* OR *Kit* OR *Vulpes macrotis Merriam* OR *gopher* OR *pocket* OR *Thomomys* spp OR *javelin* OR *Pecari tajacu* OR mountain lion OR *Felis concolor* OR mouse OR *cactus Peromyscus eremicus* OR pinyon OR *P. truei* OR pocket OR *Perognathus* spp OR muskrat OR *Ondatra zibethica* OR otter OR river OR *Lutra canadensis* OR *prairie dog* OR *Gunnison's* OR *Cynomys gunnisoni* OR *porcupine* OR *Erethizon dorsatum* OR rabbit OR cottontail OR *Sylvilagus* spp OR jack OR *Lepus* spp OR raccoon OR *Procyon lotor* OR rat OR kangaroo OR *Dipodomys* spp OR pack OR *Neotoma albigula Hartley* OR wood OR *Neotoma* spp OR *ringtail* OR *Bassariscus astutus* OR bighorn sheep OR *Ovis canadensis Shaw* OR desert shrew OR *Notiosorex crawfordi* OR vagrant OR *Sorex* spp OR skunk OR hog-nosed OR *Conepatus mesoleucus* OR *hooded Mephitis macroura* OR striped OR *M. mephitis* OR spotted OR *Spilogale putorius* OR *squirrel* OR *Abert's* OR *Sciurus aberti Woodhouse* OR *Kaibab Sub S.* OR *aberti* OR *Apache S. apache* OR Arizona gray OR *S. arizonensis* OR *Tamiasciurus hudsonicus* OR *ground Citellus* spp OR vole OR long-tailed OR *Microtus longicaudus Merriam* OR *Mexican* OR *M. Mexicanus* OR *montane* OR *M. montanus* |




**Supplementary Figure 1.** Literature search of journal papers published in English between 2008 and 2017 that reported diagnostic test validation for infectious diseases in wild mammals. Main findings from review of the 45 papers are summarized in Tables 2 and 3.


**Supplementary Figure 2.** Diagnostic sensitivities (x-axis) reported in the relevant test validation studies ($n$ = 15) of *M. bovis* published between 2008 and 2017. For test abbreviations and wild animal species, see Table 2. Dashed lines represent boundaries between studies.


**Supplementary Figure 3.** Diagnostic specificities (x-axis) reported in the relevant test validation studies ($n$ = 15) of *M. bovis* published between 2008 and 2017. For test abbreviations and wild animal species, see Table 2. Dashed lines represent boundaries between studies.