Brucellosis

Disease Monograph Series – 21

Bacteria | Brucella | Zoonotic | Cattle | Sheep | Goats | Pigs | Camels

IDRC | Bartay

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Acronyms

AU	African Union
AU-IBAR	African Union Inter-African Bureau for Animal Resources
BBAT	Buffered *Brucella* Antigen test
BBSRC	Biotechnology and Biological Sciences Research Council
BMGF	Bill and Melinda Gates Foundation
CFT	Complement fixation test
CI	Confidence Interval
CVO	Chief Veterinary Officer
DALY	Disability-adjusted life year
DG	Director General
DIVA	Differentiate infected from vaccinated animals
DVS	Director Veterinary Services
ELISA	Enzyme-linked immunosorbent assay
FAO	Food and Agriculture Organization of the United Nations
FPA	Fluorescence polarization assay
IAEA	International Atomic Energy Agency of the United Nations
IM	Intramuscular
IN	Intranasal

NGO	Non-governmental organization
OIE	World Animal Health Organization
PCR	Polymerase chain reaction
RBT	Rose Bengal test
SC	Subcutaneous
SHF	Small holder farmer
SMP-AH	Standard Methods and Procedures in Animal health Program
TPP	Target Product Profile
WHO	World Health Organization of the United Nations
ZELS	Zoonoses and Emerging Livestock Systems (Research initiative funded by DFID, BBSRC and others)

Executive Summary

Disease, etiology, epidemiology and impacts

Bacteria of the genus *Brucella*, are transmissible to a wide range of animal species. They cause Brucellosis, a widespread zoonosis consistently ranked among the most economically important zoonoses globally [1]. The most relevant species are *Brucella abortus*, *B. melitensis* and *B. suis*. The different *Brucella* species each have their host preference, but they are not host specific. Brucellosis is mainly transmitted to humans from cattle, sheep, goats, pigs and camels through direct contact with blood, placenta, foetuses or uterine secretions, or through consumption of contaminated raw animal products (especially unpasteurized milk and soft cheese). *B. melitensis* has the highest zoonotic potential, but *B. abortus* and *B. suis* are also zoonotic and of public health relevance.

In endemic areas, human brucellosis has serious public health consequences. Brucellosis affects approximately 500,000 people annually worldwide. The disease is severely under-reported in humans, and acute febrile illnesses are often mistaken for malaria. Brucellosis is an occupational disease, and people in contact with animals, including smallholder farmers and abattoir workers, are at high risk. The reported incidence of human brucellosis ranges from less than 0.01 to more than 200 cases per 100,000 population [2]. The WHO estimates the DALYs due to *Brucella* spp is 264,073 and 2 DALYs per 100,000 persons.

Incidence / Prevalence

Brucellosis is endemic in many countries; it is not always a notifiable disease, and this contributes to explaining why the disease is underreported at national and at international levels. In general terms, the number of outbreaks reported to the OIE and AU-IBAR, besides being discordant, seems to be below the number of outbreaks expected based on estimations of the observed herd prevalence and some of the publications available.

The prevalence of brucellosis varies amongst countries, but also within regions and within species. There are very limited data at national level. The majority of data is at regional level, and there is a publication bias; areas where certain Universities, NGOs or projects are active, seem to have more data - however, they might be working in that area because of the disease prevalence. Much of the literature does not differentiate between *B. abortus* and *B. melitensis*. However, it is clear that *B. melitensis* is also a problem in cattle.

Diagnostics

Brucellosis can be diagnosed by culture, serology or other tests. According to the OIE Terrestrial Manual, no single serological test is appropriate in all epidemiological situations; all have limitations especially when it

comes to screening individual animals. In situations where vaccination with smooth *Brucella* is practised, false-positive reactions may be expected among the vaccinated animals.

For the control of brucellosis at the national or local level, the Buffered Brucella Antigen Tests (BBAT), i.e. the Rose Bengal Test and the Buffered Plate Agglutination test, as well as the ELISA and the Fluorescence polarization assay are suitable screening tests. Positive reactions should be retested using a suitable confirmatory and/or complementary strategy. The prescribed tests for international trade are the BBAT, Complement Fixation Test and ELISA. Dr Saxena in India has patented 2 innovative modifications to improve the sensitivity and specificity of the RBT, and is seeking partners for commercialization.

Control

Control, and in many cases eradication, of brucellosis has been achieved in many high and middle income countries. In some of them, it only continues to be a challenge in wildlife and feral animals. However, in many low and middle income countries control is very difficult. Treatment is not a viable option as it requires the combined use of different antibiotics for long periods of time. Control programs are based on vaccination.

Usually when the prevalence is high, control is based on mass vaccination, and when the prevalence is low, a test/removal program is implemented. Control at herd level might be possible, but regional and national programs are hard to implement when resources are scarce and the veterinary services are limited.

Current vaccines for Brucellosis

The vaccines recommended by the OIE are S19 for *B. abortus* in cattle, and Rev1 for *B. melitensis* in small ruminants. However, the RB51 for *B. abortus* is also used, and it is the official vaccine in many countries. S19, Rev1 and RB51 have been used widely worldwide. They are all live vaccines, and have many disadvantages. They are pathogenic for humans, induce abortion in pregnant animals, transmit to other animals and interfere with traditional *Brucella* diagnostics (RB51, and other vaccines given via the ocular route or at low dose interfere to a less extent). The vaccines are good at preventing clinical signs, but do not prevent infection or seroconversion.

There is an obvious need for better vaccines that can overcome these issues. There is also a great need for a better understanding of cross protection. The cattle vaccines are all based on *B. abortus*, but *B. melitensis* is also a big problem in cattle. There is no consensus about the protection of the current *B. abortus* vaccines for *B. melitensis* in cattle, and the OIE does not recommend to use *B. melitensis* Rev1 vaccine in cattle. There is a need for a vaccine that confers good immunity in cattle for at least *B. abortus* and *B. melitensis.*

There are vaccines other than S19, Rev1 and RB51 that have been used in specific areas or regions; for example, the *B. abortus* strain 82, and strain 75/79-AB (a dissociated form of strain 82) that have been used widely in the Russian Federation, Azerbaijan and Tajikistan. In China, the *B. melitensis* M5 or M5-90 has been used in sheep and goats, as well as in cattle since the 1970's. Also in China, there is a commercial vaccine for *B. suis*, the strain 2 vaccine. The technical information publically available for these vaccines is limited, but they seem to have

been used successfully; it would be valuable to independently validate the claims that have been made in relation to these vaccines. A side by side comparison of the efficacy and cross-protection of the traditional S19, the low dose S19, but also 75/79 and M5 for B. *melitensis* in cattle, considering the inclusion of RB51 and Rev1, and any promising other candidates already tried in the target species, seems an obvious step.

Potential new vaccines and the way forward

As for new vaccines, there are several groups working on new candidates. Some are based on new technologies, while some are based on live bacterial mutants. Due to limited availability of validated challenge models in target animals, many of the vaccines have been only tried in mouse models which are not ideal. Results need to be interpreted carefully, as the practical value of a new vaccine is not a matter of short term protection, but long term protection, feasibility and cost. A good candidate for *B. melitensis* seems to be the strain 16MΔ*vjbR* which has been tried in different species. A very promising candidate for *B. suis* is the strain 353-1 vaccine which has already been tested in the target species (pigs) with good results. Information for both of these candidates and any other promising vaccines, should be reviewed for scientific quality and other important considerations.

As there is limited knowledge of the protective epitopes and antigens (some are known, but not all), it is unlikely that a vaccine based in a single epitope would be sufficient, a combination would more likely be needed. However, some vaccines based on combination of different Outer Membrane Proteins (OMP) seem promising. New delivery systems including nanotechnology, might be of particular use if the protective antigens were known.

Characteristics of an ideal *Brucella* vaccine, can be seen under the Target Product Profile in Section 9. There might be commercial companies working on the development and improvement of *Brucella* vaccines, but there is no information publically available. AgResults, is planning to set up a prize mechanism for the development of new vaccines early in 2016.

Commercial Brucellosis vaccines

Commercial *Brucella* vaccine production in the countries of interest is limited. For *B. abortus*, there are manufacturers in India and Indonesia of S19; there are *B. abortus* vaccines produced in other countries in the region like China or South Korea. In Africa, *B. abortus* vaccines are produced in Egypt, Nigeria and South Africa. They all produce the S19 strain, while the RB51 is available in South Africa. *B. melitensis* Rev1 vaccine is produced in India in Asia, and in Africa, it is manufactured in Egypt and South Africa. Many of the countries that use vaccine, use imported vaccines.

New diagnostics or vaccines that allow differentiation of vaccinated from infected animals at any period after vaccination, and could be used in adult animals would be valuable. They are not an urgent need, as many countries have achieved control with the currently available vaccines, which only allow differentiation of infected animals from vaccinated, when the animals are vaccinated at a young age. However, they require a solid surveillance program and good veterinary services.

Clinical disease overview

Etiology & Epidemiology

Brucellosis is caused by bacteria of the genus *Brucella*, a facultative Gram negative intracellular pathogen that affects most mammals. Six named species occur in animals*: B. abortus, B. melitensis, B. suis, B. ovis, B. canis* and *B. neotomae*. One or more unnamed species of Brucella have been found in marine mammals. Formal names proposed for marine mammal isolates are *B. maris* for all strains, or *B. pinnipediae* for strains from pinnipeds (seals, sea lions and walruses) and *B. cetaceae* for isolates from cetaceans (whales, porpoises and dolphins).

Some species of Brucella contain biovars. Species and biovars can be identified by phage lysis, and by cultural, biochemical and serological criteria. Molecular methods have been developed that could also be used for complementary identification based on specific genomic sequences. Different biovars can have differences in host, pathogenicity, cultural and serological characteristics.

The different *Brucella* species have their host preferences, but they are not host specific. There are many domestic and wildlife reservoirs. The presence of rough or smooth lipopolysaccharide is correlated to the virulence of the disease in humans.

This monograph focus on *B. abortus*, *B. melitensis* and *B. suis*; it does not include *B. ovis, B. canis* or *B. neomatae.*

- *Brucella abortus* affects mainly cattle, but other livestock and wild animals can be infected with varying susceptibility. Up to 9 biovars of *B. abortus* have been reported, but some differ only slightly.
- *Brucella melitensis* predominantly affects sheep and goats but can also cause disease in other mammalian species. There are 3 biovars of *B. melitensis* that show no difference in pathogenicity. Biovar 3 is the most commonly isolated. All breeds of goats are believed to be equally susceptible but resistance is assumed to vary in some breeds of sheep (Maltese sheep appear highly resistant, while certain fat-tailed breeds such as Awassi are highly susceptible).

- *Brucella suis* is the main cause of brucellosis in pigs. *B. suis* consists of 5 biovars. Pigs are infected by *B. suis* biovars 1, 2 or 3. The disease caused by biovars 1 and 3 is similar, while the one caused by biovar 2 differs in pathology, host range, and it is limited to Europe. *B. suis* biovar 2 is rarely pathogenic to humans, whereas biovars 1 and 3 are highly pathogenic and cause severe disease.

The natural host and zoonotic potential for each *Brucella* species can be seen in Table 1.

Table 1: Host preference for *Brucella* species in domestic animals. Source: Byndloss and Tsolis. *Brucella spp.* Virulence Factors and Immunity. *Annu Rev Anim Biosci*. 2016 Feb 15; 4:111-27

Species	Natural host	Zoonotic potential	Clinical signs	Transmission
Brucella melitensis	Small ruminants	High	Female: abortion, weak offspring, reduced milk yield Male: infertility, orchitis, epididymitis (rare)	Oral: ingestion of contaminated placenta, aborted fetus, contaminated milk
Brucella abortus	Cattle	Moderate	Female: abortion, weak offspring, reduced milk yield Male: infertility, orchitis, epididymitis (rare)	Oral: ingestion of contaminated placenta, aborted fetus, contaminated milk
Brucella suis	Pig	Moderate	Female: abortion, weak offspring Male: infertility, orchitis, epididymitis, osteoarticular disorders	Oral: ingestion of contaminated placenta, aborted fetus, contaminated milk Venereal: breeding using contaminated semen
Brucella canis	Dog	Mild	Female: abortion at 45–55 days Male: infertility, orchitis, epididymitis Both genders: bacteremia	Oral: ingestion of contaminated placenta, aborted fetus, contaminated milk Venereal: breeding using contaminated semen
Brucella ovis	Sheep	Absent	Female: abortion, weak offspring (rare) Male: infertility, orchitis, epididymitis	Oral: close contact between rams Venereal: use of infected rams during mating season

Transmission

It is a highly contagious disease and is spread through contact with aborted foetuses, vaginal or uterine discharges following abortion or birth of infected offspring, placenta and milk. The uterine discharges and abortions are highly infections. Shedding is not constant. The routes of transmission include ingestion of milk and contaminated materials, contact through mucous membranes, open wounds and conjunctiva.

The disease in pigs differs by its prolonged bacteremia, ability to be venereally transmitted (transmission occurs mainly via semen), and prolonged shedding of *B. suis* from mucosal surfaces or in urine, even in males or non-pregnant sows (which also appear capable of contributing to disease transmission).

Clinical Signs

Early bacteraemia is followed by localization of the infection particularly in the reproductive organs and cells of the monocyte-macrophage series.

Animals

The bacteria enters via invasion through mucous membranes and is localized in the reticuloendothelial system before septicemic spreads to other tissues. The most important clinical manifestation is reproductive failure. Following localization in the pregnant uterus, the bacteria cause placentitis which can lead to abortion, retained placenta or birth of weak, *Brucella*-infected offspring. In both males and females, *Brucella* spp. can induce inflammatory responses in reproductive tissues that may lead to infertility or sterility. It also produces reduced milk yields in females. Males may develop orchitis and epididymitis. Arthritis might develop in chronic infections.

In cattle, *B. abortus* causes abortions, stillbirths and weak calves; abortions usually occur during the second half of gestation (cows infected at service abort after an average interval of 225 days, while those infected at 7 months' gestation, abort about 50 days later). In fully susceptible herds, abortion rates vary from 30 – 70%. The placenta may be retained after abortion, and when it is retained, metritis is common. Lactation may be decreased. After the first abortion, subsequent pregnancies are generally normal; however, cows may shed the organism in milk and uterine discharges.

Epididymitis, seminal vesiculitis, uni- or bilateral orchitis and testicular abscesses are sometimes seen in bulls. Infertility occurs occasionally in both sexes, due to metritis or orchitis/epididymitis. Hygromas, particularly on the leg joints, are a common symptom in some tropical countries. Arthritis can develop after long-term infections. Systemic signs do not usually occur in uncomplicated infections, and deaths are rare except in the fetus or newborn. Infections in nonpregnant females are usually asymptomatic. Congenitally infected calves may remain sero-negative for at least 18 months, after which they may manifest the clinical signs. Similar symptoms occur in other ruminants including camels and water buffalo.

B. melitensis mainly causes abortions, stillbirths and the birth of weak offspring. The first sign of the presence of the disease in a susceptible herd or goats or flock of sheep is usually an abortion storm during which a high proportion of the pregnant animals abort, usually late in gestation. Animals that abort, particularly nanny goats, may retain the placenta. Sheep and goats usually abort only once, but reinvasion of the uterus and shedding of organisms can occur during subsequent pregnancies. Milk yield is significantly reduced in animals that abort, as well as in animals whose udder becomes infected after a normal birth. However, clinical signs of mastitis are uncommon. Acute orchitis and epididymitis can occur in males, and may result in infertility. Arthritis is seen occasionally in both sexes. Many non-pregnant sheep and goats remain asymptomatic. Kids or lambs born from infected females may be born weak or are asymptomatic; it is thought that some of them may become persistent latent carriers.

In pigs, the most common symptoms of *B. suis* are abortion, which can occur at any time during gestation, and weak or stillborn piglets. Vaginal discharge is often minimal and abortions may be mistaken for infertility. Occasionally, some sows develop metritis. Temporary or permanent orchitis can be seen in boars. Boars can also shed *B. suis* asymptomatically in the semen; sterility may be the only sign of infection. Swollen joints and tendon sheaths, accompanied by lameness and incoordination, can occur in both sexes. Less common signs include posterior paralysis, spondylitis and abscesses in various organs. Although some pigs recover, others remain permanently infected. Fertility can be permanently impaired, particularly in boars. Some animals remain asymptomatic. Some piglets infected *in utero* may die within a few hours of birth, the mortality rate often being very high, but others survive and retain the infection into adulthood.

Humans

Brucella sp. causes a flu-like febrile syndrome including intermittent and relapsing fever, body aches, joint pain, weakness, headache, weight loss and cough. The disease is generally chronic with different levels of severity.

Diagnosis

Brucellosis can be diagnosed by culture, serology or other tests. Unequivocal diagnosis of Brucella infections can be made only by the isolation and identification of Brucella, but in situations where bacteriological examination is not practicable, diagnosis must be based on serological methods. There is no single test by which a bacterium can be identified as Brucella. A combination of growth characteristics, serological, bacteriological and/or molecular methods is usually needed.

According to the OIE Terrestrial Manual, no single serological test is appropriate in all epidemiological situations; all have limitations especially when it comes to screening individual animals. Consideration should be given to all factors that impact on the relevance of the test method and test results to a specific diagnostic interpretation or application. In situations where vaccination with smooth *Brucella* is practised, false-positive reactions may be expected among the vaccinated animals because of antibodies cross-reacting with wild strain infection. The serum agglutination test (SAT) is generally regarded as being unsatisfactory for the purposes of international trade. The complement fixation test (CFT) is diagnostically more specific than the SAT, and also has a standardised system of unitage. The diagnostic performance characteristics of some enzymelinked immunosorbent assays (ELISAs) and the fluorescence polarisation assay (FPA) are comparable with or better than that of the CFT, and as they are technically simpler to perform and more robust, their use may be preferred.

OIE recognized tests

a) Identification of the agent:

- Bacteriology (staining, culture) and confirmation by PCR
- Nucleic acid detection: PCR

b) Serology and allergy skin reaction:

- Buffered *Brucella* Antigen test (BBAT): Rose Bengal (RBT) and Buffered plate Agglutination test (BPAT)
- Complement Fixation test (CFT)
- ELISA
- Fluorescence polarization assay (FPA)
- Brucellin skin test (not very common)

c) Milk tests: (used to test milk from the bulk tank)

- Milk I-ELISA
- Milk ring test

- Most commonly used in low & middle-income countries:

a) National laboratory: will depend if the laboratory has access to the reagents for BBAT. ELISA is also used.

b) For the control of brucellosis at the national or local level, the BBAT, i.e. the RBT and the BPAT, as well as the ELISA and the FPA are suitable screening tests. Positive reactions should be retested using a suitable confirmatory and/or complementary strategy. The prescribed tests for international trade are the BBAT, CFT and ELISA.

- Cross reactions with *Yersinia enterocolitica* O:9 should be considered as they are almost indistinguishable from true brucellosis serological reactions.

- Recent developments: Dr Saxena (College of Veterinary Science, Guru Angad Dev Veterinary & Animal Sciences University (GADVASU), Ludhiana, India), has introduced two innovative modifications to the RBT, to produce a more sensitive and specific test called “Superagglutination”. See Section 7 for more details.

- Main needs for diagnostics:

a) A sensitive test that could be used to differentiate infection from vaccination, even for animals vaccinated with the most commonly used vaccines, namely S19 or Rev1.

b) A diagnostic test that could be used at the point of care by Primary Animal Health Care (PAHC) providers.

c) Commercial kits: Cheaper kits, and kits that don’t require cold storage.

d) There are no commercially available PCR kits that claim to diagnose brucellosis.

Zoonotic disease

Worldwide, *Brucella melitensis* is the most prevalent species causing human brucellosis, owing in part to difficulties in immunizing free-ranging goats and sheep. *B. melitensis* causes Malta fever (also called Mediterranean or undulant fever) and it is one of the most important zoonoses. Brucellosis in humans is also caused by *B. abortus* and *B. suis*, resulting in a disease very similar to the one caused by *B. melitensis* (see Table 1).

In humans, consumption of raw milk and cheese made from raw milk is the major source of infection. *Brucella* is also transmitted by direct contact with infected animals, animal carcasses and aborted material.

There are no vaccines for humans worldwide (a vaccine has been used in China), and treatment by antibiotics is complex.

Immunity

Brucella triggers both antibody and cell-mediated responses. In primary infections, antibodies are not effective, and overcoming the infection depends largely on the cellular immune response. Antibodies, however, may play a role in the protection provided by vaccines and when transferred via colostrum and milk.

Brucella can invade and persist in macrophages that are in a non-activated state at the time of entry but do not seem to survive in pre-activated macrophages. The route of entry into these cells is therefore important. The infective strategy of brucellosis is believed to be one of stealth whereby it establishes itself into its favoured niche prior to the host raising an effective immune response. The host may respond by increasing the inflammatory action of macrophages but this may come too late and lead to a failure of clearance that results in the recurrent febrile episodes seen in humans.

Incidence and Prevalence in Selected Countries

Global

B. abortus is found worldwide in cattle-raising regions, except in Japan, Canada, some European countries, Australia, New Zealand, and Israel, where it has been eradicated. Eradication from domesticated herds is nearly complete in the USA. *B. abortus* persists in wildlife hosts in some regions, including the Greater Yellowstone Area.

B. melitensis is particularly common in the Mediterranean. It also occurs in the Middle East, Central Asia, around the Arabian Gulf, and in some countries of Latin America. This organism has been reported from Africa and India, but it does not seem to be endemic in northern Europe, North America (except Mexico), Southeast Asia, Australia, or New Zealand. There have been annual incidence reports of up to 78 cases per 100,000 people in the Mediterranean and Middle East. However, more than 550 cases have been reported from confined endemic areas in the Mediterranean and Middle East that have no mandatory animal control measures. In some countries where animals are controlled, such as Southern Europe, an annual incidence of 77 cases per 100,000 has been reported. Infection levels can be much higher, for example, a seroprevalence rate of 20% was identified on the Arabic Peninsula, with greater than 2% having active brucellosis.

Information available:

- OIE information: Data of outbreaks reported to the World Animal Health Organization (OIE) are not always reliable, as many countries doesn't seem to report, or to be reporting consistently over time. (**http://www.oie.int/wahis_2/public/wahid.php/Countryinformation/Countrytimelines**). McDermott in 2013 [1] showed that the number of predicted brucellosis cases per year compared the number of outbreaks reported to the OIE falls well below the number that can be expected based in the disease prevalence as shown in Table 2 below.

- AU-IBAR: The African Union Inter-African Bureau for Animal Resources also has a notification system. Data are published in the Pan African Animal Resources Year Books. Similarly to the OIE, many countries do not seem to consistently report the outbreaks.

- Peer reviewed publications and grey literature: Information for the different countries can usually be found in peer-reviewed publications or grey literature (for example Theses) on the internet. They usually contain data that concern a regional area, and not at national level.

- Systematic review: A very good source is a recent publication from McDermott [1], in which building on a previous ILRI report, they assessed 259 recent studies (period range not specified), to develop maps showing the prevalence estimates for brucellosis in the different species. The maps for brucellosis prevalence in cattle, small ruminants and humans can be seen below.

Table 2: The number of predicted brucellosis cases per year compared to the number of outbreaks reported to the World Animal Health Organisation in 2010. Source: McDermott, 2013 [1].

Region	Livestock prevalence %	Number of ruminants	Predicted cases per year	Outbreaks reported in 2010
East Africa	8.2	257,377,760	21,104,976	12
West Africa	15.5	197,716,517	30,646,060	37
South Africa	14.2	59,806,724	8,492,555	6,305
North Africa	13.8	57,629,367	7,952,853	1,073
South Asia	16.0	683,181,040	109,308,966	156
South-East Asia	2.9	21,247,586	616,180	164

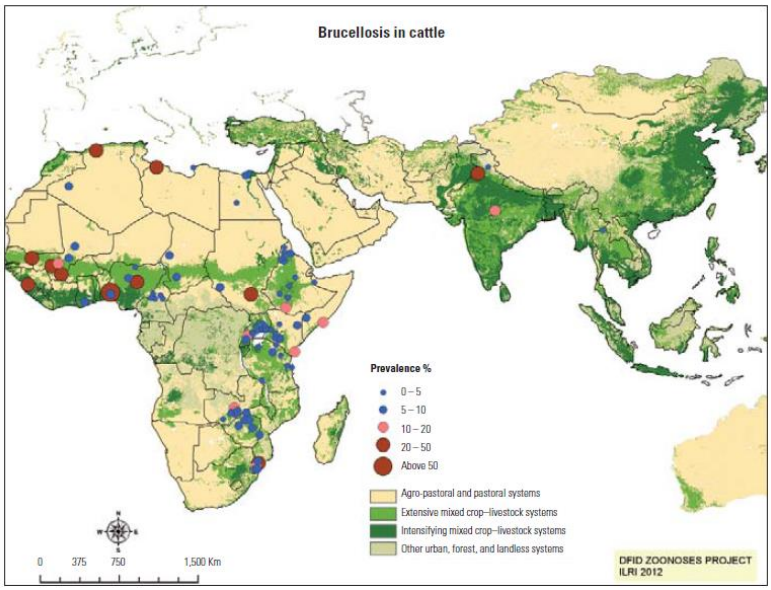


Figure 1: Results of a systematic review showing brucellosis prevalence estimates in cattle on a map of livestock production systems in Asia and Africa. Source: McDermott, 2013 [1].

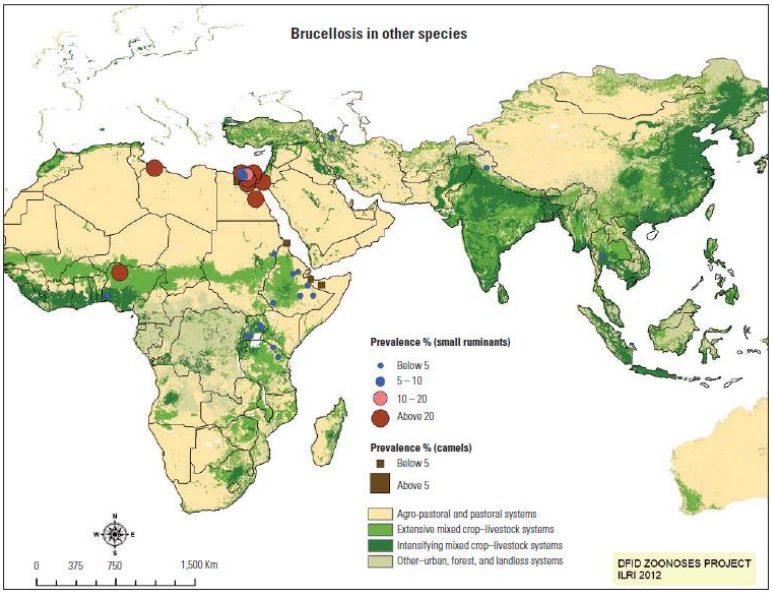


Figure 2: Results of a systematic review showing brucellosis prevalence estimates in small ruminants and camels on a map of livestock production systems in Asia and Africa. Source: McDermott, 2013 [1].

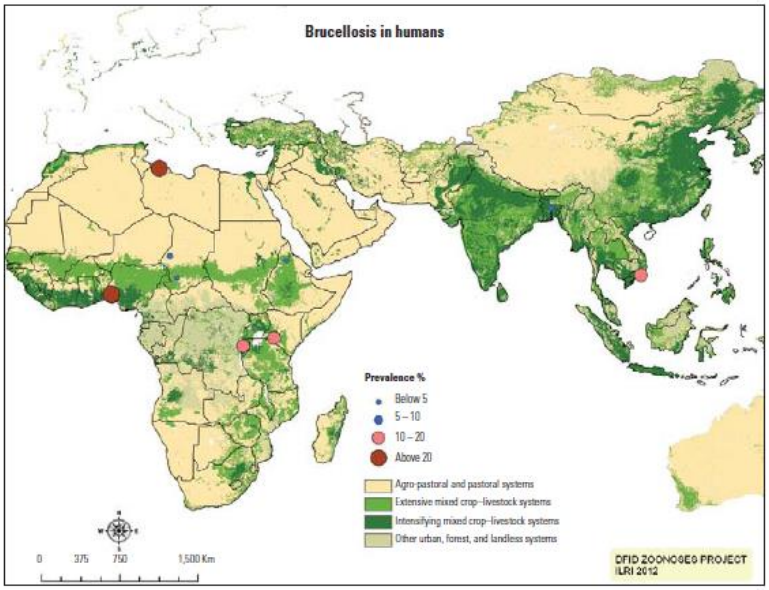


Figure 3: Results of a systematic review showing brucellosis prevalence estimates in humans on a map of livestock production systems in Asia and Africa. Source: McDermott, 2013 [1].

A more recent review in Africa, has been conducted by Boukary in 2014 [3]. The map in Figure 4 below shows the prevalence of bovine brucellosis in Africa based on the publications between 1995 and 2009 and the human outbreaks declared in 2007 in sub-Saharan Africa.

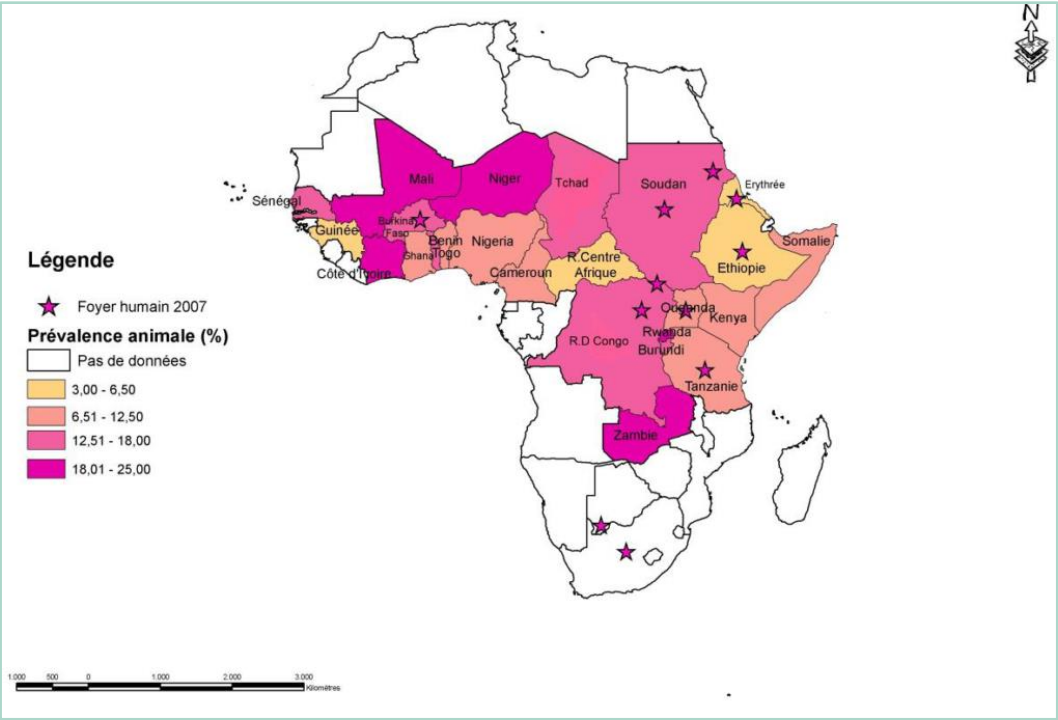


Figure 4: Prevalence of bovine brucellosis in Africa, based on publications between 1995 and 2009. Source: Boukary, 2014 [3].

Regional

Incidence data by country

There are two main sources, OIE and AU-IBAR. Data are not similar.

1- Source: OIE. **http://www.oie.int/wahis_2/public/wahid.php/Diseaseinformation/statusdetail**

Please note previous remark made on OIE information (page 7). Similar information but presented in a different manner can be seen in Annex 1.

Number of cases reported to the OIE by disease and by country:

- No information, + Present but quantitative data not known, ? Disease suspected

ASIA

Brucella abortus incidence (number new outbreaks reported)

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Bangladesh	-	-	-	+	+	+	+	+	+	-	-
India	-	6	+	3	4	10	2	5	7	7	-
Indonesia	-	+	+	+	+	+	+	+	32	-	-
Myanmar	-	3	14	1	10	3	1	0	7	3	-
Nepal	-	0	0	0	0	0	?	0	0	1	0
Vietnam	-	?	?	?	?	?	?	?	?	?	0

Brucella melitensis incidence (number new outbreaks reported)

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Bangladesh	-	-	0	0	0	+	+	+	0	-	--
India	-	-	-	-	-	-	-	-	-	-	-
Indonesia	-	-	-	0	-	-	-	-	-	-	-
Myanmar	-	-	-	0	0	1	-	1	0	1	-
Nepal	-	0	-	-	-	-	-	-	+	0	0
Vietnam	-	-	-	-	-	-	-	-	-	-	-

Brucella suis incidence (number new outbreaks reported)

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Bangladesh	-	-	0	0	0	0	0	0	-	-	-
India	-	-	-	-	-	-	-	-	-	-	-

Indonesia	-	-	-	0	-	-	-	-	-	-	-
Myanmar	-	-	-	0	0	0	0	0	0	0	-
Nepal	-	-	-	-	-	-	-	-	-	-	-
Vietnam	-	-	-	-	-	-	-	-	-	-	-

WEST AFRICA

Brucella abortus incidence (number new outbreaks reported)

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Burkina Faso	-	+	+	+	+	+	+	0	+	+	+
Ivory Coast	-	+	>1	+	+	+	+	+	+	-	-
Mali	-	+	+	-	+?	-	-	-	-	-	-
Senegal	-	-	-	-	-	-	-	?	?	?	?

Brucella melitensis incidence (number new outbreaks reported)

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Burkina Faso	-	-	-	-	-	-	-	-	-	-	-
Ivory Coast	-	-	-	-	-	-	-	-	-	-	-
Mali	-	0	-	-	+?	-	-	-	-	-	-
Senegal	-	-	-	-	-	-	-	-	-	-	-

Brucella suis incidence (number new outbreaks reported)

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Burkina Faso	-	-	-	-	-	-	-	-	-	-	-

Ivory Coast	-	-	-	-	0	0	0	0	0	-	-
Mali	-	0	-	-	-	-	-	-	-	-	-
Senegal	-	-	-	-	-	-	-	-	-	-	-

EAST AFRICA:

Brucella abortus incidence (number new outbreaks reported)

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Ethiopia	-	0	+	+	+	+	+	+	?	0	-
Kenya	-	9	24	4	21	11	7	8	10	12	6
Rwanda	-	+	-	-	-	-	-	-	12	-	-
Tanzania	-	+?	+?	+	+	+	1	+	1	+	+
Uganda	-	8	11	+	+	+	17	8	+	+	-

Brucella melitensis incidence (number new outbreaks reported)

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Ethiopia	-	0	0	0	0	2	+	0	?	0	-
Kenya	-	-	-	0	0	0	0	0	0	0	0
Rwanda	-	0	-	+	?	?	?	?	?	-	-
Tanzania	-	-	-	0	-	-	-	-	-	-	-
Uganda	-	2	5	2+	+	+	+	+	+	+	-

Brucella suis incidence (number new outbreaks reported)

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015

Ethiopia	-	-	-	-	0	0	0	0	0	0	-
Kenya	-	-	-	0	?	0	0	0	0	0	0
Rwanda	-	0	+	+	?	0	0	0	0	-	-
Tanzania	-	-	-	0	0	0	0	0	0	-	-
Uganda	-	-	?	?	0	0	0	0	0	0	-

SOUTHERN AFRICA:

Brucella abortus incidence (number new outbreaks reported)

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Madagascar	-	0	0	0	0	0	0	0	0	0	-
Malawi	-	-	-	-	-	-	-	-	-	-	-
Mozambique	-	12	13	9	22	12	8	11	15	9	-
South Africa	-	309	356	327	413	338	276	291	264	335	-
Zambia	-	-	3	13	22	14	+	13	13	19	-

Brucella melitensis incidence (number new outbreaks reported)

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Madagascar	-	0	0	0	0	0	0	0	0	0	-
Malawi	-	-	-	-	0	0	0	-	-	-	-
Mozambique	-	-	0	0	0	0	0	0	0	0	-
South Africa	-	0	1	0	0	1	0	0	0	0	-
Zambia	-	-	?	?	?	?	?	?	0	0	-

Brucella suis incidence (number new outbreaks reported)

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Madagascar	-	0	0	0	0	0	0	0	0	0	-
Malawi	-	0	0	0	0	0	0	0	-	-	-
Mozambique	-	-	-	-	+	0	0	0	0	0	-
South Africa	-	0	0	0	0	0	0	0	0	0	-
Zambia	-	-	-	-	0	0	0	0	0	0	-

The OIE, also includes zoonoses data. The number of human cases and deaths are reported by the countries. Data from the countries of interest, can be seen in the table below.

http://www.oie.int/wahis_2/public/wahid.php/Countryinformation/Zoonoses

Human cases and deaths due to Bovine TB as reported to the OIE

	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014
Bangladesh										
India										
Indonesia		C: +, D: +								
Myanmar				C: +, D: +						
Nepal						C: +, D: +	C: +, D: +	C: +, D: +	C: +, D: +	C: +, D: +
Vietnam				C: +, D: +	C: +, D: +					C: 35, D: 0
Burkina Faso	C: +, D: +	C: +, D: +								
Ethiopia	C: +, D: +	C: +, D: +	C: +, D: +	C: +, D: +	C: +, D: +	C: +, D: +		C: +, D: +		
Ivory Coast		C: +, D: +								
Kenya			C: 66, D: 5	C: 4,585, D: 0			C: +, D: +	C: +, D: +	C: 84,775, D: 0	C: 96,571 D: 0
Madagascar										
Malawi	C: +, D: +									
Mali				C: +, D: +						
Mozambique		C: +, D: +						C: +, D: +	C: +, D: +	
Rwanda		C: +, D: +					C: +, D: +	C: +, D: +	C: +, D: +	
Senegal										
South Africa		C: +, D: +	C: +, D: +	C: +, D: +	C: +, D: +	C: +, D: +	C: 26	C: +, D: +	C: +, D: +	C: 1
Tanzania	C: +, D: +		C: +, D: +	C: +, D: +					C: +, D: +	C: +, D:+
Uganda			C: +, D: +							
Zambia							C: +, D: +			
C: Cases										
D: Deaths										

2- Source: AU-IBAR.

Number of outbreaks per year as reported to AU-IBAR and published in the Pan African Animal Resources YearBook. (**http://www.au-ibar.org/pan-african-animal-resources-yearbook?showall=&limitstart**=)

Note that there is not distinction between the different types of Brucellosis. Interestingly, the number of outbreaks reported often does not match those reported to the OIE. NS= Not specified

Country	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Burkina Faso											
Ethiopia						2					
Ivory Coast	1	2									
Kenya		1		12	NS	NS		3	1	4	
Madagascar											
Malawi											
Mali											
Mozambique	8	15	12	28	21	17	19		22	21	
Rwanda											
Senegal								1	1		
South Africa	346	336	618	605	144	394	282	680	634	560	
Tanzania	1		4				1		1		
Uganda		6	6	2	19	6	29	10	16	15	
Zambia	1		4	7	11	4	4	7	11	12	

Prevalence data by country

- Sources: PubMed, *Brucella* 2014 International Research Conference proceedings, and internet engine searches (English and French when applicable).
- Efforts have been made to include the year of the study, and not the year of the publication. If they are known to be different, the year of publication is included in the reference.
- For grey literature, links have been included when possible.
- Note that not all papers have been read in full. In many cases, only the abstracts have been read. Critical evaluation of the papers for inclusion has not been conducted. If a review paper included some references, the source of the review is mentioned.

ASIA

Bangladesh

Ruminants: Most recent review for ruminants, is a PhD thesis from Rahman in 2015 [4]. It contains good detailed tables, summarising the literature review for several years (shown below). His own work in Dhaka and Mymensingh districts concludes that true exposure prevalence of brucellosis in cattle under small-scale dairy and subsistence management systems is very low (0.3%). The prevalence was high (20%) in the Central Cattle Breeding and Dairy farm. The true exposure of brucellosis in goats and sheep were also low (1%).

Pigs: The first published report was in 2012 [5]. 105 sera form 2 districts (Sirajganj and Bogra) were analysed, and 7 (6.7%) and 5 (4.8%) were found to be positive by RBT and SAT respectively.

Humans: True prevalence from Mymensingh district in high risk occupationally exposed people have been found at 4.4% and in pyretic patients at 2.7% [4]. Only *B. abortus* was identified.

Reported seroprevalence of brucellosis in cattle in Bangladesh. Source: Rahman, 2015 [4].

Year	Area (Serology)	Sample size (positive)	Tests used	Prevalence (95% CI)	References
2013	Mymensingh, Tangail, Sherpur, Sirajgonj	150 (23); 270 (23); 190 (2): 610 (71)	RBT; Rapid *Brucella* ab test kit, iELISA	11.6% (9.2-14.5)	Islam *et al.,* 2013c; Belal and Ansari, 2013; Dey *et al*., 2013
2012	Bagerhat, Bogra, Gaibandha, Mymensingh, Sirajgonj	465 (4)	iELISA, RBT, cELISA and FPA (performed in South Korea)	0.9% (0.4-2.2)	Rahman *et al*., 2012b
2011	Bagherhatt, Bogra, Gaibandha, Mymensingh and Sirajgong	188 (4)	RBT, iELISA	2.1% (0.6-5.4)	Rahman *et al*., 2011b
2010	Dinajpur, Mymensingh	182 (6)	RBT, iELISA, cELISA	3.3% (1.2-7.0)	Ahasan and Song, 2010
09	Mymensingh	200 (9); 200 (10): 400 (19)	RBT	4.8% (2.9-7.3)	Nahar and Ahmed, 2009; Rahman *et al*., 2009
2006	Mymensingh, Sherpur	300 (7)	TAT	2.3% (0.9-4.7)	Sikder *et al*., 2012
2005	Mymensingh	120 (4)	RBT, PAT, TAT	3.3% (0.9-8.3)	Amin *et al*., 2005
2004	Mymensingh	250 (5)	RBT, PAT, TAT	2.0% (0.7-4.6)	Amin *et al*., 2004
1992	Chittagonj, Comilla, Jessore, Manikgonj	350 (17)	RBT, PAT, TAT	4.9% (2.9-7.7)	Ahmed *et al*., 1992
	Sub-total	2865 (137)		4.8% (4.1-5.7)	
1970	Mymensingh	412 (76)	TAT	18.4% (14.8-22.5)	Rahman and Mia, 1970
	Overall	3127 (167)		5.3% (4.8-6.2)	

Legend: RBT: Rose Bengal Test; iELISA: indirect ELISA; cELISA: Competitive ELISA; FPA: Fluorescence Polarization Assay; PAT: Plate Agglutination Test; TAT: Tube Agglutination Test.

Reported seroprevalence of brucellosis in cattle in Bangladesh - milk ring test. Source: Rahman, 2015 [4]

Year	Area (Milk based)	Tested (Positive)	Tests used	Prevalence (95% CI)	References
2012	Chittagong	500 (25)	MRT (Individual milk)	5.0% (3.3-7.3)	Sikder *et al*., 2012
1983	Dhaka, Tangail, Mymensingh	1992 (80)	MRT (Individual milk)	4.2% (3.2-4.9)	Rahman *et al*., 1983
1981	Sirajgonj, Mymensingh, Dhaka	234 (23), 527 (40): 761 (63)	MRT (Indivudal and Bulk/herd milk)	8.3% (6.4-10.75)	Pharo *et al*., 1981; Rahman and Rahman, 1981
1978	Dhaka, Mymensingh, Tangail	490 (42)	MRT (Bulk milk)	8.6% (6.2-11.4)	Rahman *et al*., 1978
	Overall	3743 (210)		5.6% (4.8-6.3)	

Legend: MRT: Milk Ring Test.

Reported seroprevalence of brucellosis in goats and sheep in Bangladesh. Source: Rahman, 2015 [4].

Year	Area (goats)	Sample size	Tests used	Prevalence (95% CI)	References
2014	Mymensingh, Netrakona	113 (7)	RBT	6.2% (2.5-12.3)	Akhter *et al.*, 2014
2012	Bagerhat, Bogra, Gaibandha, Mymensingh, Sirajgonj, Nilphamari	154 (4), 230 (5): 384 (9)	RBT, iELISA, cELISA, FPA	2.3% (1.1-4.4)	Rahman *et al.*, 2012c,b
2011	Bagherhatt, Bogra, Gaibandha, Mymensingh and Sirajgong	127 (4); 120 (3): 247 (7)	RBT, iELISA	2.8% (1.1-5.8)	Rahman *et al.*, 2011b,a
2010	Dhaka, Mymensingh, Rajshahi	208 (8)	RBT, SAT	3.8% (1.7-7.4)	Islam *et al.*, 2010
2007	Dhaka, Mymensingh	300 (6)	RBT, PAT, TAT, MET	2.0% (0.7-4.3)	Uddin *et al.*, 2007b
1988	Mymensingh, Tangail, Manikgonj	350 (51)	PAT, TAT	14.5% (11.0-18.7)	Rahman *et al.*, 1988
	Overall	1252 (37)		2.9% (2.1-4.1)	
Year	Area (sheep)	Sample size (positive)	Tests used	Prevalence (95% CI)	References
2014	Mymensingh, Netrakona	102 (6); 101 (6): 203 (12)	RBT, iELISA	5.9% (3.1-10.1)	Ahsan *et al.*, 2014; Akhter *et al.*, 2014
2012	Bagerhat, Bogra, Gaibandha, Mymensingh, Sirajgonj	206 (14); 170 (12); 80 (1): 456 (27)	RBT, iELISA, cELISA, FPA	5.9% (3.9-8.9)	Rahman *et al.*, 2011a, 2012b,d
2011	Bagherhatt, Bogra, Gaibandha, Mymensingh and Sirajgong	130 (4)	RBT, iELISA	3.1% (0.8-7.7)	Rahman *et al.*, 2011b
2007	Dhaka, Mymensingh	60 (2)	RBT, TAT, PAT	3.3% (0.4-11.2)	Uddin *et al.*, 2007a
	Overall	839 (45)		5.4% (3.9-7.1)	

Legend: RBT: Rose Bengal test; SAT: Slow Agglutination Test; MET: 2-Mercaptoethanol Test; cELISA: Competitive ELISA; iELISA: Indirect ELISA; FPA: Fluorescence Polarization Assay; PAT: Plate Agglutination Test; TAT: Tube Agglutination Test.

India

Ruminants: There exists a wide variation in different reports on prevalence of brucellosis in animals. The table below shows a summary of the data.

References: The ones marked * were referenced by Dr Singh Sharma at a presentation during the FAO Regional Workshop on brucellosis diagnosis and control in Asia-Pacific region, 2014 (**http://www.rr-asia.oie.int/fileadmin/Regional_Representation/Programme/Emerg/2014_Brucellosis_Chiang_Mai/05.India.pdf**) but haven't been able to find the original reference.

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2014	Kolkata	Cattle	988	RBT: 4.85 ELISA: 5.46	Chakraborty et al [6]
2013	Punjab and Hariyana	Cattle and buffalo (dairy animals)		26.5	Chand and Chhabra [7]
2011	Maharashtra			40.4	Lodhe*
2010	Organized dairy farms	Dairy animals (Cattle and buffalo)		13.7	Trangadia, Rana et al [8]
2009		Yak		21.11	Bandyopadhayay, Sasmal et al [9]
2007	Rajasthan and Bihar			Cattle: 8.58 Goat: 8.85 Sheep: 7.08	Singh *
2006	Tamil Nadu			B. *melitensis*: RBT: 13.85 SAT: 9.96 ELISA: 20.35	Maher Sulima et al*
2005	Punjab	Different species of animals	973	11.23	Dhand, Gumber et al [10]

2004	Nagaland	Mithun (Indian Bison)	98	ELISA: 34 STAT: 20 RBT: 11	Rajkhowa, Rahman et al [11]
2002	Long term serological study	Cattle Buffalo		5 3	Renukaradhya, Isloor, Rajasekhar [12]
1998	Surveillance in 23 states of India	Cattle and buffalo	30,437	Cattle: 1.9 Buffalo: 1.8	Isloor, Renukaradkya et al [13]
1985	Bikaner district	Milk goats		11.45	Kappor et al*
1984	Nagpur	Bovine	953	9.7	Nawathe and Bhagwat [14]
1979	UP and Delhi	Goat Sheep Pig Cattle Buffalo Equines	1607 438 244 361 551 318	5.53 3.42 15.98 6.37 4.9 12.89	Sharma, Sethi et al [15]

Pigs: Very limited data, but already identified in 1979 (see table above)

Nagaland: 3 animals tested positive out of 53 (5.6%) by using the *Brucella* IfG flow assay [16]

Humans: The table below shows a summary of the data.

References: The ones marked * were referenced by Dr Singh Sharma at a presentation during the FAO Regional Workshop on Brucellosis diagnosis and control in Asia-Pacific region, 2014 (**http://www.rr-asia.oie.int/fileadmin/Regional_Representation/Programme/Emerg/2014_Brucellosis_Chiang_Mai/05.India.pdf**) but haven't been able to find the original referenceBikaner district: 2.97%

Year	Place of study	Remarks	No. of samples tested	No. of positive cases	% positive	References
2011	South India			68		Sathyanarayanan, Razak et al [17]
2011	Pujab	Blood of occupationally exposed group tested by PCR	116	8	7	Gemechu, Gill et all [18]
2007	Chandigarh	Blood donors	292	1	0.3	Vaishnavi et al*
2006	Bijapur, Karnatka	1988-2004, Brucellosis in adults	26948	517	1.9	Mantur [19]
2004	Bijapur, Karnatka	Brucellosis in child	5726	93	1.6	Mantur [20]
2003	Bikaner			98		Kochar, Sharma et al [21]
2002		Chronic brucellosis		28	6.8	Sen et al*
2000	Kashmir	Patients with fever of unknown origin over a period of 5 years	3532	28	0.8	Kadri, Rukshana et al [22]
1998	India	Patients with fever of unknown origin	121	12	9.9	Handa, Singh et al [23]
1998	India	Occupationally exposed individuals	50	7	14	Handa, Singh et al [23]
1979	UP and Delhi		1685		0.89	Sharma, Sethi et al. [15]

Data in Punjab state:

Dr Singh Sharma at a presentation during the FAO Regional Workshop on Brucellosis diagnosis and control in Asia-Pacific region, 2014 (as per links mentioned above)

Year	Total Samples	Positive Samples	% Positive
Upto 2002	2430	383	15.8%
2003	139	40	28.7%
2004	905	95	10.5%
2005	430	44	10.2%
2006	297	44	14.8%
2007	175	47	26.8%
2008	241	64	26.6%

Indonesia

Ruminants: Serological investigation of *Brucella* infection in beef cattle tended under extensive farming conditions in Bali, revealed a high seroprevalence (19.3%; 95% CI, 17-22) in the compliment fixation tests [24].

Data from samples tested for Bovine Brucellosis at the Disease Investigation Centre (DIC) Maros. Modified from the presentation by Dr Siswani at the FAO Regional workshop on Brucellosis diagnosis and control in Asia-Pacific region, 2014

http://www.rr-asia.oie.int/fileadmin/Regional_Representation/Programme/Emerg/2014_Brucellosis_Chiang_Mai/04.Indonesia.pdf

Year	Samples	Positive	%
2011	3524	1097	31.13
2012	5794	942	16.26
2013	5099	697	13.67

Pigs: Data from 1988 showed *Brucella* suis biotype 1 was isolated from 13.1% of the pigs slaughtered in Kapuk Jakarta, West Java and from 15.09% of the pigs slaughtered in Surabaya, East Java [25]. The prevalence of *B. suis* by means of the Rose Bengal Plate Test, was 22.3% for West Java and 14.9% for East Java. The Rose Bengal Plate Test detected more *B. suis* infected animals (73% of the infected animals) than did the Complement Fixation Test (41%) and the Serum Agglutination Test (54.5%).

Myanmar (Burma)

Very limited information is available from Myanmar (or Burma).

1977: A WHO report posted online (**http://apps.who.int/iris/bitstream/10665/156172/1/sea-hlm-137.pdf**) by consultant Dr Jan Kolar, showed the following results:

Locality of blood samples collection	Animal species	Number of specimens tested	Results						Reactors	
			SAT Titre in I.U.					RBT	No.	%
			20	40	80	160	320			
Taikkyi District 2 villages (Inywetgei and Targwa)	Cattle	65	-	-	-	-	1	1	1	1.5
	Pigs	20	-	-	-	-	-	-	-	-
Dairy farm in Rangoon	Cattle	32	-	2	2	1	-	5	5	15.6
Slaughterhouse I	Cattle	134	4	2	1	-	-	3	3	2.2
	Sheep	121	3	1	-	-	-	3	4	3.3
	Goats	179	1	3	1	1	-	5	6	3.3
Slaughterhouse II	Pigs	65	-	-	-	-	-	-	-	-

Place of milk samples collection	Kind of sample	No. of samples	No. of		Positive in MRT	
			Tested localities	Tested farms	No.	%
Rangoon milk market	bulk can* milk	145	8	47	6	4.1
Small dairy farms on the outskirts of Rangoon	bulk can milk	6	2	6	3	50.0

*One can sample is a bulk milk sample from about 7-10 cows (one can is 25-30 litres). Thus the 151 samples represent nearly 1 000 cows tested for brucellosis.

The only other source that was found, is an MSc Thesis from 2007, which focus in dairy cattle in Yangon. Prevalence on farm level was estimated at 3.83%, and on animal level at 0.47% [26].

Source: Prevalence survey of bovine brucellosis (*Brucella abortus*) in dairy cattle in Yangon, Myanmar. Thesis by Than Naing Tun, Master of Veterinary Public Health, 2007 – Ref 26.

Group	Sampling materials	No. of samples examined	No. of positive samples	Sample Prev* (%)	95 % CI**	
					Lower limit	Upper limit
1	Bulk milk tank from MCP***	**Total tanks 113**	**11**	**9.73**	**5.20**	**17.12**
2	Bulk milk from individual farm	53	14	26.42	15.68	40.58
	Overall prev* on farms level	**Total farms 366**	**14**	**3.83**	**2.19**	**6.48**
3	Blood sample from individual animals	623	25	4.01	2.67	5.95
	Overall prev* on animal level	**Total population 5280**	**25**	**0.47**	**0.31**	**0.71**

*Prevalence, **Confidence Interval, ***Milk Collecting Point

Nepal

Animals: The table below shows a summary of the information for the different species in Nepal.

Sources:

*: As mentioned on the presentation by Dr Pragya Koirala at the FAO Regional workshop on brucellosis diagnosis and control in Asia-Pacific region, 2014

http://www.rr-asia.oie.int/fileadmin/Regional_Representation/Programme/Emerg/2014_Brucellosis_Chiang_Mai/10.Nepal.pdf

: **http://www.amazon.com/Seroprevalence-Brucellosis-Different-Species-Animals/dp/3844399577

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2014	Ramecchap	Goat	502	ELISA: 5.8 RBT: 6.3	Bindari and Shrestha [27]
2013	Kailali district	Cattle, buffalo, goat	Cattle: 50 Buffalos: 67 Goats: 113	Cattle: 32 Buffalos: 13.4 Goats: 2.6	Pandeya et al [28]
2008	Different parts of Nepal	Buffalos, goats, pigs	Buffalos: 153 Goat: 70 Pig:153	Buffalos: 0 Goat: 17.14 Pig: 7.18	Birochan Shrestha**
2000		Cattle and buffalo		1.25	Joshi [29]
2000	Milk collection area of DDC	Goats	558	4.5	Joshi*
1997		Water buffalo, cattle and sheep		Water buffalos: 22.64 Cattle: 17.4 Sheep: 1.54	Pyakural*
1996	Chitwan	Dairy cattle	91	3.3	Pradhan*
1993		Cattle, buffalo, goats		Cattle: 1.28 Buffalos: 1.93 Goats: 3.7	Jha et al*
1983	Kathmandu valley	Cattle, buffalo, sheep and goats	Cattle & buffalo: 1069 Sheep and goats: 247	Cattle & buffalo: 8.7% Sheep and goats: 3.64	Joshi*
1977		Buffalos and cattle		Buffalos: 22.64 Cattle: 17.47	Pyakural and Mishra*

Humans: Dr Joshi reported in 1983 a human prevalence in the Kathmandu valley of 6.08% (87/1430). In 2000, he found a prevalence of 4.5% [29]. In another study by Aryal in 2007, the prevalence was recorded 11.93% [30].

Vietnam

Ruminants and pigs: According to the data presented by Dr Nguyen Khanh Ly at the FAO Regional workshop on brucellosis diagnosis and control in Asia-Pacific region, there was no evidence of the disease. They tested dairy cattle: 285 animals in 2011, 88 in 2012 and 70 in 2013.

http://www.rr-asia.oie.int/fileadmin/Regional_Representation/Programme/Emerg/2014_Brucellosis_Chiang_Mai/15.Vietnam.pdf.

The disease has never been reported to OIE. However there was evidence of the disease in 1962 (**http://www.cabdirect.org/abstracts/19632702734.html;jsessionid=3F86F2AFEAF4956A1221DC4DECAA4CB5**) .

Humans: In 2006, in Binh Thuan province, the seroprevalence in the Rose Bengal test among 406 patients presented with acute undifferentiated fever was 14.8%. Seven of the 64 Rose Bengal test positive samples reacted weakly positive in the *Brucella* IgM/IgG flow assay. No seroconversion was observed [31].

AFRICA

Burkina Faso

Animals:

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2013	Transhumant cattle	Cattle	464	7.3	Dean et al [32]
2009		Cattle	273	16.42	Boussini et al*
2004-2005	Ouagadougou	Cattle	1689	3.61	Boussini et al [33]
2001-2002	Hamdallaye	Cattle	290	13.2	Traore et al, 2004 [34]
2000	Peri-urban	Cattle	1107	8	Coulibaly et al [35]

*Source: Akuku, I. Brucellosis in Africa. Paper given at the Workshop "An integrated approach to controlling brucellosis in Africa". Ethiopia, 2013 [36].

Humans: Data from 1976 established a 10% prevalence in an agro-pastoral area of Burkina Faso [37].

Côte d'Ivoire (Ivory Coast)

Animals: Recent data are shown in the table below.

In a recent presentation by Dr. Kanoute, the data is not clear, but it concludes that Brucellosis seems to be an important zoonosis in small ruminants in Korhogo, and it is more likely to be *B. melitensis*.
http://www.csrs.ch/Africa2013/PDF/090_Kanoute_Youssouf.pdf

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2012	Savannah-forest region	Cattle	907	10.3	Sanogo et al [38]
2008	Pastoralist	Cattle	660	8.8	Sanogo et al*
2004	Abidjan	Cattle	Private dairy farms: 244 Traditional: 137	Private dairy: 3.6 Traditional: 4.3	Thys et al [39]

*Source: As referenced by Boukary, 2014 [3].

*Source: As referenced by Akuku, I. Brucellosis in Africa. Paper given at the Workshop "An integrated approach to controlling brucellosis in Africa". Ethiopia, 2013 [36].

- Humans: Data from the north region of Korhogo and the west region of Odienne from studies by Gidel found a prevalence of 7-8% - no year given [36].

Ethiopia

Dairy cattle: There is a very good and recent Meta-analysis review of the prevalence of brucellosis in dairy cattle by Asmare [40]. The summary of the prevalence is shown in the table below.

Author (year)	Sample size	Apparent seroprevalence	Sampling group (management system)	Diagnostic test
Bekele et al. (2000)	4,243	4.9	Semi-intensive and extensive	RBPT, CFT
Eshetu et al. (2005)	552	10	Semi-intensive and intensive	RBPT, CFT
Asmare et al. (2007)	811	2.5	Semi-intensive and intensive	RBPT, CFT
Berehe et al. (2007)	816	3.2	Extensive	RBPT, CFT
Hailemelekot et al. (2007a)	864	3.8	Semi-intensive and intensive	RBPT, CFT
Hailemelekot et al. (2007b)	326	3.7	Semi intensive and intensive	RBPT, CFT
Tolosa et al. (2008)	1,305	0.8	Extensive	RBPT, CFT
Kebede et al. (2008)	497	9.7	Extensive	RBPT, CFT
Kebede et al. (2008)	619	12.4	Semi-intensive	RBPT, CFT
Jergefa et al. (2009)	336	4.5	Semi-intensive	RBPT, CFT
Jergefa et al. (2009)	902	2.2	Extensive	RBPT, CFT
Dinka and Challa (2009)	1,106	11.2	Extensive	RBPT
Abebe et al. (2009)	177	3.9	Semi-intensive and intensive	RBPT
Haileselassie et al. (2010)	1,120	7.7	Semi-intensive	RBPT, CFT
Haileselassie et al. (2010)	848	1.2	Extensive	RBPT, CFT
Asmare et al. (2010)	1,627	1.7	Extensive	RBPT, CFT
Megersa et al. (2011a)	283	10.6	Extensive	RBPT, CFT
Amenu et al. (2010)	408	2.6	Semi-intensive and extensive	RBPT
Ibrahim et al. (2010)	610	1.9	Semi-intensive	RBPT, CFT
Tolosa et al. (2010a)	950	1.1	Extensive	RBPT, CFT
Tolosa et al. (2010b)	780	0.5	Extensive	RBPT, CFT
Degefa et al. (2011)	370	0.5	Extensive	RBPT, CFT
Degefu et al. (2011)	435	1.4	Extensive	RBPT, CFT
Megersa et al. (2011b)	900	1.6	Extensive	RBPT, CFT
Teklehaimanot and Gangwar (2011)	72	23.6	Extensive	RBPT, CFT
Teklehaimanot and Gangwar (2011)	232	11.2	Semi-intensive	RBPT, CFT
Tesfaye et al. (2011)	1,202	1.5	Intensive	RBPT, CFT
Haileselassie et al. (2011)	1,354	6.1	Extensive	RBPT, CFT
Ibrahim et al. (2010)	985	3.9	Extensive	RBPT, CFT
Yohannes et al. (2012)	55	3.6	Semi-intensive	RBPT, CFT
Yohannes et al. (2012)	351	1.7	Extensive	RBPT, CFT
Megersa et al. (2012)	575	8	Extensive	RBPT, CFT
Asmare et al. (2013)	2,334	1.9	Semi-intensive and intensive	RBPT, CFT
Tschopp et al. (2013)	417	1.7	Extensive and semi-intensive	RBPT, ELISA
Gumi et al. (2013)	862	1.4	Extensive	RBPT, ELISA

Additional information and other reports are summarised below:

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2012	Southern and central	Goats	3315	Sedentary: 0.6 Agro-pastoral: 1.9 Pastoral: 7.6	Asmare et al*

2011	Hammer and Dasenech (South Omo)	Goats	384	4.2	Ashagrie et al*
2011	Somali	Cattle		Shinle: 42.9 Jijiga: 50	Megersa et al*
2011	Dawro (Southern)	Cattle	Dawro: 104 Gedeio: 161 Hadiya: 245 Sidama: 390	Dawro: 0 Gedeio: 10 Hadiya: 35.3 Sidama: 19.2	Megersa et al*
2010-2011	Dire-Dawa (Eastern)	Camel	646	2	Warsame et al*
2010-2011	Guto-Gida (Oromia)	Cattle	406	3	Yohannes et al* 2012
2010	Sidama (Southern)	Indigenous zebu	1627	Individual: 1.6 Herd level: 13.7	Asmare et al*
2010	Peri-urban Awassa	Cattle		3.9	Abebe*
2010	Arsi-Negele (Oromia)	Cattle	400	Individual: 2.6 Herd level: 12	Amenu et al*
2010		Cattle		Individual: 3.1 Herd: 15	Ibrahim et al***
2009-2010	Merti-Arsi (Oromia)	Indigenous Arsi cattle	370	0.5	Degefa et al*, 2011
2009	Jijiga	Sheep and goats	Sheep: 430 Goats: 300	RBT: 1.64 CFT: 1.51	Mohammed***
2009	Oromia	Cattle	1106	Pastoral: 15.2 Agro-pastoral: 4.1	Dinka & Chala*
2009	Central Oromiya	Cattle		Individual: 2.9	Jergefa et al***

				Herd level: 13.6	
2008-2009	Jijiga (Somali)	Sheep and goats	Sheep: 421 Goats: 309	1.64	Bekelet et al* 2011
2008-2009	Bahir-Dar (North West)	Sheep and goats	Sheep: 270 Goats: 230	1.2	Ferede et al* 2011
2008-2009	South Wollo (Amhara)	Sheep	800	1.5	Yesuf et al* 2011
2008	Eastern Amhara	Sheep	2409	4.89	Shimeles***
2007-2008	Borana pastoral system	Cattle, camels and goats	Cattle: 575 Camels: 1073 Goats: 1248	Cattle: 8 Camels: 1.8 Goats: 1.6	Megersa et al* 2012
2007-2008	Amhara	Cattle	780	RBT: 1.28 CFT: 0.5	Tedele et al*
2007	Tigray	Indigenous cattle	816	Individual: 3.3 Herd level: 42.3	Berhe et al***
2007	Pastoral	Sheep and goats	Sheep: 563 Goats: 1005	Sheep: 3.2 Goats: 5.8	Ashenafi et al**
2007	Southern	Sheep and goats	Sheep: 2905 Goats: 1059	Sheep: 1.6 Goats: 3.2	Mengistu***
2007	North western Amhara	Cattle		4.63	Mussie et al***
2007	Sidama (Southern)	Cattle		2.46	Kassahun et al ***
2006	Pastoral	Sheep and goats	2000	RBT: 1.9 i-ELISA: 9.7	Teshale et al
2006	Southeast Somali	Camels	822	Individual: 2.43 Herd level: 10.3	Birhanu***

2005	Afar region	Sheep and goats		Sheep: 15 Goats: 16	Yibeltal et al***
2005	Borena lowlan	Camels	3218	1.8	Megersa et al***
2003	Afar, Somali and Borena	Camels	1442	RBT: 5.6 CFT: 4.2	Teshome et al**
2002	Borena (Oromia)	Cattle		50	Alem and Solomon***

*Source: Akuku, I. Brucellosis in Africa. Paper given at the Workshop "An integrated approach to controlling brucellosis in Africa". Ethiopia, 2013, Ref 36.

**Source: As referenced by Boukary, 2014 [3].

***Source: As referenced by Yohannes, 2013 [41].

Humans:

Year	Area	Remarks	No. of samples tested	% positive	Reference
2009	Northern Ethiopia	Patients with acute fever	653	Finotesalam: 6.3 Quarit: 3 Bembecha and Jiga: 0	Abebe et al*
2009		Traditional pastoral communities. Patients with febrile illness		Borena: 34.1 Hammer: 29.4 Metema: 3	Ragassa et al*
2007	Amhara	High risk groups	238	5.3	Mussie et al
2007	Sidama	High risk groups	38	3.78	Kasahun et al*
2007		Fever of unknown origin	56	3.6	Tolosa et al*
2006	Addis Ababa	High risk groups	336	4.8	Kassahun et al*

*Source: As referenced by Yohannes, 2013 [41].

Kenya

Animals:

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2014	Kajiado and Kiambu	Cattle, sheep and goats	Kajiado: 274 households Kiambu: 433 households (max 15 samples per HH)	Kajiado: 3.4 Kiambu: 1.2	Ogola et al [42]
2014	Baringo	Cattle, sheep and goats	Cattle: 149 Goats: 92 Sheep: 73	Cattle: 10.07 Goats: 13.04 Sheep: 8.23	Kosgei*
2012	Kiambu (Kajiado and Kiambo)	Various	Cattle: 1303 Goats: 310 Sheep: 455	Herd level: 6	Kenya Zoonotic Disease Unit**
2009	Eldoret	Dairy cattle	130 milk samples	0	Namanda et al***
2009	Country answer to OIE questionnaire	Cattle, small ruminant, pigs		Cattle: 0.9 Small ruminants: 1 Pigs: 0.9	Akakpo et al [43]
2007	Dagoretti	Cattle	393	1	Kang'ethe et al****
2005	Urban + Pastoral	Cattle	456	0-10	Arimi et al****
1999-2000	Nairobi and Nakuru	Dairy cattle	434 raw milk HH level 110 Informal market milk	Raw milk: 5 Informal market milk: 2.4-3.4	Kang'ethe et al [44]

*Source: Kosgein et al. 2014. Estimating prevalence in livestock and assessment of knowledge, attitudes and practices of respective communities in Baringo County, Kenya. Research application summary.

http://www.ruforum.org/sites/default/files/Kosgei.pdf

Source: **http://zdukenya.org/wp-content/uploads/2012/09/Brucellosis-study_Kiambu.pdf

***Source: Akuku, I. Brucellosis in Africa. Paper given at the Workshop "An integrated approach to controlling brucellosis in Africa". Ethiopia, 2013 [36].

****Source: As referenced by Boukary, 2014 [3].

Humans:

Year	Area	Remarks	No. of samples tested	% positive	Reference
2014	Kiambu and Kajiado		Kajiado: 433 Kiambu: 274	Individual level Kiambu: 2.2 Kajiado: 14.1 Household level: Kiambu: 5.7 Kajiado: 31.8	Ogola in 2014 [42]
2010-2011	Ijara	Febrile patients at Ijara District Hospital	384	Seroprevalence: 31.8 PCR: 15.4	Kiambi, 2012*
2000	Pastoralist area	Patients with flu like symptoms	488	13	Maiachomo et al **

*Source: Prevalence and factors associated with Brucellosis among febrile patients attending Ijara District Hospital, Kenya. MSc thesis by Stella Gaichugi Kiambi, 2012.

http://elearning.jkuat.ac.ke/journals/ojs/index.php/pgthesis_abs/article/view/208/173)

**Source: As referenced by Akuku, 2013 [36].

Madagascar

No published information has been found confirming the presence of brucellosis in livestock. There have no been official reports, so the disease might not be present.

Malawi

Animals: There is only very limited recent information about brucellosis in Malawi:

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2011	Northern region	Dairy cattle	156	Mzimba: 8.1 Nkhata: 6.3	Tebug et al [45]

Mali

Animals: There are no recent publications.

Year	Area	Species of animal	No. of samples tested	% positive	Reference
1995	Mixed areas	Cattle	867	19.7	Maiga et al*
1994	Different areas	Cattle	9466	Individual: 22 Herd level by zones: Soudanienne: 73 Sahelienne: 47 Saharienne: 13.5	Tounkara et al [46]

*Source: As referenced in Boukary, 2014 [3].

Humans:

Year	Area	Remarks	No. of samples tested	% positive	Reference
2009	Mopti	Patients with fever	150	B. *melitensis*: 58	Dao et al*

				B. *abortus*: 49	
2006	Bamako	Febrile patients		7.7	Steinmann et al**

*: Dao et al. Seroprevalence of human brucellosis in Mopti, Mali, 2009.

http://www.infectiologie.org.tn/pdf/revues/rti11/article_original2.pdf

** Referenced in Akuku, 2013 [36].

Mozambique

Animals:

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2015	Limpopo National Park	Buffalos	Buffalos: 62	Buffalos: 17.72 (RBT), 27.42 (ELISA)	Tanner et al [47]
2010	Maputo province	Cattle, sheep and goats	Cattle: 971 Goats: 752 Sheep: 260	Cattle: 14.2 Sheep & goats: 0	Manhica et al*

* Manhica, 2010: http://repository.up.ac.za/handle/2263/27114

Rwanda

Animals:

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2015	Kigali	Cattle	2017	RBT: 2.03 c-ELISA: 1.7	Manishimwe et al [48]

2009	Country answer to OIE questionnaire	Cattle		1.7	Akakpo et al [43]
2008	Nyagatare	Cattle	998	9.9	Chatikobo et al*

*Source: http://www.appropriatetech.net/files/The_prevalence_of_bovine_brucellosis_in_milking_dairy_herds_in.pdf

Humans:

Year	Area	Remarks	No. of samples tested	% positive	Reference
2011	Huye	Abattoir workers	68	14.7	Vivaldi*
2006	Huye	Women with abortion/ stillbirth	60	25	Rujeni et al [49]

* Referenced in Akuku, 2013 [36].

Senegal

Animals:

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2012	Dakar	Dairy	300	25	Tialla et al, 2014 [50]
2009	Country answer to OIE questionnaire	Cattle		20	Akakpo et al [43]
2007-2008	Tivaouane and Thies	Gobra zebus	132	1.5	Kouamo et al*
2003	Bassin Arachidier	Cattle	479 animals, 30 farms	Individual: 0.6 Herd level: 10	Unger et al [51]

* Referenced in Akuku, 2013 [36].

Humans: No recent published information has been found.

South Africa

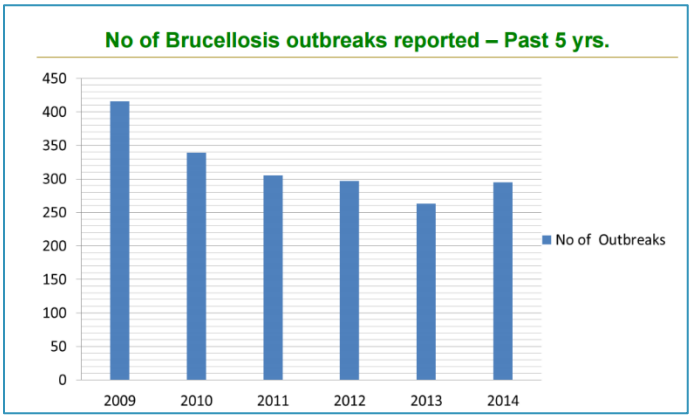
Animals:

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2010	Gauteng	Goats		B. *melitensis*	Communicable diseases communique*
2009-2013	Gauteng	Samples tested by OVI	150000	Herd prevalence: 2009: 17 2013: 21 Individual prevalence: 2009: 2.1 2013: 1	Govindsasamy et al [52]
2001-2003	KwaZulu Natal	Cattle	46025	1.45	Hesterberg et al**

*Source: http://www.nicd.ac.za/assets/files/NICD-NHLS%20Communique%20January%202011.pdf

**Referenced in Akuku, 2013 [36].

Figure 5, represents the number of brucellosis outbreaks in South Africa 2009-2014, and the location of the most recent outbreaks 2010-2014, as presented by Dr Mbizeni from the Disease Control Directorate. He mentioned that herd prevalence is about 25%, but differs per province.



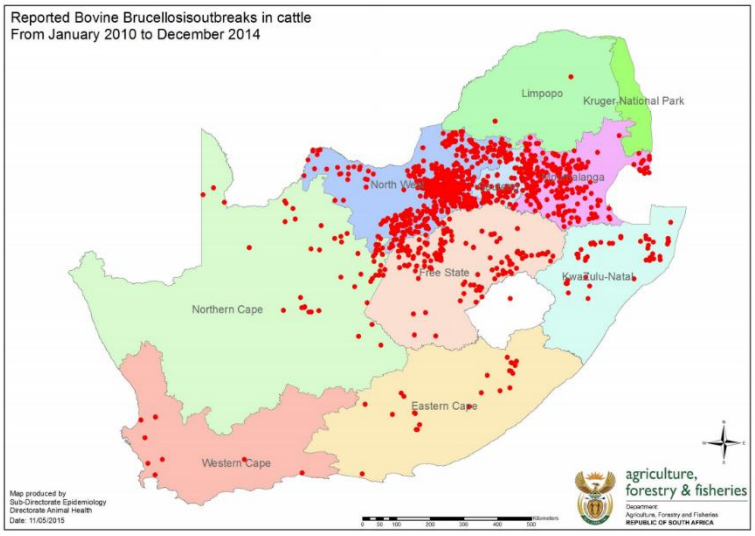


Figure 5: Recent brucellosis outbreaks in South Africa. Source: Brucellosis in South Africa: Progress and challenges. By Dr S. Mbizeni. Disease control directorate.
http://repository.up.ac.za/bitstream/handle/2263/49187/mbizeni_brucellosis_sa2015.pdf?sequence=1&isAllowed=y

Humans: No recent published information has been found.

Tanzania

Animals:

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2015	Katavi-Rukwa	Various	Cattle: 1103 Goats: 248 Buffaloes: 38 Lions: 1 Zebra: 2	Cattle: 6.8 Goats: 1.6 Buffaloes: 7.9 Lions: 50 Zebra: 0	Assenga et al [53]
2012	Morogoro	Dairy cattle	450	Milk: 29.3 Serum: 18.4	Lyimo*
2009	Country answer to OIE questionnaire	Cattle		5.8	Akakpo et al [43]
2007		Cattle and wildlife	2738 livestock 90 wildlife	Cattle: 6.2 Small rum: 6.5 Wildlife: 13	Shirima**
2005	Tanga	Milk	59	56	Swai & Schoonman, 2011 [54]
2003-2004	Tanga	Cattle	246 indigenous 409 crossbred	Smallholder: 4.1 Traditional: 7.3 Herd level Smallholder: 10.5 Herd level Traditional : 20	Swai & Schoonman, 2010 [55]
2002-2004	Tanga	Cattle: abattoir survey	51	12	Swai & Schoonman, 2012 [56]

2003	Moshi (North)	Cattle	417	Individual: 12.2 Herd level: 41.9	Swai et al, 2005**
1995-1997	Dar es Salaam (Dairy) Lugoba (Zebu)	Cattle	Dairy cattle: 343 Zebus: 2289	Dairy: 14.1 Zebu: 12.3	Weinhaupl et al [57]
1999	Iringa and Tanga	Cattle	2187	Pastoral: 1.5-17.9 Smallholder: 0.6-3.6 Parastatal farm: 2.7	Karimuribo, 2007*

*: Source: Beritlla Elias Lyimo. Prevalence of bovine brucellosis in smallholder dairy farms in Morogoro, Tanzania. MSc Thesis: **http://suaire.suanet.ac.tz:8080/xmlui/bitstream/handle/123456789/585/BERTILLA%20ELIAS%20LYIMO.pdf?sequence=1&isAllowed=y**

**Source: Akuku, 2013 [36].

Humans:

Year	Area	Remarks	No. of samples tested	% positive	Reference
2015	Katavi-Rukwa		340	1.5	Assenga et al [53]
2013	Kilosa (Morogoro)	Febrile children at Kilosa district hospital	370	*B. abortus:* 7 *B. melitensis:* 15.4	Chipwaza et al [58]
2007-2008	Moshi	Febrile admissions to 2 hospitals	453	3.5	Crump et al [59]
2004	Tanga	Volunteers various occupations	199	5.52	Swai & Schoonman

Uganda:

Animals:

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2015	South West	Cattle and goats	Cattle: 768 Goats: 315 Bovine milk: 635	Cattle: 14 Bovine milk: 29 Goats: 17	Miller et al (ahead of publication)*
2015	Throughout Uganda	Indigenous cattle	925	Individual: 8.64 Herd level: 28.7 Lake Victoria crescent: 1.78 North Eastern drylands: 19.67	Kabi et al [60] Please see Figure 6.
2013	Luwero and Nakasongola	Cattle	315	Nakasongola: 2.4 Luwero: 4.7	Nizeyimana et al [61]
2012	Kampala area	Cattle	214	Individual: 3 Herd level: 11	Jonsson ****
2011-2012	Gulu and Soroti	Cattle	Gulu: 500 Soroti: 507	Individual: 7.5 (Gulu: 6, Soroti: 9.1) Herd level: 27.1 (Gulu: 19, Soroti: 46)	Mugizi et al [62]
2011	Peri-urban	Dairy cattle	423	Individual: 5 Herd level: 6.5	Makita et al. 2011 [63]
2011	Mubende	Cattle and goats		Cattle: 11 individual, 38 herd level Goats: 36 individual, 58 herd level.	Karimu Grace et al [64]

2010	Kampala	Informal marketed milk	Milk: 117	Milk: 12.6	Makita et al. 2010 [65]
1998-2008	Makerere, Entebbe and Tororo labs	Various	17359	Overall: 10	Mwebe et al [66] Please see graphs below.
2007-2009	Kiboga, Mpigi and Kiruhura (West) and Kumi and Mbale (East)	Cattle		Mpigi: 2008: 5.3, 2009: 30 Kiruhura: 2007:8.1, 2009: 16.8 Kumi: 2007: 2.3, 2008: 6.2 HERD LEVEL: Kiboga: 2007: 77.8, 2008: 65.6 Mpigi: 2009: 70.8	Kashiwazaki et al***
2009	Dairy and Pastoral	Cattle	Dairy: 226 Pastoral: 497	Dairy: 3.3 Pastoral: 34	Magona et al **
2006	Kampala	Marketed milk samples	162	44.4	Smith, 2006
2006	Kashongi	Cattle	258	10.2	Mugizi***
2005	Pastoral	Cattle	10529	15.8	Faye et al**
2004	Peri urban	Cattle	245	42	Mwiine**
2002	Mbarara	Dairy cattle	315 herds	Individual: 15.8 Herd level: 55.6	Bernard et al***
1998	Eastern and Western Uganda	Goats	1518	Individual: 4 Herd level: 43	Kabagambe et al [67]

				B. abortus herd level: Kumi: 0 Masaka: 14 Mbarara: 29 Soroti: 2 Ssembabule: 86 *B. melitensis* Herd level: Kumi: 50 Masaka: 28 Mbarara: 71 Soroti: 33 Ssembabule: 86	

*Source: Pubmed abstract, ahead of printing: **http://www.ncbi.nlm.nih.gov/pubmed/25660343**

**Source: As referenced in Boukary, 2014 [3].

***Source: As referenced in Akuku, 2013 [36].

****Source: Ellen Jonsson, 2013. Seroprevalence and risk factors for bovine brucellosis, salmonellosis and bovine viral diarrhea in urban and peri-urban areas of Kampala, Uganda. Veterinary Bachelors Thesis.

Spatial distribution of *Brucella* antibodies among indigenous cattle in Uganda 2011- 2012. Source: Kabi et al [60]

Mwebe conducted a review of the brucellosis diagnostics between 1998 and 2008. A total of 17,359 samples were analysed serologically, of which 1,061, 15,758 and 585 samples were from Makerere, Entebbe and Tororo laboratories, respectively. The overall seroprevalence of brucellosis was 10% while from individual laboratories was 38%, 32% and 7% for Makerere, Entebbe and Tororo laboratories, respectively. Some of the data is shown in the Figure 7 below:

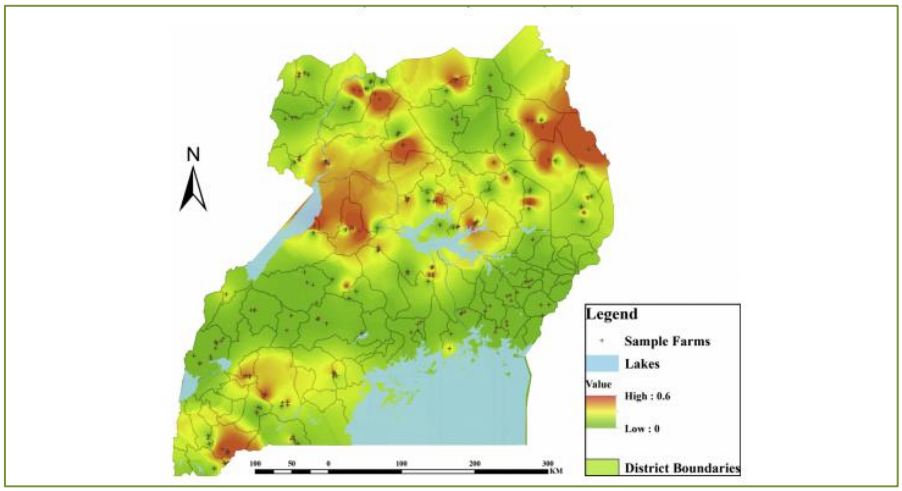


Figure 6: The spatial distribution of *Brucella* antibodies among indigenous cattle population in Uganda. Source: Kabi et al, 2015 [60]

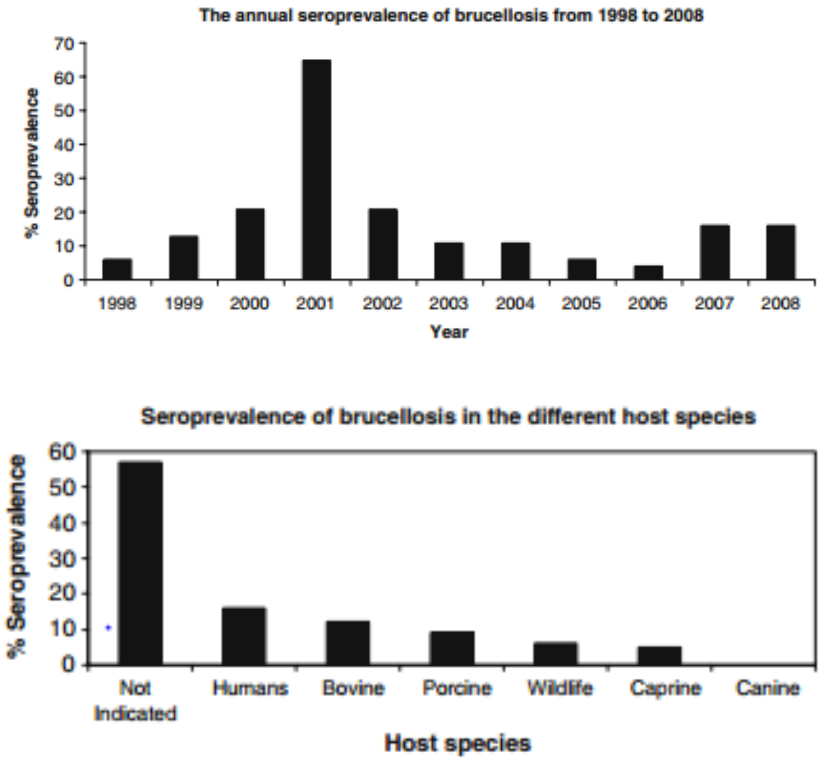


Figure 7: Brucellosis seroprevalence in livestock in Uganda from 1998 to 2008: a retrospective study. Source: Mwebe et al [66].

Humans:

Year	Area	Remarks	No. of samples tested	% positive	Reference
2015	South West		236	11	Miller et al (ahead of publication)*
2015	Kiboga	Patients attending hospital	235	17	Tumwine et al [68]
2011	Nakasongola, Kween, Kapchorwa and Kabale	Samples from every second patient with fever	513	*B. abortus*: 21.8 *B. melitensis*: 14	Nabukenya et al [69]
2011	Mubende	Hospital records		31	Karimu Grace et al [64]
2007	Kampala and Mbarara	Abattoir workers	Kampala: 161 Mbarara: 71	Kampala: 12 Mbarara: 7	Nabukenya et al [70]

Incidence: The annual incidence rate was estimated to be 5.8 (90% CI: 5.3–6.2) per 10,000 people by Makita et al [65]

*Source: Pubmed abstract, ahead of printing: **http://www.ncbi.nlm.nih.gov/pubmed/25660343**

Zambia

Animals:

Year	Area	Species of animal	No. of samples tested	% positive	Reference
2010	Chongwe, Luangwa and Kafue	Cattle	Pastoral: 48 Peri-urban: 849	Pastoral: 18.7 Peri-urban: 7.9	Chimana et al [71]
2009	Wetlands	Antelopes	44	42.9	Muma et al, 2011[72]

2009	Country answer to OIE questionnaire	Cattle		Cattle: 2.5 Sheep/goats: 4.7	Akakpo et al [43]
2008	Southern Province	Cattle	395	20.7	Muma et al, 2013 [73]
2008	Southern and Lusaka	Cattle	1323	6	Muma et al 2012 [74]
2007	Kafue flats	Cattle	886	Individual: 23.9 Herd level: 50	Muma et al 2007 [75]
2006	Lochinvar and Blue Lagoon National Park	Cattle, sheep and goats	Cattle: 1245 Sheep and goats: 280	Cattle: Individual: 14.1-28.1 Herd level: 46.2-74 Sheep and goats: 0	Muma et al, 2006 [76]

Humans: Humans: No recent published information has been found.

Economic and Social Impacts at Global and Regional Levels, and in Selected Countries

The economic and social impact of brucellosis is due to the human, livestock and wildlife disease. The economic and social impact vary by geography, livestock species, management system and capacity of the country's veterinary and medical systems. It includes direct and indirect costs as seen in Figure 8 below:

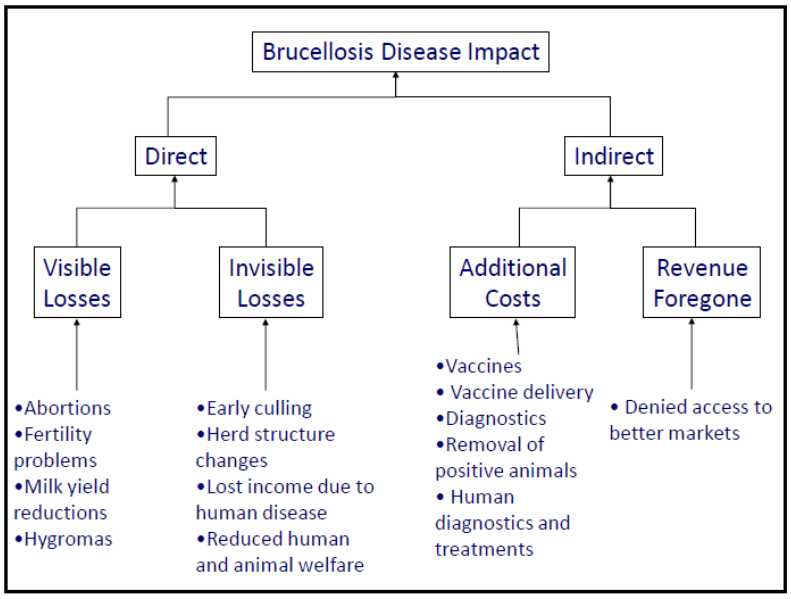


Figure 8: Brucellosis disease impact. Source: Cost-benefit analysis of brucellosis control. Presented by Mieghan Bruce and Jonathan Rushton at the Sub regional meeting on brucellosis control Skopje, TFYR Macedonia, Nov 2014.
http://www.fao.org/fileadmin/user_upload/Europe/documents/Events_2014/Bruc_skopje/CBA_brucellosis_FAO_Macedonia_Nov_2014.pdf

Livestock impact

Cattle: Losses are caused by abortion and later permanently reduced fertility and chronically lowered milk yields in affected animals (10-15% reduction). In previously unexposed and unvaccinated cattle, *B. abortus* spreads rapidly and abortion storms are common. The abortion rate varies from 30% to 80%. In herds where this organism has become endemic, only sporadic symptoms occur and cows may abort their first pregnancies. McDermott (2002) estimated that seropositive cattle were 4.6 times more likely to abort. In a study conducted by McDermott in South Sudan, he found that positive cows had approximately 10% less calves. Abortions are less common in water buffalo cows than cattle. Deaths are rare in adult animals of most species.

Small ruminants: The relative importance of *B. melitensis* for sheep and goats varies with the geographic region, and can be influenced by husbandry practices and the susceptibility of sheep breeds in the region. Management practices and environmental conditions significantly influence the spread of infection. Lambing or kidding in dark, crowded enclosures favours the spread of the organism, while open air parturition in a dry environment results in decreased transmission. The abortion rate is high when *B. melitensis* enters a previously unexposed and unvaccinated flock or herd, but much lower in flocks where this disease is enzootic. The animals usually abort only during the gestation when they are first infected. Inflammatory changes in infected mammary glands usually reduce milk yield by a minimum of 10%, but there are reports of up to 28% in goats (Alton 1985). Fertility in males can be permanently impaired. Deaths are rare.

Pigs: In domesticated pigs, the abortion rate from *B. suis* varies widely, from 0% to 80%.

Good analysis of the economics of brucellosis impact and control in low-income countries has been published by Mc Dermot in 2013 [1] and includes an extensive literature review. Some of the data reviewed on the impact of brucellosis mentioned includes:

- Studies on the economic production loses of bovine brucellosis are reasonably consistent across a range of production systems in Africa, with losses estimated at 6% to 10% of the income per animal.
- At the end of the last century, economic losses for Argentina were estimated at US$60 million per year or US 1.20 per bovine when the prevalence was around 5%.
- In Nigeria losses were estimated at US 575,605 per year or US3.16 per bovine with a prevalence 7-12%.
- Productivity losses from *B. melitensis* are less documented. One study in India estimated the annual economic loss at Rs 1180 (US$21) and Rs 2121.82 (US$ 38) per infected sheep and goat respectively. *B melitensis* usually occurs in outbreaks rather than in a more regular endemic pattern.
- Brucellosis in pigs has productivity and economic impacts but there is little information on their magnitude in low income countries.

If a country has a control program, a cost-benefit analysis of the program can be done, using local data if possible. Some points to consider are the extra costs of brucellosis (the basic costs of the new control program, and increased livestock numbers) and the Revenue foregone (if there is test and slaughter policy, it would include the lost revenue from a culled dairy cow, and unintentional consequences, e.g. abortion due to vaccination of a pregnant animal). Benefits include the costs saved (for not implementing control efforts and from reduced human cases) and extra revenue from an improved livestock productivity from losses avoided due to a reduced prevalence, and lost income avoided by reducing number of sick people (based in presentation by J. Rushton, Skojpe 2014). The private and public costs to be evaluated when considering or evaluating control programs have also been recently summarised by Mc Dermott [1] and are shown in Figure 9 below.

	Actors	Cost of illness	Cost of prevention	Intangible and opportunity costs
Private	Individuals and households	Treatment (e.g. medication), loss of household production	Risk mitigation such as boiling milk	Disutility of ill health per individual (DALYs) Disutility of ill health for friends, family, etc.
Private	Livestock sector	Treatment, herd slaughter, market loss due to risk of infected meat and milk, mortality, morbidity, lower production, loss of exports	Increased biosecurity, vaccination*, and procedures to control disease along the value chain (e.g. pasteurisation)	Future emerging disease Loss of animal genetic resources Loss of opportunities occasioned by spending on disease prevention and cure
Public	Health sector (human and animal)	Treatment (hospital provision, etc.) Outbreak costs, movement restrictions, culling, vaccination	Risk mitigation such as movement control and vaccination* Disease surveillance Research	
Public	Economy	Indirect effects on economic development, ecosystem services and tourism	Biosecurity, avoiding wildlife and vectors Disease surveillance Research	

Dark grey boxes: market prices available and commonly included in economic assessments of disease
Light grey boxes: market prices not available so costs need to be estimated through other methods
White boxes: prevention costs reflect efficiency and effectiveness of public and private service provision. Usually there are few data and only rough estimates are made
Black box: included in health metrics (DALYs).
*a number of costs (for example, vaccination) produce benefits for both the private sector (better livestock production) and the public sector (fewer human infections)
DALYs: disability-adjusted life years

Figure 9: Costs to be considered and estimated in planning brucellosis control and eradication programs. Source: McDermott, 2013 [1].

Analysis by the World Bank:

The World Livestock Disease Atlas – a quantitative analysis of global animal health data [77], published by the World Bank (with cooperation of OIE and FAO) in 2011 is an attempt to understand which livestock diseases cause the heaviest losses, which countries suffers the worst disease-related losses and which livestock species are most affected. **http://www-wds.worldbank.org/external/default/WDSContentServer/WDSP/IB/2012/02/17/000356161_20120217030841/Rendered/PDF/668590WP00PUBL00Livestock0Atlas0web.pdf**

The World Livestock Disease Atlas bases its analysis on the Livestock Units (LSU). Each species has a LSU value, and the losses of LSU have been given a value. See Figure 10. For more information on the methodology description, please refer to the World Bank Atlas itself (pages 6 & 7). Brucellosis is one of the top 10 diseases causing losses for cattle, buffalos and small ruminants, as shown in Figure 11. However, looking at the data in detail, there are few data from sub-Saharan Africa and Asia.

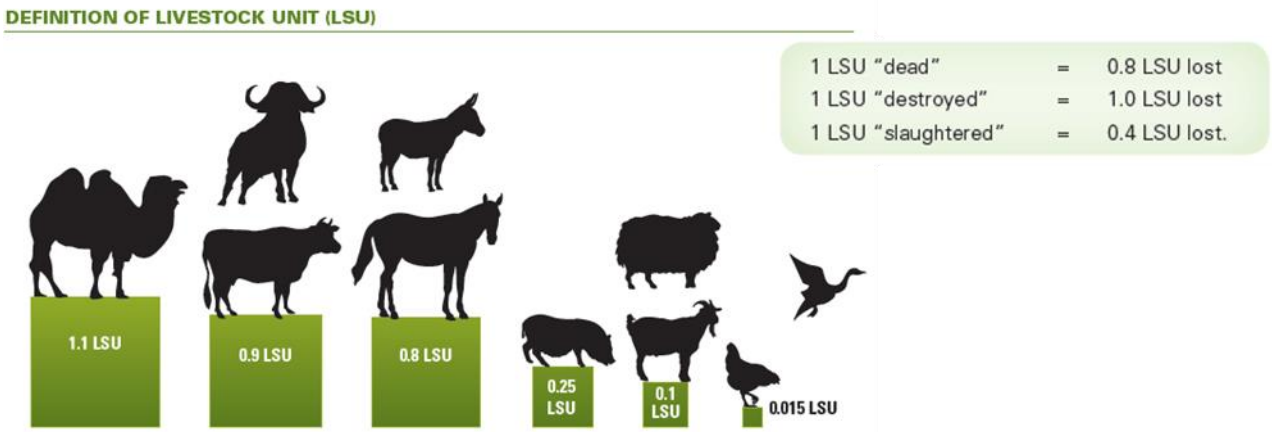


Figure 10: Livestock Units. Source: World Livestock Disease Atlas – The World Bank, 2011 [77].

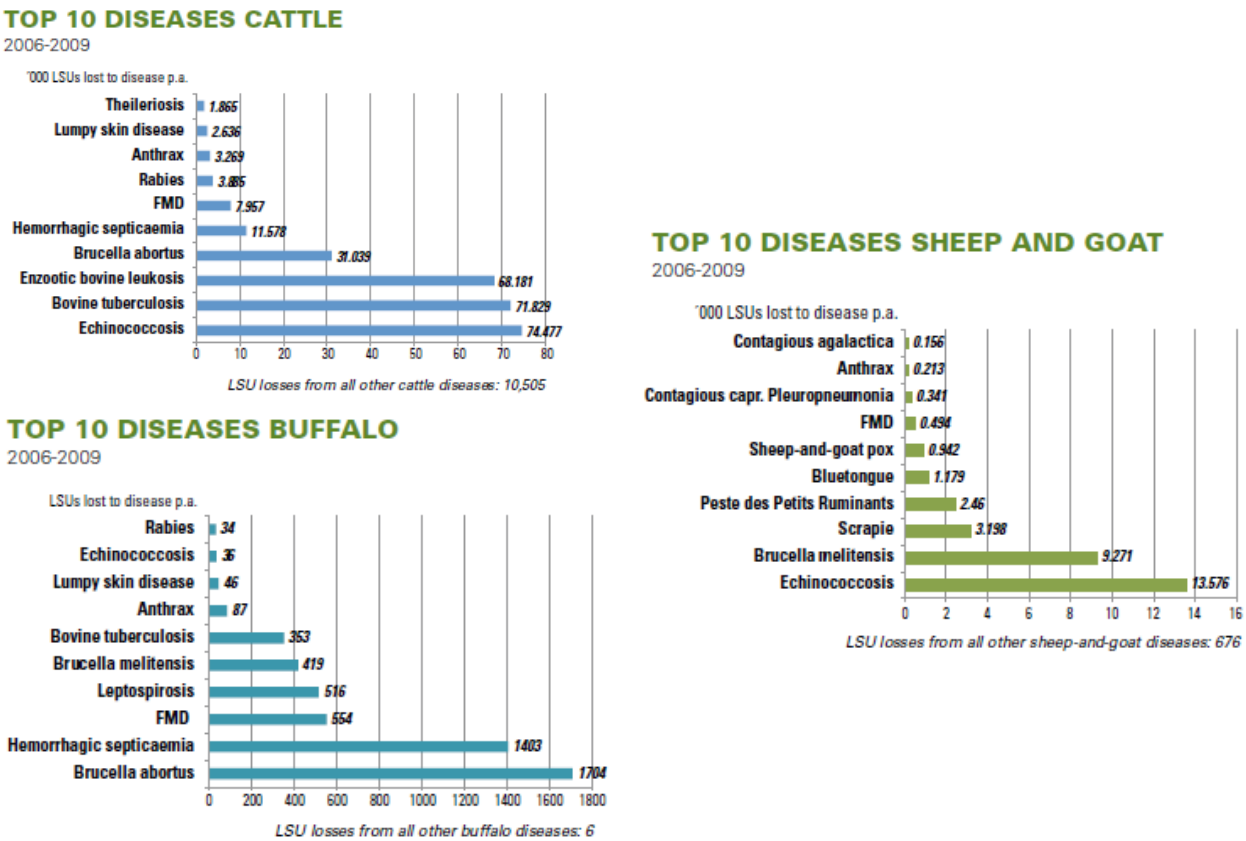


Figure 11: Top 10 diseases in terms of LSU losses for cattle, buffalo, and sheep & goats. Source: World Livestock Disease Atlas – The World Bank, 2011 [77].

Humans:

Worldwide millions of humans are at risk, especially in developing countries where the infection in animals has not been brought under control, heat treatment procedures of milk are not routinely applied, and food habits such as the consumption of raw milk and poor hygienic conditions favour human infection. Brucellosis is also an occupational disease; most cases tend to occur in abattoir workers, veterinarians, hunters, farmers, and livestock keepers. People who do not work with animals usually become infected by ingesting unpasteurized dairy products. Brucellosis is also one of the most easily acquired laboratory infections. In humans, brucellosis usually produces a grave and debilitating disease that may become chronic and requires prolonged treatment. Complications are seen occasionally, particularly in the undulant and chronic forms. The most common complications are arthritis, spondylitis, epididymo-orchitis and chronic fatigue. Neurological signs occur in up to 5% of cases. Brucellosis is rarely fatal if treated; in untreated persons, the case fatality rate vary from less than 2% to 5%. Deaths are usually caused by endocarditis or meningitis. The incidence and severity of disease varies with the species of *Brucella*. *B. melitensis* is considered to be the most severe human pathogen in the genus

Brucellosis affects approximately 500,000 people annually worldwide [78]. The disease is severely under-reported in humans, and acute febrile illness are often mistaken for malaria or other febrile diseases – an example in Tanzania showed that of 870 febrile patients, 60% were clinically diagnosed with malaria, but it was the actual cause in only 1.6% [59]. The reported incidence ranges from less than 0.01 to more than 200 cases per 100,000 population [2].

A recent systematic review on the burden of brucellosis [80], concluded that the incidence varied significantly within regions and within countries and aggregated data do not capture the complexities of disease dynamics and at-risk populations may be overlooked. Also as many brucellosis endemic countries do not have strong health systems, passively acquired data likely underestimates the true burden.

Disability adjusted life years (DALY's): The WHO Estimates of the global burden of foodborne diseases Report, published in December 2015, (http://www.who.int/foodsafety/publications/foodborne_disease/fergreport/en/), estimates the **Disability adjusted life years (DALYs) due to *Brucella* spp is 264,073 and 2 DALYs per 100,000 persons**. See Figure 12 and Table 2.

	Median number of DALYs	Median DALYs per 100,000 persons
***Brucella* spp**	264,073	2
E. granulosus	183,573	0.6
M. tuberculosis	607,775	9
T. solium	2,788,426	41

Figure 12: WHO estimates of the global burden of foodborne diseases of interest for IDRC.
Data source: WHO estimates of the global burden of foodborne diseases: foodborne burden epidemiology reference group 2007-2015

DALYs have been previously calculated for specific countries like Mongolia, where it was used to model the benefit of a brucellosis control program, which would have a cost of US$ 19 per DALY averted [79] (as a rule of thumb, interventions that cost less than US$ 150 per DALY averted are “attractive”, and less than US$25 are “highly attractive”[1]).

Abbreviations: NoV = Norovirus; Camp = *Campylobacter* spp.; EPEC = Enteropathogenic *Escherichia coli*; ETEC = Enterotoxigenic *E. coli*; STEC = Shiga toxin-producing *E. coli*; NTS = non-typhoidal *Salmonella enterica*; Shig = *Shigella* spp.; Vchol; *Vibrio cholerae*; Ehist = *Entamoeba histolytica*; Cryp = *Cryptosporidium* spp.; Giar = *Giardia* spp.; HAV = Hepatitis A virus; Bruc = *Brucella* spp.; Lmono = *Listeria monocytogenes*; Mbov = *Mycobacterium bovis*; SPara = *Salmonella* Paratyphi A; STyph = *Salmonella* Typhi; Toxo = *Toxoplasma gondii*; Egran = *Echinococcus granulosus*; Emult = *E. multilocularis*; Tsol = *Taenia solium*; Asc = *Ascaris* spp.; Trich = *Trichinella* spp.; Clon = *Clonorchis sinensis*; Fasc = *Fasciola* spp.; Flukes = Intestinal flukes; Opis = *Opisthorchis* spp.; Parag = *Paragonimus* spp.; Diox = Dioxin; Afla = Aflatoxin.

Figure 13: Scatterplot of the global burden of foodborne diseases per 100,000 population and per incidence case Source: WHO Estimates of the global burden of foodborne diseases, 2015. (Note: axes use log scales). The red arrow points at Brucella spp. Green arrows point at other diseases of interest for IDRC (*T. solium*, *Mycobacterium bovis* and *E. granulosus*)

Impact on specific focus countries:

There are no published reports about the specific economic or social impact of brucellosis in the countries of interest. Specific country evaluations, usually refer to the assessment of benefit-cost ratio of brucellosis control programs, as for example has been done in Nigeria and Mongolia [1], and more recently in Kirghizstan. Different types of benefits and costs of animal brucellosis mass vaccination in Mongolia are seen in Figure 14 below.

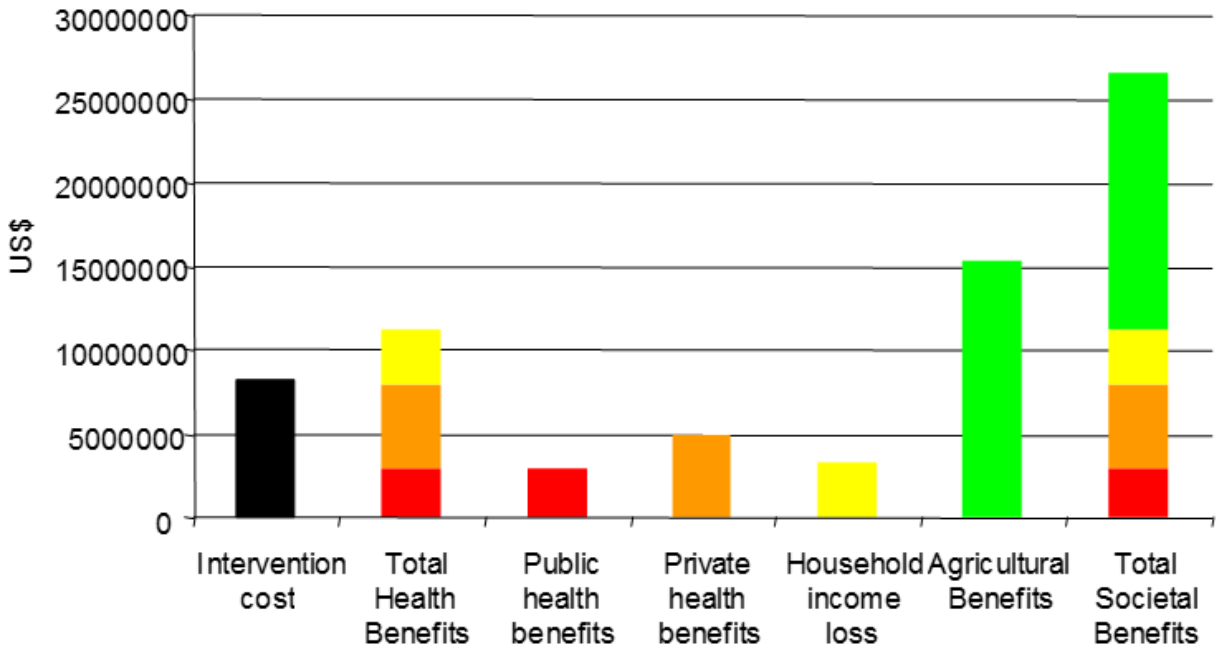


Figure 14: Different types of benefits and costs of animal brucellosis mass vaccination in Mongolia (Source: Bassirou Bonfoh, Economics of brucellosis, presentation at the workshop on integrated approach to controlling brucellosis in Africa, Addis Ababa, 2013)

Disease Prevention and Control Methods

Treatment (Control)

Livestock suffering from brucellosis are generally not treated. *Brucella* spp may undergo L-transformation when exposed to certain antibiotics, resulting in a cell wall deficient form [81]. The effect in preventing serological detection and resultant creation of carrier animals is not clear.

However, it has been demonstrated that long and complex treatments can successfully eliminate shedding of organisms from long-term carriers in cattle [82] and small ruminants [83], but it is believed to be economically unviable. For example the most practical, effective and least expensive regimen for sheep and goats required long acting oxytetracycline 25 mg/kg IM every 2 days for 4 weeks, combined with streptomycin 20 mg/kg IM every 2 days for 2 weeks.

No treatment has proved effective and economically feasible in treating pigs. In general, antibiotic therapy in pigs has been effective in limiting the bacteremic stage of the disease, but after therapy was discontinued, viable *B. suis* were still present in tissues. In carefully selected circumstances it would probably be possible to suppress multiplication of *B. suis* in vivo sufficiently to alleviate clinical signs and shedding.

Recent developments: Dr Steven Olsen (USDA) has been doing trials to evaluate the new macrolids against *B. melitensis* in sheep. Preliminary results indicate that they are not effective during the abortion stage; they did not prevent abortion (presumed the foetus were already colonised at the time of treatment) but further analysis is ongoing. He would like to pursue this line of research (Dr Olsen, personal communication).

Prophylaxis (Prevention)

Biosecurity measures to ensure the disease does not enter the herd are useful but might be very difficult to implement in the settings that characterise the developing world. New animals entering the herd, as well as semen, should come from *Brucella* negative herds/farms. Animals entering the herd should be quarantined and tested, before they are allowed to mix with the remaining animals.

Vaccination is a very effective way of prophylaxis. The different types of vaccines, their advantages and disadvantages, are discussed in Section 6. Livestock vaccines currently available are effective in reducing production losses and reducing transmission, but do not prevent the animals getting infected, or seroconverting after exposure to virulent strains.

Options and strategies for control programs at national, sub-national or regional level:

Control of brucellosis is a long term program that should be adapted to the local circumstances. The most successful efforts to control and in many cases eradicate brucellosis have been in high and middle income countries (and one low income country, Nigeria). The general pattern has been to establish a diagnostic and surveillance system and estimate the prevalence and distribution of brucellosis. Based on the prevalence results, different strategies might be applied (see Figure 15 below). Initial control measures, including vaccination, may be implemented to reduce an initial high prevalence. From there, testing, quarantine and slaughter with compensation policies are established. Sometimes special measures are required in late stages for high risk populations. Often, the final stages are the most difficult, when prevalence rates are low and the cost of finding the final positive animals is very high. Complications arise if wildlife reservoirs exist [1].

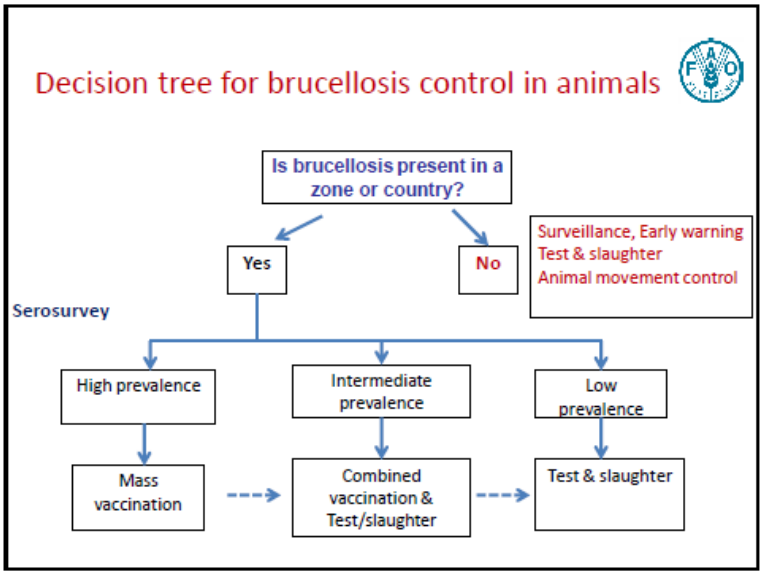


Figure 15: Decision Tree for brucellosis control as recommended by FAO (Source: Strategies and options for control and surveillance of brucellosis by Ahmed Elldrissi. Presented at the Sub regional meeting on brucellosis control Skopje, TFYR Macedonia, Nov 2014).
http://www.fao.org/fileadmin/user_upload/Europe/documents/Events_2014/Bruc_skopje/Brucellosis_strategies_Skopje.pdf)

When implementing test and slaughter, there are important points to consider: where do replacement animals come from? Are there enough funds to compensate farmers? Are animals individually identified to ensure seropositive animals are correctly identified? It is socially and culturally acceptable? (e.g. culling cows in Hindu areas).

Attempts to control and eradicate brucellosis in middle-income countries using the classical approaches have been much less successful. These include the attempts in Mongolia which progressed at a very slow pace, as well as less than successful control programs in Egypt, Israel (*B. melitensis*), Macedonia, India and the Azores. In low and middle income countries, more targeted control measures may be more realistic. Under conditions of high to moderate prevalence, inadequate veterinary resources, inability to control livestock movement, widespread brucellosis in feral animals or wildlife, livestock owners unaware of the importance of the programme or not strongly committed to public disease control, or limited diagnostic capabilities, targeted mass vaccination of all animals (including adults) might be the optimal tool for reducing level of infection. Reduction of prevalence through targeted and time-bound vaccination campaigns may be economically beneficial as it could stop the spread of an outbreak of *B. melitensis*. Such approach has been reported to be successful in Tunisia and Morocco [1]. The strategy chosen will depend of the country resources, the epidemiological situation, the political will, the legal framework (for example legislation required for test, slaughter and compensation), veterinary services and laboratory infrastructure, animal movement control, animal/herd identification practices and availability of good quality vaccines.

AU-IBAR has developed Standard Methods and Procedures (SMPs) for control of Brucellosis in the Greater Horn of Africa [84]. In the considerations for vaccination, it is stated that an effective vaccination requires coverage of over 80% of the eligible animal population, and vaccination carried out for a period greater than twice the average production life (over 10 years in sheep and goats). They suggest that in the context of the region, it may be possible to combine vaccination campaigns for brucellosis with those being implemented for other diseases like PPR or CBPP.

As for considerations of the different scenarios in the Greater Horn of Africa, they define high-prevalence, endemic situation in small ruminants, when there is over 5% herd prevalence and in those cases mass vaccination is recommended. Where risk factors cannot be controlled (for example, under conditions of transhumance), vaccination is recommended even when the prevalence is lower.

Advantages and disadvantages of the different brucellosis control strategies, can be seen in Table 3 below.

Table 3: Advantages and disadvantages of Brucellosis control strategies:
Source: Brucellosis in Sheep and Goats. European Commission. Scientific Committee on Animal Health and Animal Welfare.SANCO.C.2/AH/R23/2001

Strategy	Advantages	Disadvantages
Mass vaccination	1. Reduces zoonotic impact 2. Herd immunity quickly established 3. Effective disease control and reduction in losses due to disease 4. Well accepted by owners 5. Easy to manage and economical 6. Flock immunity can be maintained by vaccinating young animals	1. Vaccine induced abortions in pregnant animals 2. Distinguishing infected form vaccinated animals is not feasible in the short term 3. Infected animals remain on farm for some time
Vaccination of young animals and test and slaughter of older infected animals	1. Minimises vaccine induced abortions 2. Serological response reduced in vaccinated non-infected animals allowing test to differentiate infected and vaccinated animals	1. Herd immunity slowly established (unless moving from mass vaccination strategy) 2. Serological test to differentiate infected and vaccinated animals are not optimal and cannot be relied upon for accurate diagnosis of an individual animal
No vaccination Test and slaughter	1. If successful will result in elimination of the infection in the region 2. Diagnostic test are more accurate in non-vaccinated animals but still not optimum	1. Risk of epidemics and subsequent human infection 2. Higher cost 3. Need efficient veterinary services (animal identification, laboratory support, movement control) 4. Suitable for low disease prevalence areas only 5. Removal of protective cover of vaccination may allow disease prevalence to increase 6. May require whole herd slaughter to be effective

Disease situation and government policies by country

Tables 4 and 5 below have been partially completed with information from Akakpo, Teko-Agbo and Kone presented at an OIE conference in 2009 [43], and updated with data published by Akuku [36], data obtained by the consultant earlier in the year, and data from a brucellosis workshop conducted by the Brucellosis ZELS project in Dakar in June 2015 (data not published, but kindly shared by Dr Javier Guitian). It also includes information from the questionnaires sent to the DG and DVS offices of the different countries.

Table 4 covers the disease situation (if it is notifiable or not), the presence of official surveillance and/or control programs, and the treatment situation. Table 5 refers to vaccination.

The definitions that were given to the respondents are:

[1]Surveillance: is the systematic ongoing collection, collation and analysis of data and the timely dissemination of information to those who need to know so that action can be taken.

[2]Control: a programme which is approved, and managed or supervised by the Veterinary Authority of a country for the purpose of controlling a vector, pathogen or disease by specific measures applied throughout that country, or within a zone or compartment of that country.

Table 4: Official status, official programs and treatment for Brucellosis in the countries of interest. (Ba: *B. abortus,* Bm: *B. melitensis,* Bs: *B. suis).*

Country	Notifiable (yes/no)	Official surveillance[1] program (yes/no) (if yes, active or passive)	Official control[2] program (yes/no)	Treatment (Chemotherapy)	
				Treatment authorised (yes/no)	Frequently practiced (yes/no)
ASIA					
Bangladesh #	Ba: Yes Bm: No Bs: N/A	No	No	No	-
India					

Indonesia					
Myanmar # (Burma)	Yes	Ba, Bm: Yes, passive Bs: No	No	No	Yes
Nepal #	Yes	Yes, passive	No	No	No
Vietnam #	No	No	No	No	Yes
AFRICA					
Burkina Faso &	Yes	Yes*	Yes	No	No
Côte d'Ivoire # (Ivory Coast)	Yes	Yes, Passive	Yes	No	
Ethiopia *		No			
Kenya #	Yes	Yes, active/passive # No**	No	No # Yes &	No
Madagascar					
Malawi #	Yes	No	No # Yes &	Yes # No &	No
Mali #	- # Yes &	Ba: yes, passive Bm, Bs: -	Ba: Yes # Bm, Bs: N/A # No***	No	No
Mozambique &				No	Yes
Rwanda %. #	Yes	Yes***	Yes***	No #	No #
Senegal &	Yes		Yes		
South Africa					
Tanzania #	Yes	Yes, passive #	No	No	No
Uganda #	No	No # Yes, passive*	No	No	Yes (only supportive)

Zambia # &	Yes	Ba, Bm: Yes, active Bs: No	Ba, Bm: Yes Bs: No	No	No # Yes &

Countries mark indicates the main source. If different answers have been found, they are marked within each box.
Data from the questionnaire submitted as part of this monograph to the DG/DVS offices.
&: Data from Akakpo 2009
* Data from communications between the consultant and various country representatives in May 2015.
** Source: Data from Akuku, 2013
*** Source: Data from Craighead et al. "Brucellosis in West and Central Africa: Situation Analysis (ZELS project report submitted for publication) kindly provided by Dr Javier Guitian.
% During the workshop conducted in June 2015, and described in Craighead et al. "Brucellosis in West and Central Africa: Situation Analysis (ZELS project report submitted for publication), the participant from Rwanda reported the existence of a national brucellosis surveillance and control programme. Surveillance activities are carried out in abattoir and in live animals, as well as vaccination of young female cattle using RB51. Further testing is carried out on animals produced for the 'One family, one cow' programme where any positive animals are culled. Through this system positive small ruminants have also been identified.

Table 5: Vaccination for Brucellosis in the countries of interest.
(Ba: *B. abortus,* Bm: *B. melitensis,* Bs: *B. suis)*

Country	Vaccination			
	Compulsory vaccination (yes/no)	Who pays for the vaccine (Government, farmers, combination, others-specify)	Who delivers the vaccine (official, private vaccinators or both)	Species vaccinated (cattle, sheep, goats, pigs, poultry)
ASIA				
Bangladesh #	No	-	-	-
India				
Indonesia				
Myanmar # (Burma)	No	Ba: Farmers Bm, Bs: -	Ba: Private Bm, Bs: -	Ba: Cattle Bm: sheep/goat
Nepal #	No	N/A	N/A	N/A
Vietnam #	No	Farmers	Private vaccinators	Ba, Bm: cattle

				Bs: pigs
AFRICA				
Burkina Faso &	Not authorised	-	-	-
Côte d'Ivoire (Ivory Coast) #	No	Farmer	Private vaccinators	Cattle
Ethiopia				
Kenya #	No	Farmer	Both	Cattle, sheep, goats
Madagascar				
Malawi &, #	Not authorised	-	-	-
Mali &	Not authorised	-	-	-
Mozambique				
Rwanda #	No	Government	Official	Cattle
Senegal				
South Africa				
Tanzania #	No	Ba: Farmers Bm, Bs: Not done	Ba: private vaccinators Bm, Bs: Not done	Ba: cattle
Uganda #	No	Ba, Bm: Combination (but mainly farmers)	Ba, Bm: Both (government and private)	Ba: cattle Bm: goats
Zambia #	No	Ba, Bm: Farmer	Ba, Bm: Both	Ba, Bm: cattle

Countries mark indicates the main source. If different answers have been found, they are marked within each box.
Data from the questionnaire submitted as part of this monograph to the DG/DVS offices.
&: Data from Akakpo 2009
-: Questionnaires received, but no information provided.

Vaccines Available

There are several different types of vaccines for brucellosis. Tables 6 and 7, show a summary of the characteristics of the main vaccines for *B. abortus*, *B. melitensis* and *B. suis*, based on the information from the OIE Terrestrial Manual, Discontools, and the most recent publications on brucellosis vaccines reviews, including publications from Dorneles in 2015 [85], Avila-Calderon [86], Yang [87] and Olsen [88] in 2013, and Siadat in 2012 [89]. It also includes specific reviews for vaccines from Russia [90] and China [91].

B. abortus

There are 2 vaccines recognized by the OIE for *B. abortus* in cattle: the Strain 19 (S19) is the reference vaccine, and the RB51. Both are live vaccines and are widely used. There used to be an inactivated vaccine, the 45/20, but it has been discontinued. In South Africa, OBP produces S19 low dose (1 to 10 X 10^8 cfu/dose). This low dose vaccine triggers CFT antibodies for a limited period which can be used to monitor seroconversion, but the animals remain negative to c-ELISA. This low dose vaccine has been used during outbreaks to provide good immunity also in adult animals while preventing a strong serological response. See Table 6.

In Russia over 50 vaccine strains have been evaluated [90], and 5 have been incorporated into veterinary practice (S19, 104-M, 82, 75/79-AB and KB17/100). The SR-*B. abortus* strain 82, is the most commonly used, and it is commercially available manufactured by S*hchelkovo Biocombinat* (**http://biocombinat.ru/en/catalog/32/425/**). It was approved for use in 1974, but can cause abortions in pregnant cattle. The other vaccine widely used since 1997, is the strain 75/79-AB (which seems to be a dissociated form of strain 82) and is also manufactured by S*hchelkovo Biocombinat* (**http://biocombinat.ru/en/catalog/32/424/**). Both have weak agglutinogenic properties, and provide good immunity. The main advantage of 75/79AB is that it does not seem to produce abortions in cattle.

There are several patents filled for *Brucella* vaccines, however, it is difficult to know if they are being pursued or not.
https://www.lens.org/lens/search?q=%28title%3A%28brucellosis+AND+vaccine+AND+%28*abortus*+OR+*melitensis*+OR+suis%29%29+%7C%7C+abstract%3A%28brucellosis+AND+vaccine+AND+%28*abortus*+OR+*melitensis*+OR+suis%29%29+%7C%7C+claims%3A%28brucellosis+AND+vaccine+AND+%28*abortus*+OR+*melitensis*+OR+suis%29%29%29&dates=%2Bfiling_date%3A20100101-20151030&l=en&p=0&n=50

Some patents for *B. abortus* vaccines have been more widely publicised:

1. In 2009, it was announced that Drs Delvecchio, R.A. Ugalde, J.E. Ugalde and D.J. Comerci, were awarded United States patent # 7,541,447 B2, for a live attenuated vaccine that prevents brucellosis. The brucellosis Delta-pgm vaccine is a live attenuated and genetically defined mutant with a deleted portion of the phosphoglucomutase gene. This deletion mutation results in a substantially less virulent organism which has retained its protective ability as a vaccine. Since it is a deletion it also has no capability to revert to a virulent organism. A master seed lot of the vaccine has been produced and used in several cattle studies. Standard production methods using bacterial fermentation are used to produce the Delta-pgm vaccine. The vaccine does not interfere with diagnostic methods for brucellosis and it induces a higher degree of protection in comparison with S-19 strain. Dr. Delvecchio is President and founder of Vital Probes, Inc. a biotechnology firm in Pennsylvania that is seeking investors to commercialise the vaccine. According to their website, Licensure of the vaccine is available on a per country or a global scale. They have been contacted to find the latest information, but no reply has been received.

http://www.vitalprobes.com/randd.php?rdlink=006,
http://www.vitalprobes.com/news.php?article_id=20090605094159

http://www.iib.unsam.edu.ar/bioemprendedores/wp-content/uploads/2015/05/Brucellosis-Vaccine_V1-Ing-072015.pdf

2. In August 2013, the patent of a *Brucella abortus* S19 vaccine expressing green fluorescent protein (S19-GFP) was announced by the National University (UNA), University of Costa Rica (UCR) and the Public University of Navarra (Spain) This recombinant vaccine would allow the differentiation between vaccinated and naturally infected animals. An accompanying ELISA has also been developed and patented. It would seems this vaccines is not commercially available.

(**http://albeitar.portalveterinaria.com/noticia/12438/actualidad/patentan-una-vacuna-contra-la-brucelosis-que-diferencia-los-animales-con-infeccion-natural-de-los-vacunados.html**).

(**http://www.google.com/patents/WO2011067446A1?cl=en**).

B. melitensis

There is only one vaccine recognized by the OIE for use in sheep and goats for B. *melitensis*, the Rev1. In China, the M5 (or M5-90) vaccine, derived from strain M28 was developed in Harbin, and has been used widely in goats and sheep since 1970 (91, 92). It is commercially produced by the China Animal Husbandry Group. According to the publications (91,92), M5-90 can be used in pregnant animals, however the commercial manufacturer recommends not to use in pregnant animals. Some information was obtained from the following link: **http://baike.baidu.com/view/2532416.htm**. It seems that the vaccine can also be given as an indoor or outdoor aerosol, but that route would create concerns for human safety, and transmission to all animal including

lactating ones, that would transmit the *Brucella* in milk. The manufacturers of M5-90 say that the vaccine is pathogenic for humans, so they need to use protection during aerosol vaccination, but no further guidance is given (information provided by Ms Shumin Li). The manufacturers of M5 also say that the vaccine can be used in cattle, but it is not clear if it is for protection against *B. abortus*, *B. melitensis* or both. See Table 7.

B. melitensis vaccines for cattle: According to the OIE Terrestrial Manual, it is not infrequent to isolate *B. melitensis* in cattle in countries with a high prevalence of this infection in small ruminants. There has been some debate on the protective efficacy of S19 against *B. melitensis* infection in cattle and it has been hypothesised that Rev.1 should be a more effective vaccine in these conditions. However, there is very little information related to this issue. Evidence proving that S19 is able to control *B. melitensis* at the field level is also scanty. No experiments have been reported showing the efficacy of Rev.1 against *B. melitensis* infection in cattle. Moreover, the safety of this vaccine is practically unknown in cattle. Until the safety of Rev.1 in cattle of different physiological status and efficacy studies against *B. melitensis* under strictly controlled conditions are performed, this vaccine should not be recommended for cattle.

Brucella suis

The only commercial pig vaccine for the prevention of *B. suis* is produced in China (**http://www.cahic.com/**).

http://www.cahic.com/pham/index.php?optionid=357&auto_id=570. The manufacturers were contacted via the web to obtain additional information, but not reply was obtained. Research conducted by Ms Shumin Li, clarified that the manufacturers claim that the vaccine can be used orally in pregnant animals, but no IM. The manufacturers also claim duration of immunity for cattle, sheep and goats, but it is not clear for which type of Brucella. As for interference with serology, it would seem that even if it is a smooth strain, the interference with diagnostic tests is not long term. See Table 7.

http://www.ncbi.nlm.nih.gov/pubmed/3541425

A promising experimental vaccine, is strain 353-1. It is a natural rough mutant that does not induce immune responses as detected on the traditional diagnostic tests, is not shed after vaccination, and is clinically safe in pigs [93]. Dr Steve Olsen who is leading the USDA team involved in the development of this vaccine, has provided further information (please see Section 7, note 1, page 48)

Human vaccines

China is one of the few countries to have a vaccine for humans, the strain M-104 vaccine, which has also been used in Russia. It is a *B. abortus* isolated from the foetus of an aborted calf in 1950 by a Russian scientist; tests indicated the M strain had low virulence, stability and high immuno-antigenicity. The scratch vaccination was used in China to introduce five billion bacteria and achieved 90% of protection and 12 month duration. The

vaccine has been adopted for use in humans since 1965. However, the epidemiology of the human brucellosis situation in China become more severe during 2005-2010 [94].

Table 6: Comparison of the different *B. abortus* vaccines

	B. abortus			
	Strain 19	RB51	45/20	Strain 82
Status	In use. Recognized by OIE (Reference vaccine).	In use. Recognized by OIE.	Used, but stopped	In use: Russian Federation, Azerbaijan, Tajikistan and others
Type	Live: *B. abortus* biovar 1 (Smooth)	Live: *B. abortus* biovar 1 (Rough)	Killed: *B. abortus* biovar 1 (Rough)	Live: *B.abortus* biovar 6
Origen	Naturally attenuated by room temperature for 1 year	Subculture on medium with rifampicin and penicillin	Isolated after 20 passages in guinea pigs.	Selecting colonies from an aborted bovine foetus.
Target species	Cattle	Cattle	Cattle and sheep	Cattle
Other species	Water buffalo	Safe in water buffalo (but does not protect natural Brucella infections). Safe in small ruminants.		
Protection against other Brucella strains	*B. melitensis* : Debatable that it is protective against *B. melitensis* in cattle (OIE), DISCONTOOLS says it is effective. It is protective against *B. melitensis* in sheep, but Rev1 is better. *B. suis* : ? *B. ovis* : ?	*B. melitensis* : No *B. suis* : No *B. ovis* : No		
Indications	Female calves 3-6 months of age	Calves		Heifers 3-6 months.
Immunity	Lasting immunity to moderate challenge, but precise duration is unknown.	Long immunity to moderate challenge, but duration unknown. In risk areas, revaccinate after 12 months of age. Booster suggested after 4-5 years	Two consecutive vaccinations, 6-12 months apart.	Repeat in heifers after 10 months. Immunity lasts 1 year.
Route	Usually SC (or conjunctival)	SC	IM	SC
Dose	Calves SC: 5-8 $x10^{10}$ viable organisms. Adults SC: reduced dose 3 $x10^{8}$ - 3 x 10^{9} but some side effects. Conjunctival any age: 5$x10^{9}$ viable organisms	Calves 4-12 months: SC: 1-3.4 $x10^{10}$ organisms. Reduced dose 1$x10^{9}$ recommended for adults		
Serology on standard tests	Positive (induces anti-LPS Ab). Prolonged high titres with booster vaccination	Negative (does not induce anti-LPS Ab), even on booster vaccination. No seroconversion in RBT and CFT, but detectable with ELISA.	Not completely free of the O-chain, can induce Ab detectable by serology	Intermediate: it express some O Ag on its surface, but humoral response less robust and shorter. No response in agglutination tests

Continued: Comparison of the different *B. abortus* vaccines

	B. abortus			
	Strain 19	RB51	45/20	Strain 82
Pathogenicity	Moderate to high	Low		
Efficacy	Highly effective in reducing production losses and disease transmission. Less efficacious at preventing infection (& seroconversion). Efficacy is challenge dose-dependant	Similar to S 19, but there is not generalized agreement. Never proven more effective than S19.	Lack of sufficient protection after challenge	Similar to S19
Zoonotic characteristics	Significant human pathogen	Reduced pathogenicity compared with S19, but still infections, and it is resistant to rifampicin, one of the most potent antibiotics used for Brucellosis		
Use in pregnant animals	Low dose may cause significant abortions (3.2%) and high titres	Occasional abortions (less than 0.2%). Some claims are higher.	Safe.	Not recommended for pregnant cattle
Other side defects	Significant reduction in milk production has been reported. Recovered 10% milk samples. Can't be used in males due to persistent orchitis.	Not safe in males.	When used live, reverts to S pathogenic form when injected in cattle.	
First used	1923	Mid 1990's		Russia: 1974
Large scale use	Yes	Yes		Yes, in Russia
Others		More expensive than S19	Was used in some EU countries to replace S19, but was stopped due to the be variability in protection and	Strain 75/79-AB (a dissociated form of strain 82) seems not to induce abortions in cattle.

Table 7: Comparison of the different *B. melitensis* and *B. suis* vaccines

	B. melitensis			*B. suis*	
	Rev 1	M5 or M5-90	H38	Strain 2	353-1
Status	In use. Recognized by OIE (Reference vaccine).	In use: China	Experimental. Abandoned	In use (China only)	Experimental
Type	Live (Smooth)	Live: *B. melitensis* biovar 1	Killed	Live: *B.suis* biovar 1 (strain 2) (Smooth)	Live (Rough)
Origen	Passage on streptomycin media. Resistant to 2.5u/mL streptomycin and susceptible 5 IU penicillin G.	*B. melitensis* virulent strain M28 passaged through chicken		Laboratory adopted, isolated from an aborted sow and attenuated by serial passage.	
Target species	Small ruminants	Goats and sheep	Mice and cows	Pigs	
Other species	Little known about Rev1 preventing melitensis in cattle. OIE does not recommend the use in cattle.	Cattle		Sheep, goats and cattle	
Protection against other Brucella strains	*B. abortus*: One study showed to be more protective than S19 in cows, however there are also reports of virulence. *B. ovis*: Yes *B. suis*:			*B. abortus*: Yes *B. melitensis*: Yes, but Rev1 is better. Others say no. *B. ovis*: Contradictory information.	
Indications	Lambs 3-6 months				
Immunity	Solid and durable immunity, but declines with time. Revaccination advisable in endemic areas.	Three years		Immunity declined compared to S19 and RB51. Two-three years.	Robust humoral and cell-mediated
Route	SC or conjunctival	SC, intranasal, aerosol		Oral (water)	SC or orally
Dose	0,5-2 x10^9 CFU/dose	Cattle SC: 25x10^9, indoor aerosol 25x10^9, outdoor aerosol 40x10^9. Goats & sheep SC or IN: 1x10^9, indoor aerosol: 1x10^9, outdoor aerosol: 5x10^9, oral 25x10^9.		10x10^9 bacteria	10^{10} CFU/dose
Serology on standard tests	SC: Positive Ab response. Used conjunctival to minimise response.	Yes. Cattle: up to 6 months in 5-10% animals by cELISA, but usually less than 3 months. Goats and sheep: not detected	Persistent Ab titres	Does not induce persistent Ab. Strange being smooth strain?	Does not produce serological response on conventional tests
Pathogenicity	Safe enough to be used in young rams or billy goats			Less than S19 and Rev1 in mice	
Efficacy	Highly effective in reducing production losses and disease transmission. Less efficacious at preventing infection (& seroconversion).		Lack of sufficient protection after challenge	Highly effective in reducing production losses and disease transmission. Less efficacious at preventing infection (& seroconversion).	

Continued: Comparison of the different *B. melitensis* and *B. suis* vaccines

	B. melitensis			*B. suis*	
	Rev 1	M5 or M5-90	H38	Strain 2	353-1
Zoonotic characteristics	Yes. More virulent than S19.	Yes			
Use in pregnant animals	Can induce abortions.	It seems to be safe			
Other side defects	Occasional excretion into the milk				
First used	1957	China: 1970		China: 1980's	
Large scale use	Yes: Tajikistan, Portugal	Yes: China		Only China	
Others	It shows instability, so QC is essential. Subject to varying its morphological and immunological properties				

Commercial vaccines manufactured in Africa and Asia

The information summarised in Tables 8 and 9 below, is based on information from The Center for Food Security and Public health, Iowa State University (**www.cfsph.iastate.edu/vaccines/index.php** and Vetvac (**www.vetvac.org**). More details have not been gathered, as another consultant has been commissioned to perform this task.

Table 8: Manufacturers of *Brucella abortus* vaccines in Africa and Asia.

Manufacturer	Country	Name & Strain	Vaccine Type	Countries distribution
AFRICA				
Veterinary Vaccine Research Institute	Egypt	*Brucella abortus* Strain 19 Vaccine	Live	Arab Rep, West Bank and Gaza
NVRI	Nigeria	*Brucella* S19 Vaccine	Live	
OBP	South Africa	*Brucella* S19	Live	Namibia
MSD Animal Health (Merck)	South Africa	RB-51®	Live	

ASIA				
Qilu Animal Health Products Factory	China	Brucellosis vaccine A19	Live	
China Animal Husbandry Group	China	Bovine Brucellosis S19 (for pig & sheep)	Live	
China Animal Husbandry Group	China	M5 or M5-90 (for cattle & sheep)	Live	
Hester Biosciences Limited	India	*Brucella abortus* S19	Live	
Indian Immunologicals Limited	India	Bruvax S19 Cattle & buffalo	Live	
Institute of Animal Health and Veterinary Biologicals	India	*Brucella abortus* S19	Live	
Pusvetma	Indonesia	Brucivet S19	Live	
CAVAC	South Korea	BoviShot® Brucel RB51	Live	

Table 9: Manufacturers of *Brucella melitensis* vaccines in Africa and Asia.

Manufacturer	Country	Name & Strain	Vaccine Type	Countries exported
AFRICA				
OBP	South Africa	*Brucella* Rev.1	Live	Namibia
Vaccine Research Institute	Egypt	*Brucella melitensis* Vaccine Rev1	Live	

ASIA				
Indian Immunologicals Limited	India	Bruvax Rev 1	Live	

Commercial vaccines imported into Africa and Asia

The information summarised Table 10, is based on the same sources mentioned in Table 9, as well as a questionnaire sent to the Directors of Veterinary Services office and regulators of the countries of interest. Note that some vaccines might have been imported under DVS dispensation, and they are not necessary licensed in the country.

Table 10: Commercial *Brucella* vaccines imported into the countries of interest

Country	Vaccine name	Strain or type	Country of origin	Doses imported 2015	Doses imported 2014	Doses imported 2013	Doses imported 2012
ASIA							
Bangladesh	-	-	-	-	-	-	-
India							
Indonesia							
Myanmar (Burma)	-	-	-	-	-	-	-
Nepal	-	-	-	-	-	-	-
Vietnam	-	-	-	-	-	-	-
AFRICA							
Burkina Faso							

Côte d'Ivoire (Ivory Coast)	-	-	-	-	-	-	-
Ethiopia	Bruce19 Vac	S19 Live	Jordan				
	BRUCEVAC (Full, Reduced, or Conjunctival)	Rev1	Jordan				
Kenya	-	-	-	-	-	-	-
Madagascar							
Malawi	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Mali	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Mozambique							
Rwanda	-	RB51	USA	10,000	5,000	2,000	-
Senegal							
South Africa							
Tanzania	-	-	-	-	-	-	-
Uganda	-	S19	Various	4,000	16,000	0	60,000
Zambia	-	S19	South Africa	26,790	63,900	39,000	-
	-	RB51	South Africa	6,250	6,000	1,600	-

- Questionnaire received, no information provided.

Other comments

JOVAC, the manufacturer from Jordan was also sent a questionnaire designed for key importers into the region. They confirmed that they export *B. abortus* S19 vaccine (Bruce19 vac) to Asia and Africa, and *B. melitensis* Rev1 (Brucevac) also to Africa and Asia. They did not specify the countries or the volumes.

Characteristics of Ideal Vaccine Candidates for Smallholders

The Target Product Profiles (TPPs) reflect the availability and utility of current agents and incorporate features that will be necessary to improve on the current products and to address unmet needs, taking into account the particular requirements of the poorest livestock keepers.

The TPPs are more robust when they include the opinions and consider the needs of the different stakeholders. While efforts have been made to encompass them, the TPP showed in Table 11 below, should be considered a proposal, a live document subject to improvements.

Information on current vaccines has been obtained from the datasheet of different products. An example of each is mentioned in the links below:

RB51: **http://www.msd-animal-health.co.za/products/rb_51/020_product_details.aspx**

S19: **http://www.msd-animal-health.co.in/products/*Brucella*/020_product_details.aspx**

Rev1: **http://www.czveterinaria.com/en/productos/rev-1.html**

Rev1 ocular: **http://www.czveterinaria.com/en/productos/ocurev.html**

Table 11: Target Product Profile (TPP) *Brucella* vaccine – Proposal:

	Attribute	Minimum (current available vaccine)	Ideal
1	Antigen	Immunogen with protective antigens for *Brucella abortus* **OR** *B melitensis*	Immunogen with protective antigens to *Brucella abortus, B. melitensis, B. ovis* **AND** *B. suis*

2	Indication for use	For active immunization of cattle OR sheep and goats. Some strains are not indicated for adult animals or males.	For active immunization of cattle, water buffalo, sheep, goats and pigs of all ages and sexes.
3	Recommended species	Cattle or sheep and goats	Cattle, buffalo, sheep, goats and pigs. Also all susceptible animals, including susceptible wildlife that may get in contact with domestic livestock.
4	Recommended dose	Cattle: 2 - 5 ml SC Sheep and goats: 1-2 ml SC Intraocular: 0.035 ml (one drop)	Same dose for all species (2 ml)
5	Pharmaceutical form	Reconstituted injectable solution/suspension	Ready to use solution/suspension
6	Route of administration	SC or conjunctival (*B. melitensis* M5 China: aerosol)	SC, Intramuscular or conjunctival
7	Regimen - primary vaccination	Single dose	Single lifetime dose
8	Regimen - booster	S19: No RB51: Single annual booster (if desired, but not required) Rev1: No	Lifelong immunity after primary vaccination
9	Epidemiological relevance	Protection against *B. abortus* OR *B. melitensis*	Protection against *B. abortus, B. melitensis, B. ovis* AND *B. suis*.
10	Recommended age at first vaccination	S19: Heifers 3-8 months of age. RB51: Heifers 4 - 10 months of age with 2 mℓ administered SC. Revaccinate with full dose 12 – 16 months of age. Rev1: 4-6 months of age, 3 months for reduced dose	From 1-2 months of age, when other vaccines are applied.
11	Onset of immunity		One week following primary vaccination

12	Duration of immunity	At least 1 year	Lifelong immunity
13	Expected efficacy	To prevent disease & prevent mortality.	To prevent infection and transmission in 100% of the animals. No disease & no mortality in vaccinated animals after virulent challenge.
14	Expected safety	Local reaction can occur at the site of injection. Mild temperature increase might occur. Risk of abortion in pregnant animals. Bulls: can cause persistent orchitis	No post-vaccinal reactions at any age. Safe for pregnant animals at any stage. Safe for all sexes at any age.
15	Withdrawal period	S19: RB51: 3 weeks Rev1: 21 days meat, 90 days milk	Nil for milk and meat
16	Special requirements for animals	Do not vaccinate un-healthy animals. Do not vaccinate pregnant animals or animals in lactation. Avoid antibiotic therapy before and after vaccination for a period of 21 days.	Vaccinate all animals
17	Special requirements for persons	Several as they are pathogenic for humans: Avoid direct contact. Do not eat, drink or smoke during administration of the vaccine. Burn or sterilize container after use.	None
18	Package size	5-25 doses	Multiple pack size from 5 doses
19	Price to end user		

20	Storage condition and shelf-life as packaged for sale	Stable at 4-8°C for 12 months	Stable at 30°C for 24 months
21	In-use stability	S19: 2 hours RB51: Rev1:	24 hours or greater
22	Other: Interference with diagnostics	Interfere with some (or all) available diagnostics	Do not interfere with diagnostics regardless of route of administration or age.

Combination vaccines:

There are many combinations that might be of interest. They will vary depending on the species and geography.

For cattle, a combined vaccine with Tuberculosis could be of great value, especially for dairy on small holder farmer settings and cooperatives. FMD could also be considered.

For small ruminants, combinations with any vaccine routinely used in the area, for example clostridium, could be of interest. Of public health importance is also hydatid disease.

For pigs, it will really depend on the geography. In SE Asia, combination with FMD and CSF could be good. In Africa, pigs are rarely vaccinated. Ideally, any vaccine that could be combined with ASF would be of great value. From the public health point of view, combination with cysticercosis would be of value.

Limitations

Scientific quality: The publications and data from the different research groups, should be carefully evaluated. The use of good science and good experimental design with use of proper controls, adequate numbers, suitable challenge model, reproduction of results by them and by independent groups, and appropriate analysis has not been verified for this monograph. If any of these projects were to be pursued, a detailed peer review taking into account the above considerations is strongly recommended.

Other considerations for vaccine improvement and development:

1. The murine model is not as good model as it seems. *Brucella* is not a natural host and tends to produce splenic and liver colonisation in mice, while in the other animals affects mostly the lymphoreticular system. The responses of inbred strains of mice do not accurately reflect the immune responses of heterozygous livestock. It has previously been observed that data form murine models has failed to predict immunogenicity or efficacy of vaccines in domestic animals [88]. Attention should be given to vaccines evaluated in the target species.
2. There is a lack of knowledge on protective epitopes. It is not likely that a single epitope will produce a robust immune response. Vaccines expressing one epitope might not produce robust immunity. Some antigens have been identified with protection, but not all. The role of antibodies is not clearly known.
3. The different species of *Brucella* have over 90% homology. Therefore, it is expected that many strains will give protection. However, it is important to evaluate what will work with a single dose, duration of immunity (in years), cost of delivery, etc..
4. However, it is questionable if a *Brucella ovis* vaccine will protect across species as it is quite different, and there are some species limitations. For example, *B. abortus* in pigs tends to be cleared quickly.
5. Many vaccines will work if there is an annual vaccination policy. The key point is which one provides better protection. A side by side analysis of the different vaccines would be very valuable. For example, there is contradictory information about efficacy of the different vaccines for *B. melitensis* in cattle. A side by side comparison of the current vaccines (including S19, RB51, Rev1) with some of the most promising candidates (ideally the ones already evaluated in target species) for *B. melitensis* in cattle would be very valuable.
6. Live vaccines prevent infection (and abortions), but they do not stop colonisation (shedding in milk in lactating animals).

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2. The Center for Food Security & Public Health. Iowa State University, USA.

   Brucellosis: **http://www.cfsph.iastate.edu/Factsheets/pdfs/brucellosis.pdf**

   Brucella abortus: **http://www.cfsph.iastate.edu/Factsheets/pdfs/brucellosis_abortus.pdf**

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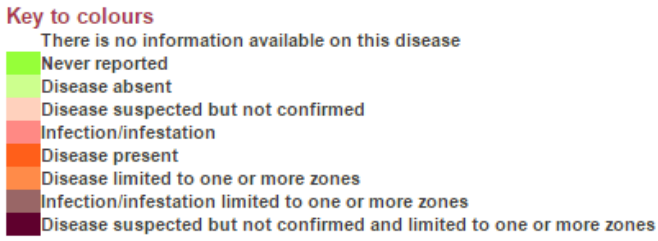
ANNEX 1: Additional data on disease presence and incidence

Reports to OIE on *Brucella abortus*:

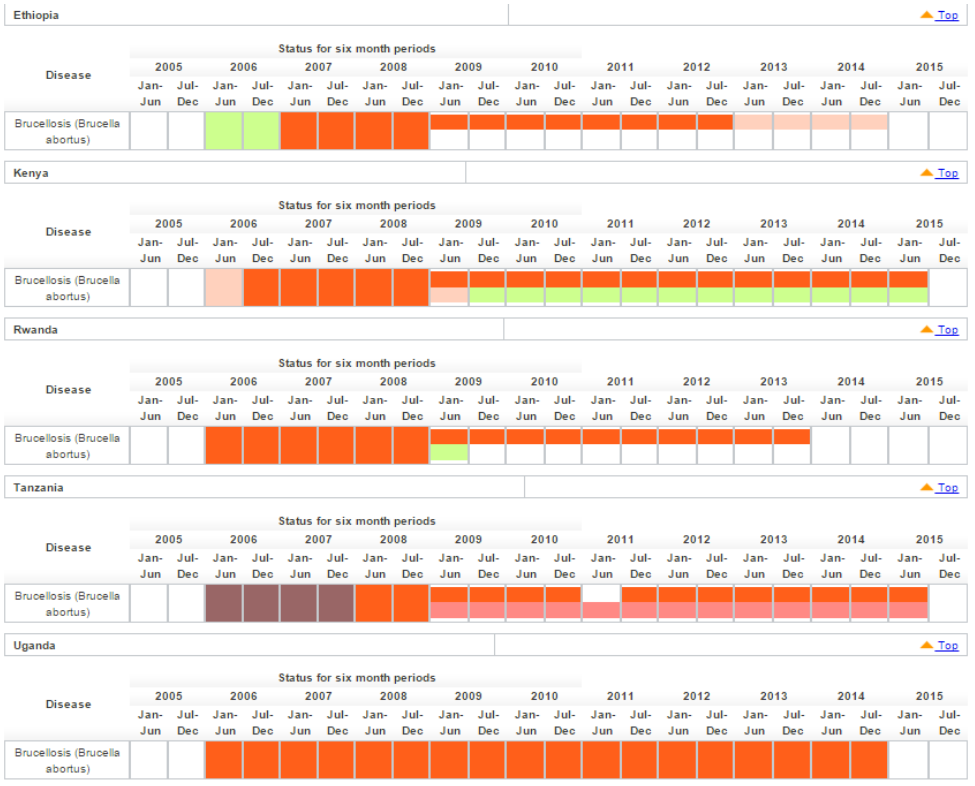


When different animal health statuses between domestic and wild animal population are provided, the box is split in two: the upper part for domestic animals, and the lower part for wild animals.

***Brucella abortus* in Asia: Bangladesh, India, Indonesia, Myanmar, Nepal and Vietnam**

Brucella abortus in Western Africa: Burkina Faso, Ivory Coast, Mali and Senegal

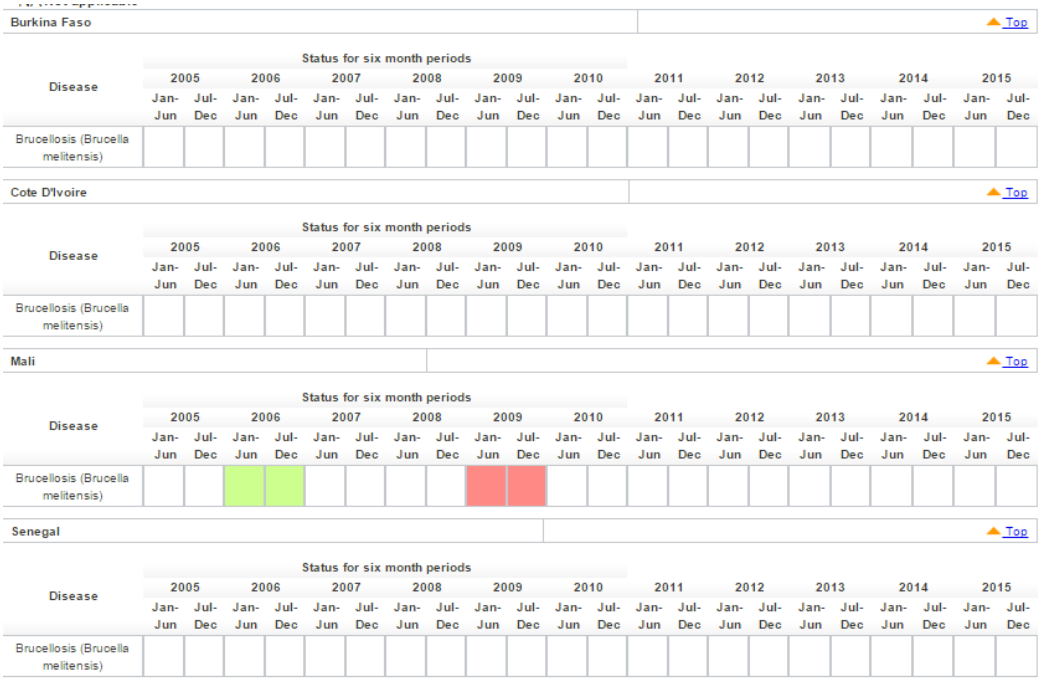
Brucella abortus in Eastern Africa: Ethiopia, Kenya, Rwanda, Tanzania and Uganda



Brucella abortus in Southern Africa: Madagascar, Malawi, Mozambique, South Africa and Zambia

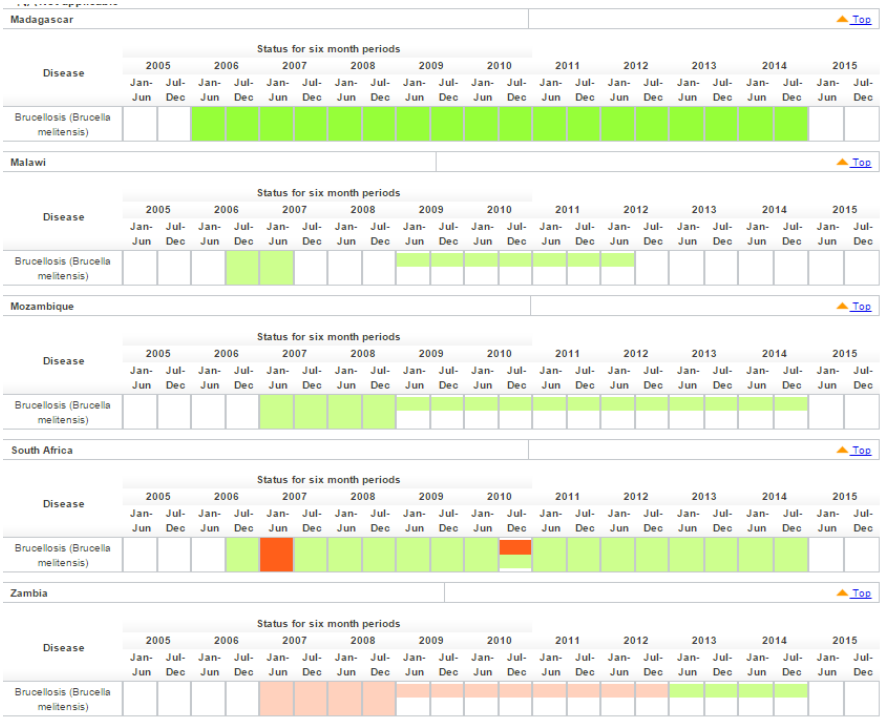
Brucella melitensis in Asia: Bangladesh, India, Indonesia, Myanmar, Nepal and Vietnam

Brucella melitensis in Western Africa: Burkina Faso, Ivory Coast, Mali and Senegal

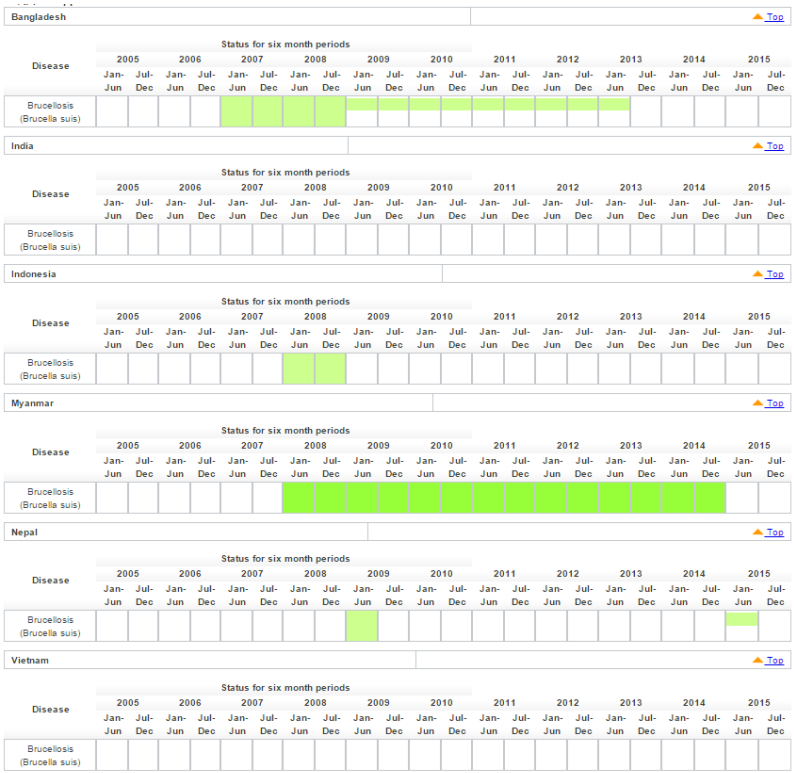


Brucella melitensis in Eastern Africa: Ethiopia, Kenya, Rwanda, Tanzania and Uganda

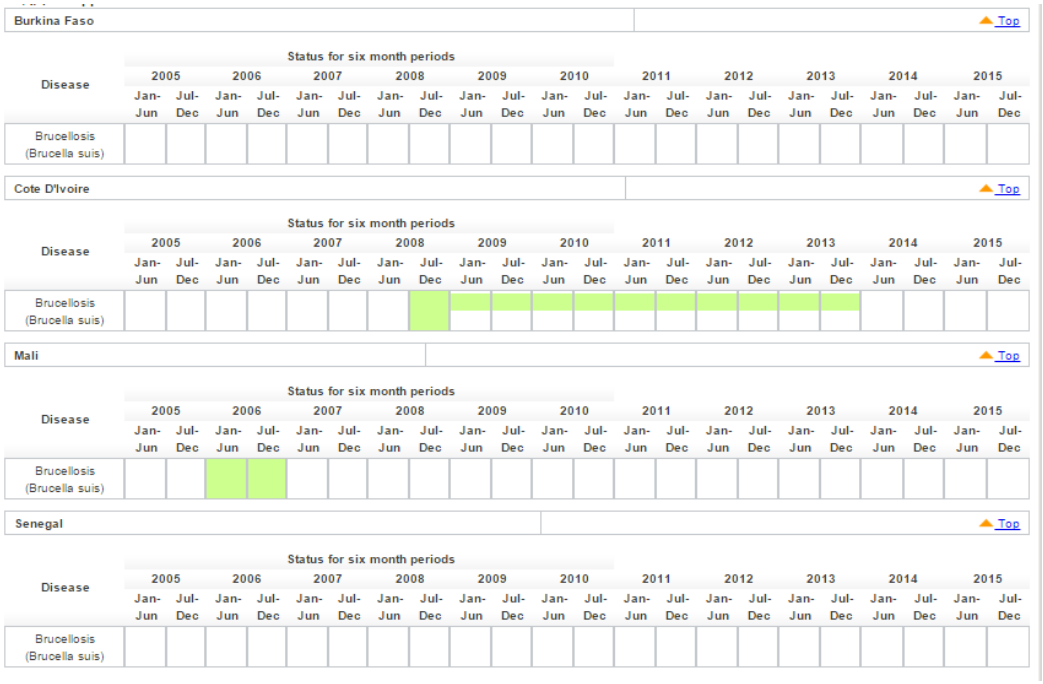
Brucella melitensis in Southern Africa: Madagascar, Malawi, Mozambique, South Africa and Zambia



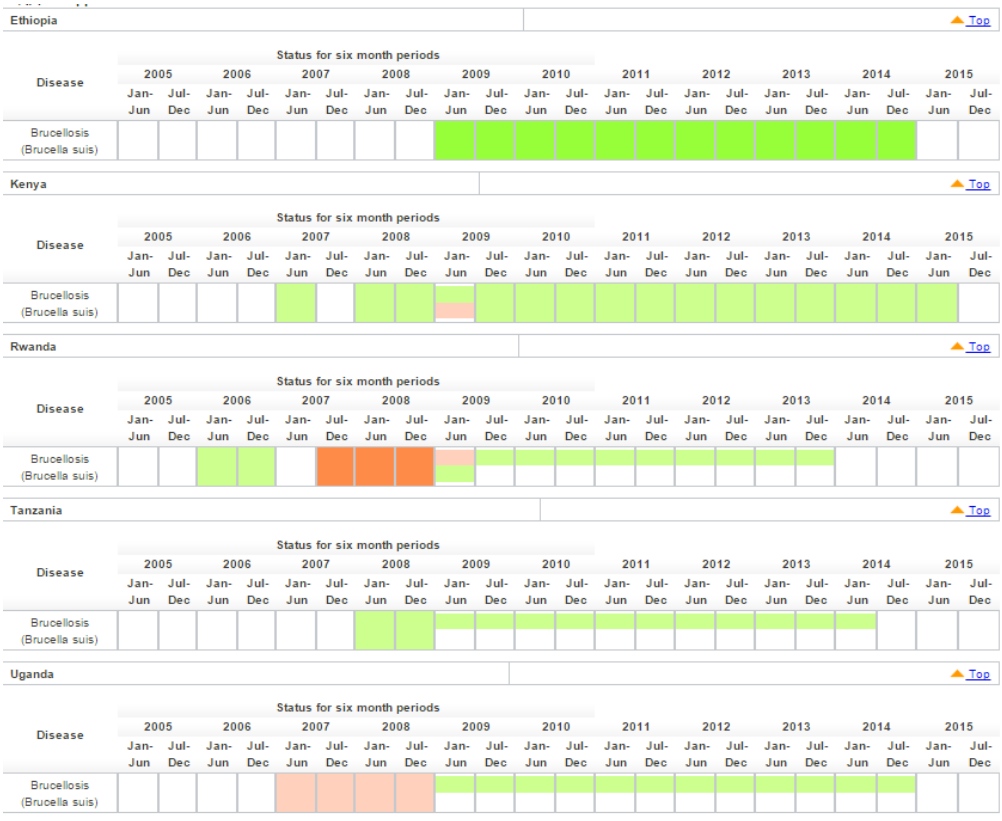
Brucella suis in Asia: Bangladesh, India, Indonesia, Myanmar, Nepal and Vietnam



Brucella suis in Western Africa: Burkina Faso, Ivory Coast, Mali and Senegal



Brucella suis in Eastern Africa: Ethiopia, Kenya, Rwanda, Tanzania and Uganda



Brucella suis in Southern Africa: Madagascar, Malawi, Mozambique, South Africa and Zambia