General principles of surveillance of bovine tuberculosis in wildlife

ANITA MICHEL

FACULTY OF VETERINARY SCIENCE, UNIVERSITY OF PRETORIA &

OIE COLLABORATING CENTRE FOR TRAINING IN INTEGRATED LIVESTOCK AND WILDLIFE HEALTH AND MANAGEMENT

Tuberculosis in a nutshell

- **Causes of tuberculosis: Mycobacteria of the *M. tuberculosis* complex**

  - Human TB: *M. tuberculosis*
  - TB in cattle
  - humans — *M. bovis*
  - wildlife

- ***M. tuberculosis* complex**
  - *M. tuberculosis*
  - *M. africanum*
  - *M. canettii*
  - *M. bovis*
  - *M. microti*
  - *M. caprae*
  - *M. pinnipedii*
  - *M. orygis*
  - *M. suricattae*
  - *M. mungi*
  - Dassie bacillus
  - (M. bovis BCG)

Tuberculosis in wildlife

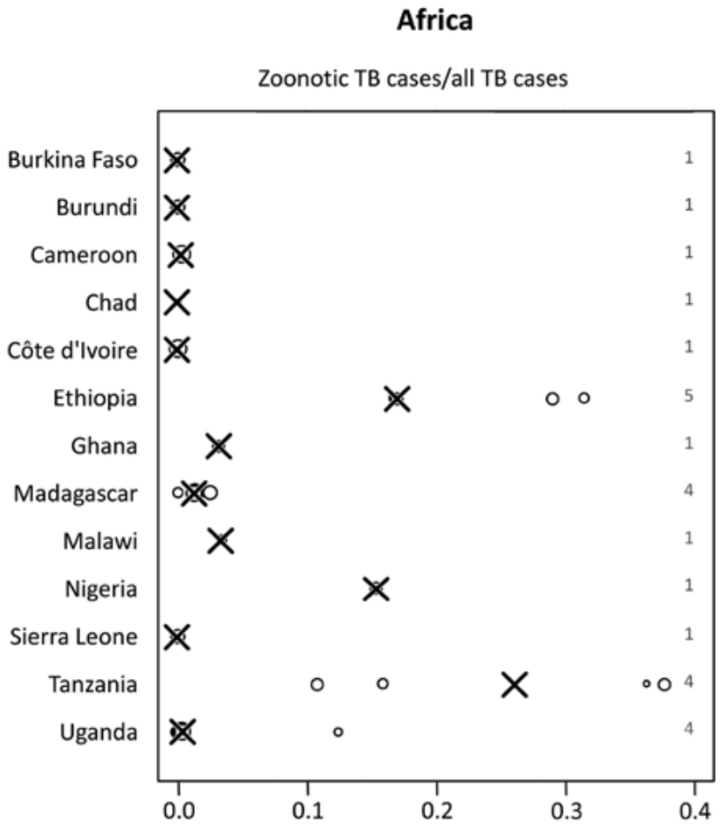







Tuberculosis in humans

- Nearly 9 million new cases worldwide every year
- 1.5 million deaths every year
- Zoonotic TB (*M. bovis*) estimated proportion:
  - developed countries: <1.4% of human TB cases
  - Africa: 2.8% (0-37%) or (7/100 000)
- Human TB (*M. tuberculosis*) in cattle: excretion via milk?
- Diagnostic challenge: If contracted by ingestion – extrapulmonary TB – not detected by sputum examination
- *M. bovis* is resistant to pyrazinamide (1 of 4 first-line anti-TB drugs)



Wildlife tuberculosis (*M. bovis*) in a nutshell

- **Chronic** and debilitating infectious disease
- Transmission mostly respiratory or via ingestion
- **Multi-host** disease (any mammal species can be affected)
- Maintenance hosts and spill-over hosts
  - Maintenance host population has the ability to maintain the infection without becoming re-infected from another species: e.g. cattle, African buffalo, European badger, Opossum, bison, wild boar ...
  - Spill-over host: Infection transmitted from maintenance host to an incidental hosts

- Multi-host pathogen in a multi-species environment

Maintenance hosts of bovine TB – examples

- African buffalo - South Africa, Uganda
- Kafue lechwe - Zambia
- European badger - UK
- Red deer - Spain
- Wild boar - Spain
- Wood bison - Canada
- Elk - Canada
- White-tailed deer - USA
- Brushtail possum - New Zealand

Different roles of wildlife hosts – dependent on epidemiological setting

- European badger

	High significance	Low significance
UK	•	
Spain		•

- Wild boar

	High significance	Low significance
Spain	•	
Italy		•

- Red deer

	High significance	Low significance
Spain	•	
UK		•

What determines the role of a wildlife host?

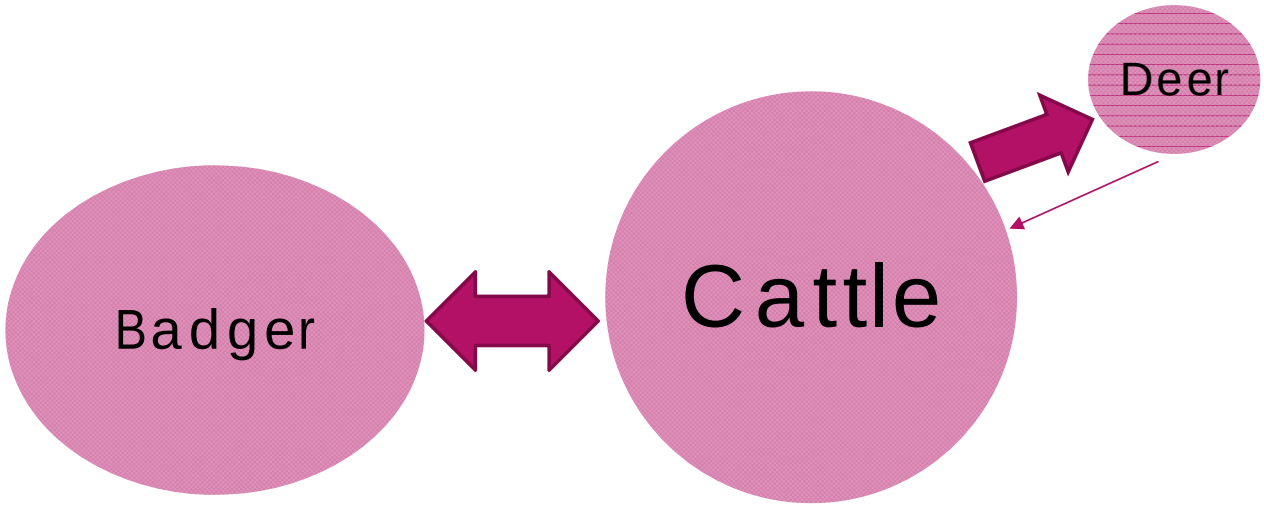
The role of wildlife hosts depends on several factors

- Host population density
- Intra-species transmission rate
- Effective inter-species contact rate
- Inter-species transmission rate
- BTB prevalence
- Longevity of host species
- *M. bovis* in the environment

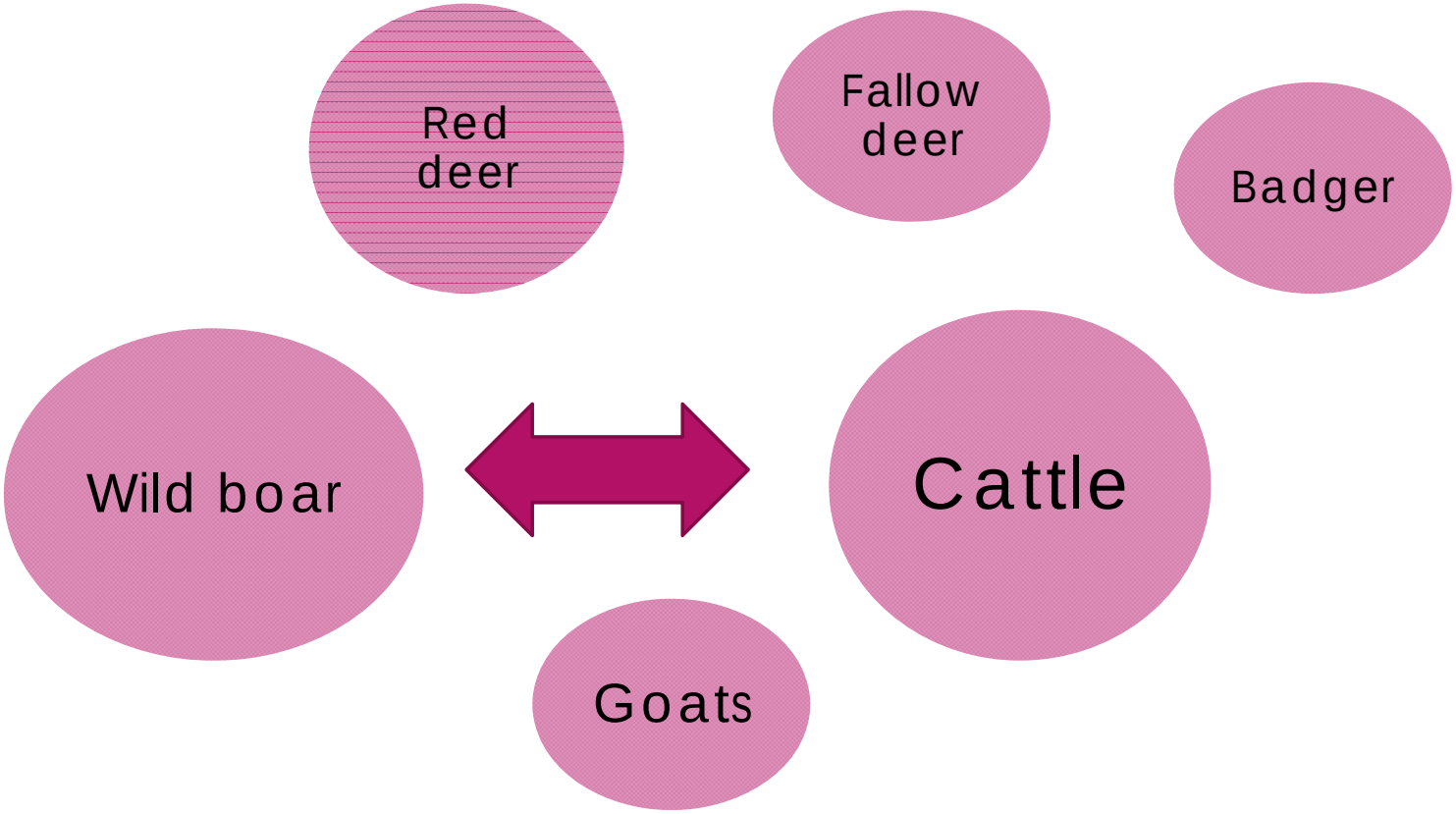
Thresholds for disease persistence apply!

Country specific settings/complexities

1. United Kingdom



2. Spain



3. South Africa

Table 1. *Mycobacterium bovis* in free/semi-free ranging wildlife in South Africa

Common name	Scientific name	Location	References
Common duiker	*Sylvicapra grimmia*	Agricultural farmland	(Paine, Martinaglia 1929)
African buffalo	*Syncerus caffer*	GKNPC[1] and other game parks[2]	(Bengis et al. 1996)
Lion	*Panthera leo*	GKNPC and other game parks	(Michel et al. 2006, Hlokwe et al. 2011, Keet et al. 1996)
Cheetah	*Acinonyx jubatus*	GKNPC	(Keet et al. 1996)
Leopard	*Panthera pardus*	GKNPC	(De Vos et al. 2001, Michel et al. 2009, Michel et al. 2006)
Greater kudu	*Tragelaphus strepsiceros*	Multiple game parks and agricultural farmland	(Paine, Martinaglia 1929, Thorburn, Thomas 1940, Michel et al. 2009, Keet et al. 2001)
Spotted hyaena	*Crocuta crocuta*	GKNPC and other reserves	(Michel et al. 2009, Michel et al. 2006, Michel 2002)
Chacma baboon	*Papio ursinus*	GKNPC and other parks	(Keet et al. 2000),(Michel et al. 2009, Michel et al. 2006, Keet et al. 1996)
Honey badger	*Mellivora capensis*	GKNPC	(Michel et al. 2006, Michel 2002)
Large spotted genet	*Genetta tigrina*	GKNPC	(De Vos et al. 2001)
Warthog	*Phacochoerus africanus*	GKNPC and other parks, agricultural farmland	(Michel et al. 2009, Michel et al. 2006)
Bushpig	*Potamochoerus larvatus*	HiP	(Michel et al. 2009, Michel et al. 2006)
Impala	*Aepyceros melampus*	GKNPC	(Michel et al. 2006)
Bushbuck	*Tragelaphus scriptus*	GKNPC	(Bengis, De Klerk-Lorist & Keet 2012, Hlokwe, van Helden & Michel 2014)
Eland	*Taurotragus oryx*	Other game parks	(Michel et al. 2006)
Blue wildebeest	*Connochaetes taurinus*	GKNPC	(Hlokwe, van Helden & Michel 2014)
Banded mongoose	*Mungos mungo*	GKNPC	(A Brüns, unpublished data)
Giraffe	*Giraffa camelopardalis*	GKNPC	T.M. Hlokwe, pers. comm Nov 2013
Wild dog	*Lycaon pictus*	GKNPC	T.M. Hlokwe, pers. comm Jan 2014
Nyala	*Tragelaphus angasii*	Other game parks	(Hlokwe, van Helden & Michel 2014)
Black rhinoceros*	*Diceros bicornis*	Other game parks	(Espie et al. 2009) (Keep, Basson 1973).

[1] Greater Kruger National Park Complex

[2] Including provincial and private game reserves and game farms

Surveillance

("close watch over an animal population")

is a key element for management of prevention, control and eradication programs through early detection (*true for wildlife TB?)*

Bovine TB surveillance in cattle

- **TO PROTECT LIVESTOCK POPULATIONS**
  - Market access
- **TO PROTECT HUMANS**
  - Food safety

What happens if effective TB surveillance (and action) is reduced in cattle?

Cattle

- Meat inspection misses x % cases:

Median time to detection: 302 weeks

Intra- and inter-herd prevalence rising

Bovine TB surveillance in wildlife

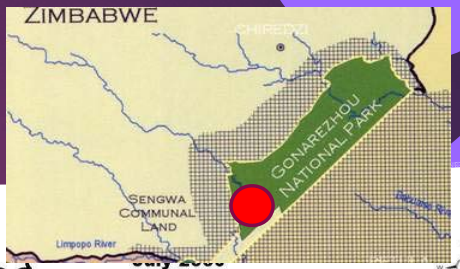
- **TO PROTECT LIVESTOCK POPULATIONS**
  - Cattle, goats, pigs
- **TO PROTECT HUMANS**
  - Food safety
  - Hunters
- **WILDLIFE CONSERVATION**
  - e.g. Iberian lynx

Bovine TB surveillance in wildlife - Aims?

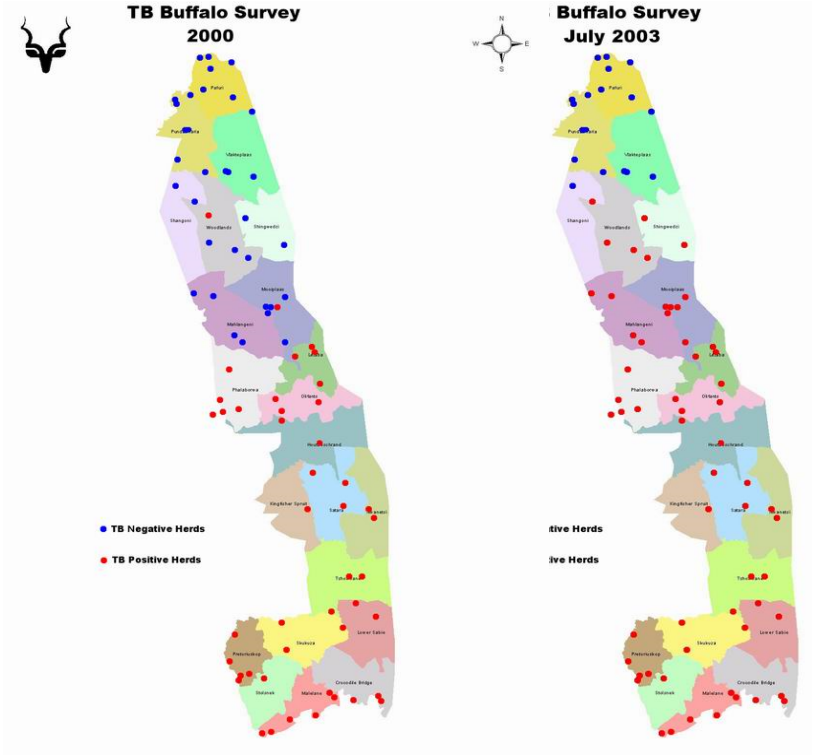
- Freedom from bovine TB
- "Early" detection

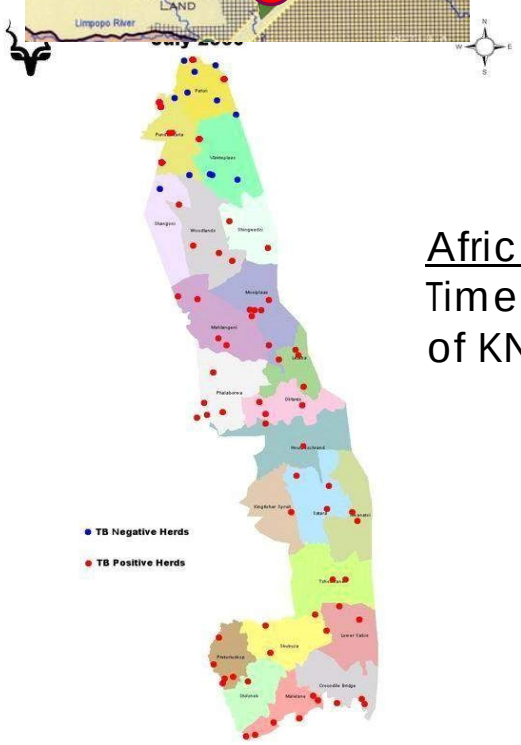
- Evaluate trends in TB prevalence
  - in a known infected host species
  - In an affected area (all susceptible species)
- Identify host species
- Determine the role of host species
- Monitor the temporal and spatial spread of infection
- Measure progress/effectiveness of control programmes
- Cornerstone in the eradication of infection

Surveillance as a vehicle to knowledge about wildlife TB



2008





<u>African buffalo</u>

Time to spread full length of KNP (350 km): 50 years

TB Surveillance components

Domestic cattle

- Routine tuberculin testing*
  - E.g. annual, every 2 y
- Movement testing
- Slaughterhouse surveillance*
  - No. of animals with suspect tuberculous lesions sent for laboratory examination
  - No. of animals with laboratory confirmation by culture / histopathology

*best practice for BTB surveillance (EFSA)

Wildlife

Low sensitivity

- Passive (scanning) surveillance on hunted wildlife
- Passive surveillance on animals found dead or moribund
- Active surveillance

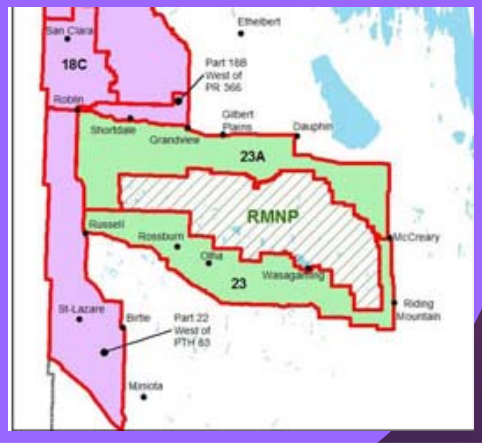
High sensitivity

  - collection of samples according to pre-determined sampling framework e.g. cage trapping, immobilisations, lethal sampling

Surveillance – wildlife

Canada

Bovine TB surveillance zone, Manitoba, Canada

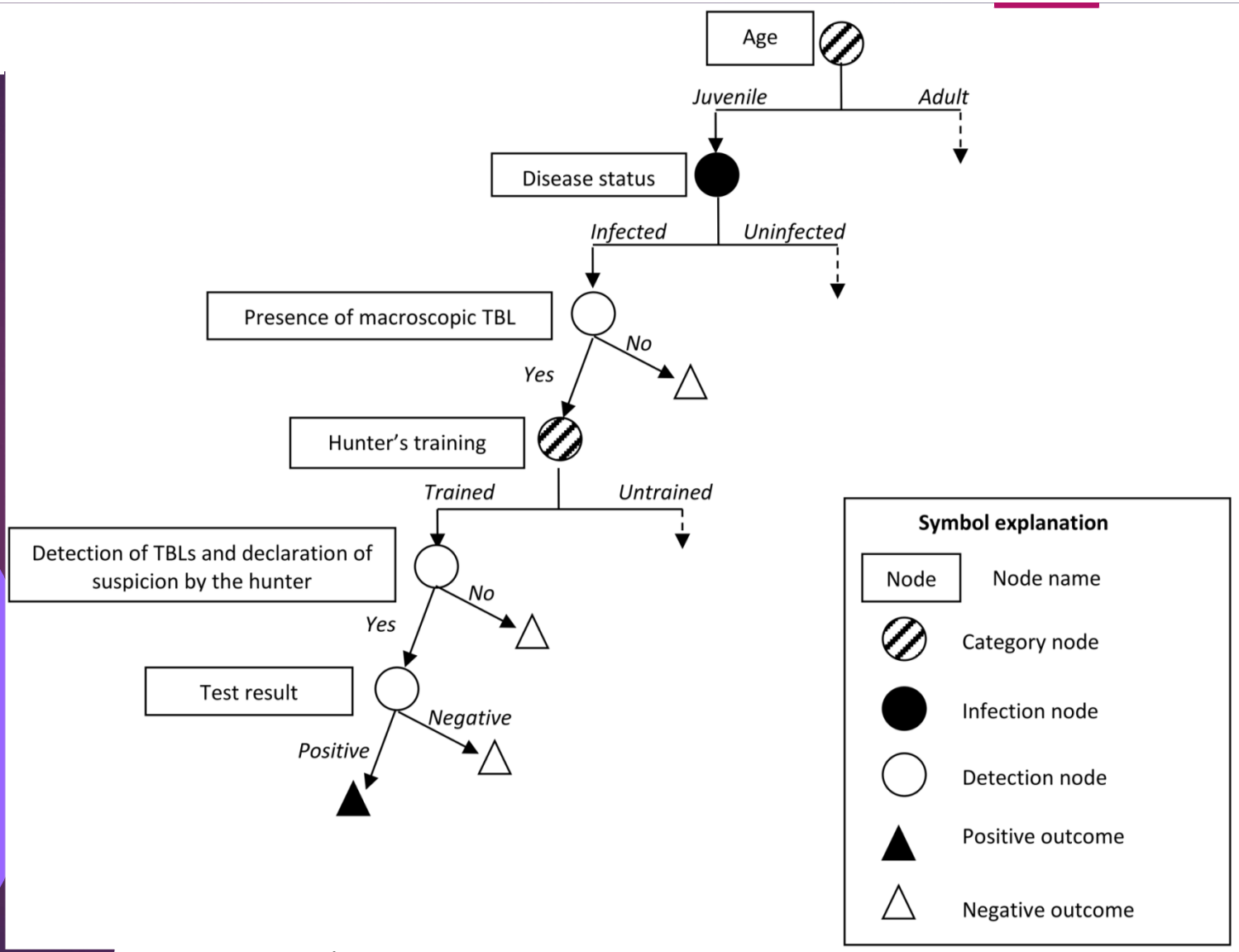


- Elk and deer hunters in the Bovine TB Surveillance Area are asked to submit elk and deer heads and lungs. All samples submitted will be examined for lesions symptomatic of this disease and those with suspicious lesions will be sent for culture.
- Cattle within the ***Bovine TB Management Area*** are tested to detect infected animals.

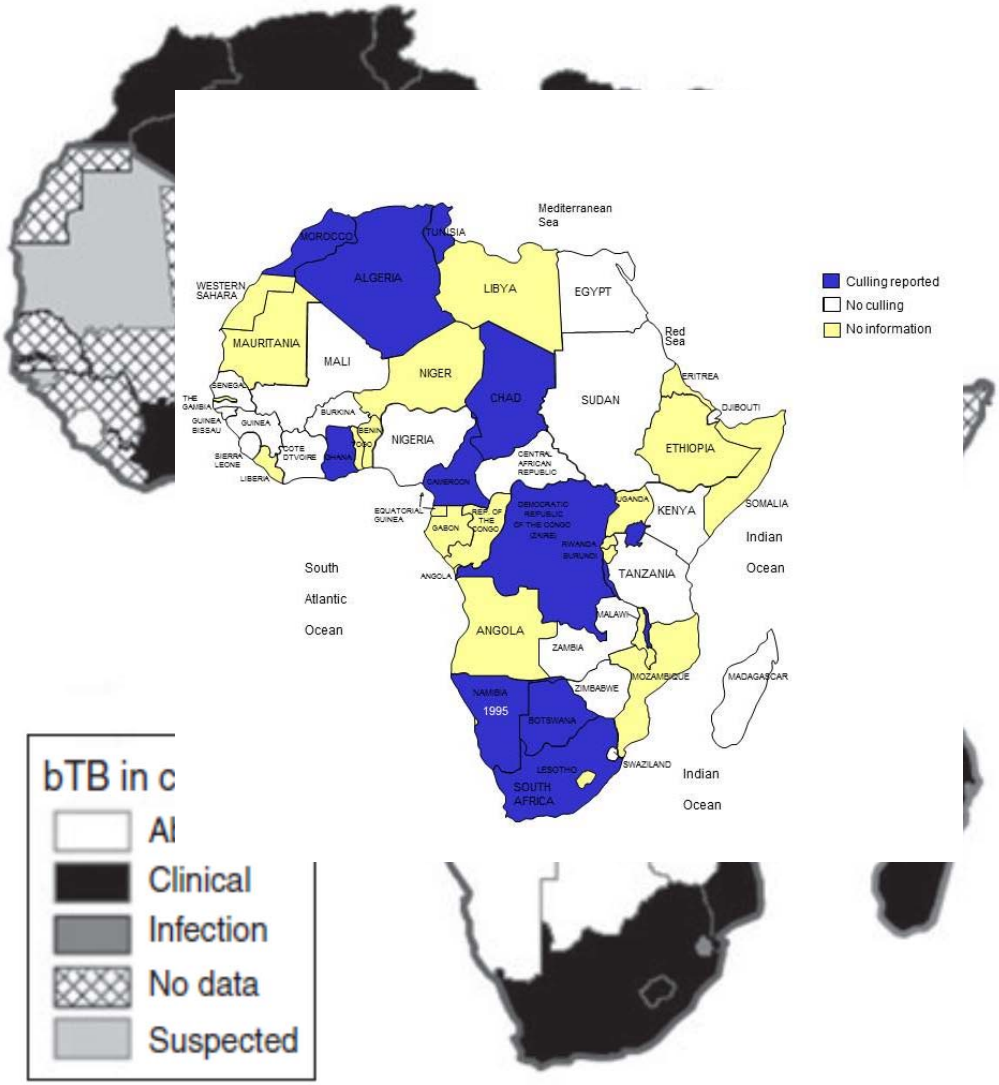
Surveillance – wildlife

France

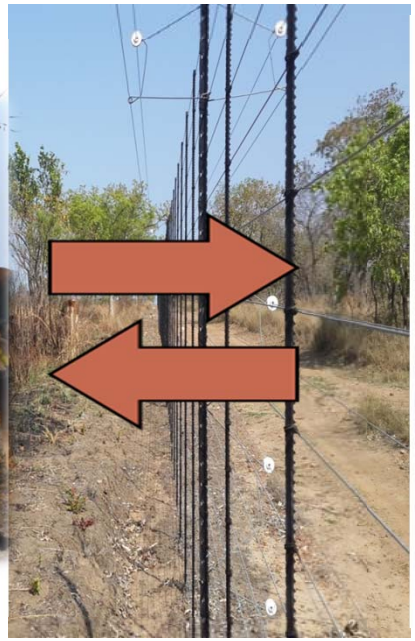
Scenario tree for passive scanning surveillance



Rivière et al. (2015) Sensitivity of Bovine Tuberculosis Surveillance in Wildlife in France: A Scenario Tree Approach. PLoS ONE 10(10): e0141884. doi:10.1371/journal.pone.0141884


Mediterranean Sea
MOROCCO
TUNISIA
ALGERIA
LIBYA
EGYPT
WESTERN SAHARA
MAURITANIA
MALI
NIGER
CHAD
SUDAN
Red Sea
ERITREA
DJIBOUTI
SENEGAL
THE GAMBIA
GUINEA BISSAU
GUINEA
BURKINA
BENIN
NIGERIA
ETHIOPIA
SIERRA LEONE
LIBERIA
COTE D'IVOIRE
GHANA
TOGO
CAMEROON
CENTRAL AFRICAN REPUBLIC
EQUATORIAL GUINEA
GABON
REP. OF THE CONGO
DEMOCRATIC REPUBLIC OF THE CONGO ZAIRE
UGANDA
KENYA
SOMALIA
RWANDA
BURUNDI
TANZANIA
Indian Ocean
South Atlantic Ocean
ANGOLA
MALAWI
ZAMBIA
MOZAMBIQUE
MADAGASCAR
ZIMBABWE
NAMIBIA
1995
BOTSWANA
SWAZILAND
LESOTHO
SOUTH AFRICA
Culling reported
No culling
No information
bTB in c
Al
Clinical
Infection
No data
Suspected

Is *M. bovis* transmitted from cattle to wildlife and back?



Can TB surveillance in wildlife be made practical and affordable?

Can TB surveillance in wildlife be made practical and affordable?

Prioritisation

- Most important: maintenance host species
  - African buffalo
  - Greater kudu

- Pathogen filters:
  - large felids
  - Warthogs

Can TB surveillance in wildlife be made practical and affordable?

Opportunities for convenience sampling

- Humane removal of moribund animals
- Victims of drought, poaching, road accidents
- Compulsory pre-movement testing of buffalo
- Conservation projects
- Disease investigations
- Wildlife hunting (60% of wildlife in SA is privately owned)
- Wildlife translocations
  - Organised, planned and frequent (70 000 – 200 000 head of game p.a in South Africa)

Diagnostic tools for surveillance of wildlife TB

Lethal sampling

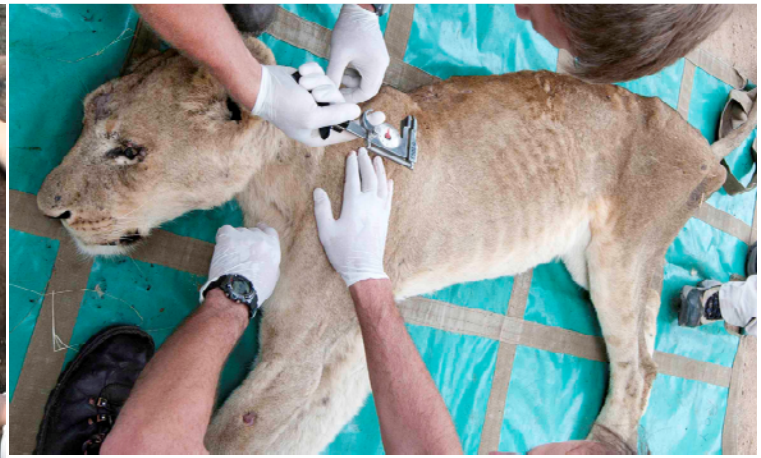
- Culture in combination with PCR (speciation) – all species
- Histopathology
- Histopathology in combination with PCR (amplification of MTBC DNA)

Live sampling

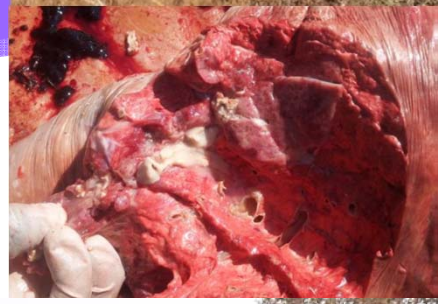
- Intradermal tuberculin test (cattle, buffalo)
- Interferon gamma assay (cattle, buffalo, bison)
- Antibody ELISA (wild suids)

Which test to use in live animals?

- Skin test requires 2 chemical immobilisations 3 days apart
- Test can only be repeated after 3 months
- Not validated (except for buffalo)



Development of new tests is key to improve/enable TB surveillance in wildlife
- e.g. Interferon gamma ass



Lion

- Possible BTB maintenance host
- Tuberculin skin testing not practical

Rhinoceros

- TB is a well recognised health threat to captive rhinos in zoos
- Sale of white rhino generates major income for KNP and HiP
- Tuberculin skin test is not applicable

Elephant

- *M. tuberculosis* is the main cause of TB in elephants in zoos worldwide and in domesticated elephants in Asia (Angkawanish et al 2013)
- Tuberculin skin test is not applicable

Laboratory facilities

- Basic facilities close to wildlife sampling
  - Fridge, -20C freezer, centrifuge, 37C incubator
  - Portable fridge
  - Stock of consumables (not expired): blood collection tubes, serum storage system
- Specialised diagnostic facilities at national level
  - TB culture, PCR
  - Histopathology
- Specialised research facility at regional level
  - Sequencing for phylogenetic studies and genotyping & metadata analysis

Bovine TB surveillance exercise

Group discussions

In Southern Africa a game reserve was newly established in 1995 and has been stocked with a founder population of buffalo from TB negative populations. A variety of plains game species and lions has been introduced between 2000 and 2005. As from 2007 buffalo auctions have been held on an annual basis during which on average 50 buffalo were sold following negative TB test results.

In 2011, TB testing of 3 buffalo captured for that year's auction tested positive and were confirmed by isolation of M. bovis. The game reserve is placed under quarantine.

Which surveillance activities would you implement and why (Aims)?

Which information would you require beforehand (re animal populations)?

Which surveillance strategy would you recommend to other game reserves?

Scenario – New Zealand

- The Animal Health Board (AHB), supported by the Government of New Zealand, have made good progress in the eradication of bovine TB in cattle over several decades. Both prevalence and incidence rates have steadily decreased with the result that certain regions did not experience outbreaks in cattle herds in several years while in other regions (on the west coast) sporadic cases continue to occur.
- Ongoing research has shown that >90% of outbreaks are caused by **wildlife**

Group discussions 1

A specialist group is tasked to develop a conceptual framework for a TB surveillance programme.

- In your opinion, what is the overall aim and the specific objective(s) of this TB surveillance programme?
- Propose a reasonable hypothesis for this surveillance programme

Group discussions 1

- Overall aim and the objective(s) of this TB surveillance programme

- Surveillance for what?
  - To eradicate bovine TB from the livestock population by
    - Eradication of bovine TB from possums and other possible wildlife maintenance hosts

- Hypothesis? If maintenance host populations can no longer transmit M. bovis to spillover hosts cattle, the risk of transmission to cattle becomes negligible

Group discussions 1

Action plan

Action	Who?	By when?	M & E
Action 1			
Action 2			
Action 3			

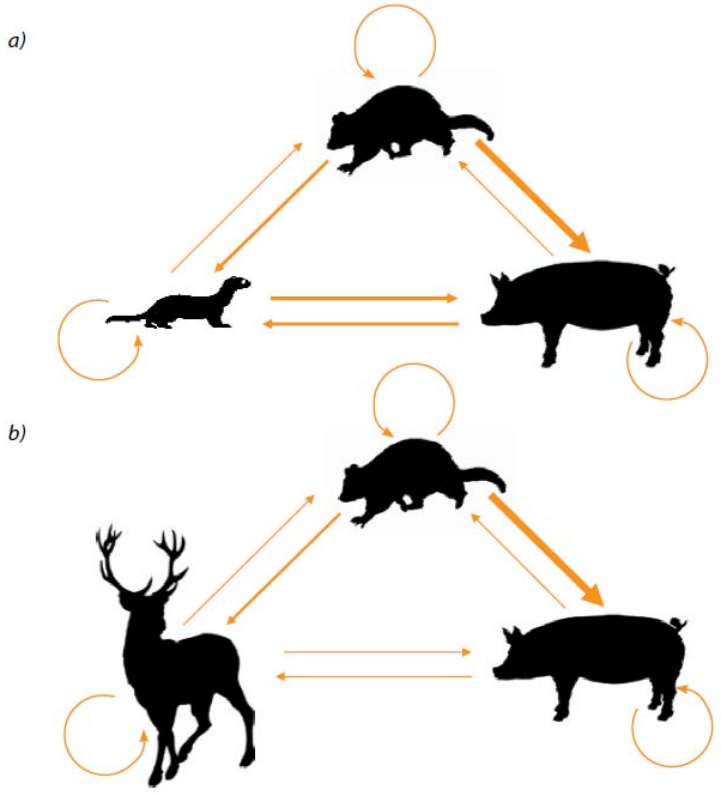
Group discussions 2

A specialist group is tasked to develop a conceptual framework for a TB surveillance programme.

- Which information (relating to animal populations) must be available before a meaningful framework can be developed?

Group discussions 2

- Which information (relating to animal populations) must be available before a meaningful framework can be developed?
  - Species involved in the transmission cycle in the area of interest: possums, ferrets, feral pigs, deer
  - Host status of each species involved
  - Intra- and interspecies TB transmission
  - Combined role of these hosts (possum-pig-ferret complex and possum-pig-deer complex) in maintaining TB and spillback to cattle?



Group discussions 3

- Which surveillance strategies can you suggest for the relevant wildlife species?

Group discussions 3

- Which surveillance strategies can you suggest for the relevant wildlife species?
  - Possums: culling (pest!) –confirmation not required anymore
  - Feral pigs: hunters to submit heads for culture of head lymph nodes
  - Ferrets: Cage traps and culling – culture
  - Deer: Hunters to submit heads and lungs – culture
  - Road kills

Case study – New Zealand

- Maintenance host: brush-tailed opossum
  - Population reduced by lethal control ~~risk of~~ transmission to domestic cattle minimised
- Other free-ranging hosts: deer, ferrets, feral pigs
  - What is the combined role of these hosts (possum-pig-ferret complex and possum-pig-deer complex) in maintaining TB and spillback to cattle?
  - Intra- and interspecies TB transmission
- Multi-host TB models for forest and grassland areas
  - Forest area: possum control outweighed the influence of deer or pigs in transmitting Tb to possums
  - Grassland area: ferret-pig-ferret transmission effective to maintain TB in absence of possums. This means Tb can only be successfully eliminated if the population of either pigs or ferrets is controlled in addition to possums