Characterization and evolution of countries affected by bovine brucellosis (1996 - 2014)

Short title

Evolution of bovine brucellosis in the world (1996-2014)

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Summary

This paper describes the global distribution and temporal evolution of bovine brucellosis due to *Brucella abortus* during a 19-year period (1996 – 2014) using the information officially reported to the World Organisation for Animal Health (OIE) by veterinary services of 156 countries. Variables that can influence the health status of bovine brucellosis (i.e., year, per capita Gross Domestic Product (GDP), continent, and bovine population) were also analysed. Countries were classified into three categories of health situations: *ENZOOTIC*: countries infected, which may have been free of brucellosis but for periods of fewer than 3 years; *NON-ENZOOTIC*: countries where the disease was present but that had at least a 3-year period without the disease; and *FREE*: countries where the disease remained absent during the whole period. The countries free from bovine brucellosis, or in the process of eradication, were located in Oceania and Europe, while the more affected regions were Central and South America, Africa, and parts of Asia. Among the Non-Enzootic countries, the results showed that a very high proportion managed to control the disease during the period of study, with a sharp decline in the percentage of infected countries from 71% in 1996 to 10% in 2014. Among the Enzootic countries, a much smaller proportion managed to control the disease, with a slight drop in the percentage of infected countries from 92% in 1996 to 80% in 2014. A relationship was found between the status of the disease and the availability of economic resources; thus, countries with a high GDP per capita tended to be free from bovine brucellosis. On the other hand, countries with a larger bovine population showed a greater probability to have the disease present. An increase in surveillance programmes and implementation of control policies were observed during the period of study.

Key words: bovine brucellosis, brucellosis, global distribution, Handistatus, OIE, WAHIS

1. Introduction

Bovine brucellosis is widespread and is of major importance due to its impact on both animal and human health (Alves et al., 2015). According to the World Health Organization estimates, approximately 400,000 people become infected yearly from *Brucella* by a foodborne route, with almost half of the cases appearing in the Eastern Mediterranean Region (World Health Organization, 2015). It causes significant economic losses in cattle production due to reproductive disorders (placentitis, metritis, retention of the placenta, and abortion in pregnant cows and epididymitis, vesiculitis, and orchitis in bulls) and the consequent reduction in milk production and increase in calving intervals. The annual economic losses attributable to bovine brucellosis have been estimated to be US$ 448 million in Brazil (Santos, Martins, Borges, & Paixão, 2013) and US$ 3.4 billion in India (Singh, Dhand, & Gill, 2015).

Control of bovine brucellosis requires significant resources and sustained efforts. Several epidemiological factors linked to the disease can complicate its control and eradication: 1) the presence of wildlife reservoirs (Bengis, Kock, & Fischer, 2002), 2) the spill-over effect (Schumaker, 2013), and 3) the difficulties of clinical diagnosis due to non-specific symptoms, which make bovine brucellosis underestimated at the farm level when diagnostic tests are not applied (de Figueiredo, Ficht, Rice-Ficht, Rossetti, & Adams, 2015; Godfroid et al., 2013). Brucellosis is a neglected disease in endemic developing countries, and the main reasons for this are the absence of specific clinical signs, the lack of systematic application of laboratory tests, which are essential for its diagnosis (Díaz, Casanova, Ariza, & Moriyón, 2011), and difficulty in attracting the attention of health authorities.

In accordance with its characteristics, bovine brucellosis control and eradication can also be complicated by several factors, such as the socio-cultural practices associated with the country in which it occurs. The disease is more controlled in dairy bovine production systems than in beef-only farms (de Alencar et al., 2016). Extensive beef-cattle animals located in agro-pastoral systems are exposed to an environment (water-points and pastures) contaminated by reproductive discharges (Adamu et al., 2016) of other herds or flocks that are moving through different pastures depending on food availability (Jackson, Nydam, & Altier, 2014). Likewise, nomadic livestock populations, low herd biosecurity, and lack of farmer sensitization (Alhaji, Wungak, & Bertu, 2016; Aznar et al., 2015) can contribute to the persistence of the disease.

Availability of sufficient economic resources is of paramount importance in bovine brucellosis control and eradication, as it is a determining factor in the capacity of the Veterinary Service to respond to an epidemiological episode. In most cases, co-operation between government and industry is key for coordinating efforts and eradicating the disease (More, Radunz, & Glanville, 2015). Some examples of this success are the eradication of the disease in the Czech Republic (Kouba, 2003) and in the United States in domestic animals (Ragan, 2002).

Meanwhile, in a country where there is inadequate economic investment in health policies, this impedes the application of appropriate control measures over time (Howe, Häsler, & Stärk, 2013; Ibironke, McCrindle, Fasina, & Godfroid, 2008; Kouba, 2003; McDermott, Grace, & Zinsstag, 2013; Pavade, Awada, Hamilton, & Swayne, 2011; Ragan, 2002).

Despite the global importance of bovine brucellosis, few studies have described its global distribution and long-term evolution (Lopes, Nicolino, & Haddad, 2010; Seleem, Boyle, & Sriranganathan, 2010). Such studies provide useful information on disease trends in different world regions and on surveillance and control strategies implemented according to the situation of the disease.

The main objective of this paper was to characterize and describe changes in bovine brucellosis-affected countries in the period 1996 - 2014 in order to improve the understanding of the mechanisms applied for its control and eradication. To do this, 18 years of bovine brucellosis data at the international level were used to 1) characterize the countries' health situations as regards bovine brucellosis; 2) determine the characteristics associated with each health situation in the countries; 3) present the evolution of the proportion of affected countries falling into each health situation; 4) describe the evolution of surveillance programmes and implementing control policies addressing each health situation; and 5) evaluate the stability of these surveillance programmes and implementing control policies over time. The findings should provide valuable information about the status of the disease worldwide and insights for improving the measures necessary to minimize the impacts of this disease.

2. Materials and methods

2.1. Materials

The data used to determine the health status of countries, surveillance programmes, and control policies implemented, as well as yearly figures on national bovine populations, were obtained from the World Organization for Animal Health (OIE), which has a mandate that includes ensuring transparency in the global animal disease situation. These data are submitted to the OIE by the National Veterinary Authorities of 180 Member Countries, who have the legal obligation to report information concerning highly impacting animal diseases, including bovine brucellosis. Additionally, more than 20 other countries and territories provide information to the OIE on a voluntary basis. Data used in this study were derived from two related collection systems. From 1996 to 2004, countries provided information stored in Handistatus II (OIE, 2017a); from 2005 to 2014, countries provided information via the World Animal Health Information System (WAHIS) (OIE, 2017b). A quality check was performed, and inconsistencies or missing records in the information collected by the OIE were systematically clarified by contacting the National Veterinary Services of the reporting countries. To be consistent with the data over these 19 years, only the 156 countries that remained Members of the OIE during the whole study period (1996-2014) were considered for the study (42 countries located in Africa, 25 in America, 40 in Asia, 45 in Europe, and 4 in Oceania).

Information on national Gross Domestic Product (GDP), corresponding to annual income values per capita (in US$), was obtained from the World Bank for the period between 1996 and 2014, and its value was deflated to the year 2014 for comparison purposes (The World Bank, 2017). The average deflated GDP over the period of analysis was then calculated for each country. Census data (number of animals) of bovine and bubaline populations were obtained from WAHIS for each country and year evaluated (OIE, 2017c).

2.2. Methods

2.2.1. Classification of countries based on their health situation from 1996 to 2014

Countries were classified into three categories of health situations from 1996 to 2014: a) *FREE countries*: countries where the disease remained absent throughout the whole study period; b) *NON-ENZOOTIC countries*: countries where the disease was present for one or more years, but there was at least a 3-year period without the disease (according to *OIE Terrestrial Animal Health Code* (OIE, 2017d), a period of 3 years represents the minimum time needed to reach disease-free status); and c) *ENZOOTIC countries*: countries where the disease was present and for which all periods of absence were less than 3 years.

Countries were mapped according to their health situation using Quantum GIS version 2.18.11 (Quantum GIS Development Team, 2017).

2.2.2. Country characteristics associated with each health situation and their evolution

The health situation of bovine brucellosis along the period was described, and the status of bovine brucellosis was compared with the economic resources and bovine populations of countries.

The evolution of surveillance programmes and implementing control policies are described for the three defined groups of countries. Reporting at least one of the following measures was considered as a proxy for the application of a ***surveillance programme***: "disease notifiable", "monitoring', "screening", "targeted surveillance", "general surveillance". Countries that applied at least one of the control measures included in WAHIS ("control of movements within the country", "stamping out", "modified stamping out", "zoning", "vaccination") were classified as ***implementing control policies***.

For each country, the continuity of the surveillance and control measures was evaluated by counting the number of times there was a switch from "activities applied" to "no activities applied" and vice versa. The Chi-squared test was calculated, and the results were plotted for the three groups of countries.

2.2.3. Statistical analysis

For the comparison of the GDP and population size with the three categories of countries, normality of the data was tested using the Shapiro-Wilk test. As the tests showed non-normality distributions (Shapiro-Wilk test, $p<0.05$) in all cases, the differences between the three groups were evaluated using a non-parametric test, the Kruskal-Wallis test. Pairwise comparisons were tested using the Mann-Whitney U test. All statistical analyses were performed using R software version 3.3.3 (R Development Core Team, 2017).

The relationship between the absence or presence of the disease in the countries and the years and health categories was evaluated using a Generalized Linear Model (GLM) with a binomial distribution (for the model, Enzootic health category was considered the reference). GLM were also used with the application, or not, of surveillance programmes and control policies using the same explanatory variables as the disease status model.

3. Results

The global distribution of countries based on their health situation from 1996 to 2014 is presented in Figure 1. The majority of the countries (67.3%) are classified as *ENZOOTIC*, especially those from America and Asia. Europe has most of the *NON-ENZOOTIC* countries, with the Free countries being located in Eastern and Northern Europe and Oceania (Table 1).

Figure 2 shows that Enzootic countries had much lower GDP values than *FREE* and *NON-ENZOOTIC* countries (median of $2,694 *vs* $12,140, and $18,191, respectively). The differences between the three groups were statistically significant (Kruskal-Wallis Chi-squared = 24.2, df = 2, p-value <0.001), and the Pairwise comparisons between groups also showed significant within-group differences ($p<0.001$).

The bovine population size showed different patterns between the three groups: the median of the bovine population in *ENZOOTIC* and *NON-ENZOOTIC* countries was higher than in *FREE* countries (median of 3 and 2.5 vs 0.55 million, respectively) (Figure 3). The differences were statistically significant (Kruskal-Wallis Chi-squared = 17.8, df = 2, p-value < 0.001), and the Pairwise comparisons showed a significant difference between *ENZOOTIC* and *FREE* countries (p<0.001) but not between *ENZOOTIC* and *NON-ENZOOTIC* countries.

The health situation was very different in the *ENZOOTIC* and *NON-ENZOOTIC* groups. Countries categorized as *NON-ENZOOTIC* had a lower probability of reporting the disease than Enzootic countries (OR=0.09), and the presence of the disease decreased significantly, with an OR=0.92 (Table 2). In *NON-ENZOOTIC* countries, the percentage of affected countries considerably decreased from 71% in 1996 to 10% in 2014. In *ENZOOTIC* countries, the percentage of affected countries remained between 80% and 94% during the studied period (Figure 4).

The application of surveillance programmes increased significantly over the period (Table 2) but without a clear trend (Figure 5). There were no differences between the groups.

Countries from the *ENZOOTIC* group applied control policies more often than the *NON-ENZOOTIC* and *FREE* group countries (OR=0.49 and OR=0.35, respectively). The control policies increased 0.02 each year (Table 2, Figure 6).

With regards to surveillance programmes and the implementation of control policies, another important aspect is the stability of the measures throughout the period. In total, 47% of Free countries maintained surveillance without variations, while these percentages were 33% and 30% for *NON-ENZOOTIC* and *ENZOOTIC* countries, respectively. The median number of times that countries switched from applying surveillance policies to not, or vice versa, was 2 in

Enzootic countries and 1 in *NON-ENZOOTIC* and *FREE* countries, with no significant differences between the groups (Kruskal-Wallis Chi-squared = 4.8345, df = 2, p-value = 0.089) (Figure 7).

Implementing control policies in affected countries were maintained, with no variations in 38% of *ENZOOTIC* countries and 19% of *NON-ENZOOTIC* countries. The median number of changes of control policies was 1 in *ENZOOTIC* countries and 3 in *NON-ENZOOTIC* countries, but the differences between groups were not significant (Kruskal-Wallis test p-value = 0.08) (Figure 8).

4. Discussion

Bovine brucellosis is one of the priority animal diseases due to its impact on public health, economics, and trade (OIE, 2014). Historical health data at a global level can help to understand the evolution of diseases as well as improve the surveillance programmes and the management of animal diseases, Therefore, they can be very useful in health policy planning by the Veterinary Services (Stärk & Häsler, 2015). These results provide a good picture of the health distribution and evolution of bovine brucellosis in the world and in different regions.

More than two-thirds of the countries encountered enzootic situations, with this group being comprised mostly of developing countries, consistent with other studies. Corbel (1997), reported that the disease is a major problem in the Mediterranean region, western Asia, and parts of Africa and Latin America. Regional studies in South America found countries with a high prevalence of brucellosis for a long period of time. The reasons for this enzootic situation have been attributed to the limited economic resources invested for the diagnosis and control of infectious diseases, being discontinuous, non-systematic measures, and a lack of incentives in beef cattle to achieve the brucellosis-free certification, among other reasons (Aznar, Samartino, Humblet, & Saegerman, 2014; Moreno, 2002). Another study of Sub-Saharan Africa describes the role of different wild mammals as reservoirs and a lack of diagnosis, both at individual and population levels, as reasons for endemicity in this region (Ducrotoy et al., 2017). Finally, Ali et al. (2017) and Lindahl-Rajala et al. (2017) showed high incidence rates in livestock in Central Asia and the Middle East areas due to the close contact between people and livestock and that brucellosis is considered a neglected zoonosis.

Thirty countries remained free of bovine brucellosis during the whole period of analysis, and 21 countries showed the presence of the disease in one or more periods of three years without being reported. These numbers might be overestimated given that, in some countries, diseases can remain under-reported due to deficient surveillance.

There are important geographic variations in bovine brucellosis status. The success of Oceania countries was based on a strict control programme that included animal identification, classification of herds according to their health status, severe restrictions on the movement of cattle between areas, monitoring of herds, compensation to producers for elimination of positive animals, optimization of laboratory procedures, registration of data on epidemiological information, and training for all participants (Shepherd, Simpson, & Davidson, 1980; Tweddle & Livingstone, 1994). In addition, the absence of known wildlife reservoirs in these countries has been contributed to the maintenance of the status (Radunz, 2006).

Since the 1940s, European countries have implemented programmes for the brucellosis eradication; in 1964, the European Union (EU) established a common eradication programme. More recently, they have established combined clinical surveillance and risk-based screening of herds to have early warning in case of a resurgence to allow for a rapid response (Hénaux &

Calavas, 2017). As a result of these policies, 44% of European countries were brucellosis-free during the whole period. Despite the eradication programme, some countries of Southern Europe remain infected. Some authors (Calistri et al., 2013; Taleski et al., 2002) have suggested the following reasons to explain the difficulties of bovine brucellosis eradication in this region: lack of stability of eradication policies, lack of epidemiological data, difficulties of disease eradication in rural areas, lack of laboratory capabilities, and the existence of wildlife reservoirs.

In Africa, Asia and the Americas, the impact of the disease is still huge, and many factors are involved in the endemicity of the disease (Lindahl-Rajala et al., 2017):

- *Lack of eradication policy*: a test-and-slaughter programme with compensation to producers is not implemented in many countries due to insufficient financial resources (Cárdenas, Melo, & Casal, 2017; Ducrotoy et al., 2017; Ibironke et al., 2008). The predominant strategy of eradication in Latin America is a voluntary programme based on removing positive animals from the herd. This strategy is very advantageous for dairy farmers because milk is better paid, but this is not the case for beef farmers. Similar conditions have been pointed out in Africa, where the trade dairy products require baseline information about the health of dairy cattle due to the public health implications (Terefe, Girma, Mekonnen, & Asrade, 2017). In Asian Hindu-culture countries, elimination of infected animals is not feasible due to the prohibition of slaughtering cattle. Finally, the absence of veterinary services in remote areas may have contributed to the high occurrence of the disease (Mekonnen, Kalayou, & Kyule, 2010).
- *Lack of a surveillance strategy and disease monitoring:* Insufficient financial resources of governments is a big constraint to the establishment of surveillance and control actions against bovine brucellosis in sub-Saharan Africa (Ibironke et al., 2008). Control of animal

movements is of paramount importance to limit the spread of infections, but it is not always applied. In India, there is no pre-movement control of animals; furthermore, selling positive-reactor animals to other farmers is a usual practice (Singh et al., 2015). The same situation has been described in Africa, where the exchange of bulls for mating between herds and the free introduction of new cattle is common (Alhaji et al., 2016). Finally, other species can become infected and spread the infection, but they are neglected in the brucellosis surveillance activities (Cárdenas et al., 2017).

- *Natural disasters:* Tropical countries are periodically affected by different meteorological phenomena, such as drought, with the consequent poor body conditions and low resistance against diseases. The highest density of animals during the dry seasons along the riverfronts facilitates contacts between animals (Alexander et al., 2012; Deqiu, Donglou, & Jiming, 2002). Tropical storms and floods can increase the movement of animals and disrupt bovine brucellosis-control measures over certain periods of time (Cárdenas et al., 2017).
- *Livestock production systems:* Some pastoral areas have high sero-prevalence that is related to the movements of animals through different pastures depending on food availability (Jackson et al., 2014). This allows contact with animals from other herds or flocks, either directly or indirectly through the water points and pastures contaminated by reproductive discharges (Adamu et al., 2016). The transhumance production systems are common in Africa, and pastoralists have little sensitization or health education on this disease (Alhaji et al., 2016). In developing countries, livestock production is based on small farmers, where a subsistence economy prevails. These are traditional systems of pastoral agriculture, with mixed extensive systems that depend on the available natural resources and that are not well regulated. This is in contrast with developed countries that base their production on modern

systems, with high economic investment (Herrero, Thornton, Gerber, & Reid, 2009).

A strong relationship was observed between economic resources and health situations of countries in this study, in which developing countries, with lower resources, are more exposed to enzootic situations. Goutard et al. (2015) also described that implementation of control and eradication plans is difficult in enzootic countries with a low GDP per capita.

These results also highlight the relationship between the size of the bovine population and the health situations of countries: Countries with a high bovine census were also associated with enzootic situations, as had been previously observed in other studies (Calistri et al., 2013; Yoon et al., 2010). In contrast, high GDP per capita and small bovine populations were associated with free countries (Godfroid et al., 2013; Ragan, 2002). Economic resources enable proper surveillance implementation and the introduction of control strategies, and small bovine populations might be correlated with fewer animal movements, leading to a reduction in the risk of introducing the disease (Economides, 2000).

A gradual increase in the implementation of surveillance programmes for bovine brucellosis has been observed over the years. Eradication of the disease is possible, but it needs strong economic resources and support. An important step towards this goal is the implementation of adequate surveillance activities. The odds ratio observed in the results indicate that there was a significant increase of surveillance efforts in the study period.

The implementation of control programmes in Enzootic countries, and especially vaccination, was greater in comparison to the Free and Non-Enzootic countries. However, there was not a trend in Enzootic countries to increase the implementation of control measures along the study period.

Less than 50% of the countries maintained their surveillance policies without variations during the entire period of study. In some cases, variations are a response to new problems or new situations, but, in some cases, variability is a reflection of planning errors or budget constraints, which can be a problem for bovine brucellosis control.

It is important to consider several limitations of this study. First, there was a possible bias due to the two different tools used for reporting (Handistatus until 2004, and WAHIS until 2014). Both interfaces and storage platforms are distinct (Jebara, Cáceres, Berlingieri, & Weber-Vintzel, 2012), the second one being more complete. Additionally, the verification procedure performed by the OIE on data provided by countries before publication evolved over time. It is reasonable to assume that the information provided in recent years is more reliable than that provided in the 1990s because there is an in-depth process of verification of the information before publication by the OIE.

Additionally, since 2002, the OIE has implemented an active search of non-official information in order to increase the sensitivity of the OIE reporting system (WAHIS). This information is evaluated in the context of the animal health situation prevailing in the country or region concerned and, where appropriate, verified with the OIE Members for the purposes of official confirmation and potential publication. The disease report allows for the early warning and monitoring system for emergency situations and for detailed knowledge of the epidemiological situation (OIE, 2017e; Thiermann, 2005). To minimize bias as much as possible due to inaccurate reports sent by Member Countries or due to the lack of information in some specific years, this study permitted the verification of historical data by communication between the OIE and the corresponding countries. Through this approach, 90% of the information was verified, with 6% of the information being added to the database with the aim of updating and completing the historical information.

In addition, bovine brucellosis is a neglected disease in some regions of Africa and Asia (Ducrotoy et al., 2014, 2017; Hegazy, Moawad, Osman, Ridler, & Guitian, 2011; Lindahl-Rajala et al., 2017). Therefore, the accuracy of official information provided by these countries for bovine brucellosis could be limited. Finally, another bias is related to the number of countries included in the analysis (156) *versus* all existing countries in the world (more than 193 according to the UN) (United Nations, 2017).

It would be desirable to update these analyses in the future, including adding more explanatory factors and sources of information, such as data from human health or from regional platforms, to avoid under-reporting. Other approaches, such as space-time model analysis, with the inclusion of time-dependent variables, may help to understand the relationship between factors and to predict areas with the highest potential for bovine brucellosis. Updating such an analysis in the future would likely show continuous improvement of the bovine brucellosis situation, as eradication strategies are ongoing throughout the world. An alternative method to improve the estimation is to identify countries that have implemented programmes to eradicate the disease and to understand the disease over time in affected areas, not only the presence and absence in the country.

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Conflict of interests statement

The authors declare that they have no conflicts of interest.

References

Adamu, S. G., Atsanda, N. N., Tijjani, A. O., Usur, A. M., Sule, A. G., & Gulani, I. A. (2016). Epidemiological study of bovine brucellosis in three senatorial zones of Bauchi State, Nigeria. Veterinary World, 9(1), 48-52. doi:10.14202/vetworld.2016.48-52

Alexander, K. A., Blackburn, J. K., Vandewalle, M. E., Pesapane, R., Baipoledi, E. K., & Elzer, P. H. (2012). Buffalo, bush meat, and the zoonotic threat of brucellosis in Botswana. PLoS One, 7, e32842. doi:10.1371/journal.pone.0032842

Alhaji, N. B., Wungak, Y. S., & Bertu, W. J. (2016). Serological survey of bovine brucellosis in Fulani nomadic cattle breeds (*Bos indicus*) of North-central Nigeria: Potential risk factors and zoonotic implications. Acta Tropica, 153, 28-35. doi:10.1016/j.actatropica.2015.10.003

Ali, S., Akhter, S., Neubauer, H., Melzer, F., Khan, I., Abatih, E. N., . . . Ahmed, H. (2017). Seroprevalence and risk factors associated with bovine brucellosis in the Potohar Plateau, Pakistan. BMC Research Notes, 10(1), 73. doi:10.1186/s13104-017-2394-2

Alves, A. J. S., Rocha, F., Amaku, M., Ferreira, F., Telles, E. O., Filho, J. H. H. G., . . . Dias, R. A. (2015). Economic analysis of vaccination to control bovine brucellosis in the States of Sao Paulo and Mato Grosso, Brazil. Preventive Veterinary Medicine, 118, 351-358. doi:10.1016/j.prevetmed.2014.12.010

Aznar, M. N., Linares, F. J., Cosentino, B., Sago, A., La Sala, L., León, E., . . . Perez, A. (2015). Prevalence and spatial distribution of bovine brucellosis in San Luis and La Pampa, Argentina. BMC Veterinary Research, 11, 209. doi:10.1186/s12917-015-0535-1

Aznar, M. N., Samartino, L. E., Humblet, M. F., & Saegerman, C. (2014). Bovine brucellosis in Argentina and bordering countries: Update. Transboundary and Emerging Diseases, 61(2), 121-133. doi:10.1111/tbed.12018

Bengis, R. G., Kock, R. A., & Fischer, J. (2002). Infectious animal diseases: The wildlife/livestock interface. Rev Sci Tech, 21(1), 53-65.

Calistri, P., Iannetti, S., Atzeni, M., Di Bella, C., Schembri, P., & Giovannini, A. (2013). Risk factors for the persistence of bovine brucellosis in Sicily from 2008 to 2010. Preventive Veterinary Medicine, 110, 329-334. doi:10.1016/j.prevetmed.2012.12.008

Cárdenas, L., Melo, O., & Casal, J. (2017). Evolution of bovine brucellosis in Colombia over a 7-year period (2006–2012). Tropical Animal Health and Production, 50(1), 19-27. doi:10.1007/s11250-017-1395-4

Corbel, M. (1997). Brucellosis: An overview. Emerging Infectious Diseases, 3, 213-221. doi:10.3201/eid0302.970219

de Alencar, M. A. L. A., Ferreira, F., Neto, J. S., Dias, R. A., Amaku, M., Grisi-Filho, J. H., . . . Gonçalves, V. S. P. (2016). Large-scale study of herd-level risk factors for bovine brucellosis in Brazil. Acta Tropica, 164, 226-232. doi:10.1016/j.actatropica.2016.09.016

de Figueiredo, P., Ficht, T. A., Rice-Ficht, A., Rossetti, C. A., & Adams, L. G. (2015). Pathogenesis and immunobiology of brucellosis: Review of brucella–host interactions. The American Journal of Pathology, 185, 1505-1517. doi:10.1016/j.ajpath.2015.03.003

Deqiu, S., Donglou, X., & Jiming, Y. (2002). Epidemiology and control of brucellosis in China. Veterinary Microbiology, 90(1-4), 165-182. doi:10.1016/s0378-1135(02)00252-3

Díaz, R., Casanova, A., Ariza, J., & Moriyón, I. (2011). The rose bengal test in human brucellosis: A neglected test for the diagnosis of a neglected disease. PLoS Neglected Tropical Diseases, 5, e950. doi:10.1371/journal.pntd.0000950

Ducrotoy, M., Bertu, W. J., Matope, G., Cadmus, S., Conde-Álvarez, R., Gusi, A. M., . . . Moriyón, I. (2017). Brucellosis in sub-saharan Africa: Current challenges for management, diagnosis and control. Acta Tropica, 165, 179-193. doi:10.1016/j.actatropica.2015.10.023

Ducrotoy, M. J., Bertu, W. J., Ocholi, R. A., Gusi, A. M., Bryssinckx, W., Welburn, S., & Moriyón, I. (2014). Brucellosis as an emerging threat in developing economies: Lessons from Nigeria. PLoS Neglected Tropical Diseases, 8, e3008. doi:10.1371/journal.pntd.0003008

Economides, P. (2000). Control of zoonoses in cyprus. Revue Scientifique et Technique de l'OIE, 19, 725-734. doi:10.20506/rst.19.3.1246

Godfroid, J., Al Dahouk, S., Pappas, G., Roth, F., Matope, G., Muma, J., . . . Skjerve, E. (2013). A "One Health" surveillance and control of brucellosis in developing countries: Moving away from improvisation. Comparative Immunology, Microbiology and Infectious Diseases, 36, 241-248. doi:10.1016/j.cimid.2012.09.001

Goutard, F. L., Binot, A., Duboz, R., Rasamoelina-Andriamanivo, H., Pedrono, M., Holl, D., . . . Roger, F. L. (2015). How to reach the poor? Surveillance in low-income countries, lessons from experiences in Cambodia and Madagascar. Preventive Veterinary Medicine, 120(1), 12-26. doi:10.1016/j.prevetmed.2015.02.014

Hegazy, Y. M., Moawad, A., Osman, S., Ridler, A., & Guitian, J. (2011). Ruminant brucellosis in the Kafr El Sheikh governorate of the Nile Delta, Egypt: Prevalence of a neglected zoonosis. PLoS Neglected Tropical Diseases, 5, e944. doi:10.1371/journal.pntd.0000944

Hénaux, V., & Calavas, D. (2017). Evaluation of the cost-effectiveness of bovine brucellosis surveillance in a disease-free country using stochastic scenario tree modelling. PLoS One, 12, e0183037. doi:10.1371/journal.pone.0183037

Herrero, M., Thornton, P. K., Gerber, P., & Reid, R. S. (2009). Livestock, livelihoods and the environment: Understanding the trade-offs. Current Opinion in Environmental Sustainability, 1(2), 111-120. doi:10.1016/j.cosust.2009.10.003

Howe, K. S., Häsler, B., & Stärk, K. D. C. (2013). Economic principles for resource allocation decisions at national level to mitigate the effects of disease in farm animal populations. Epidemiology and Infection, 141(1), 91-101. doi:10.1017/s095026881200060x

Ibironke, A. A., McCrindle, C. M., Fasina, F. O., & Godfroid, J. (2008). Evaluation of problems and possible solutions linked to the surveillance and control of bovine brucellosis in sub-saharan Africa, with special emphasis on Nigeria. Vet Ital, 44, 549-556.

Jackson, D. S., Nydam, D. V., & Altier, C. (2014). Prevalence and risk factors for brucellosis in domestic yak Bos grunniens and their herders in a transhumant pastoralist system of Dolpo, Nepal. Preventive Veterinary Medicine, 113(1), 47-58. doi:10.1016/j.prevetmed.2013.09.016

Jebara, K. B., Cáceres, P., Berlingieri, F., & Weber-Vintzel, L. (2012). Ten years' work on the World organisation for animal health (OIE) Worldwide animal disease notification system. Preventive Veterinary Medicine, 107(3-4), 149-159. doi:10.1016/j.prevetmed.2012.08.008

Kouba, V. (2003). A method of accelerated eradication of bovine brucellosis in the Czech Republic. Revue Scientifique et Technique de l'OIE, 22, 1003-1012. doi:10.20506/rst.22.3.1447

Lindahl-Rajala, E., Hoffman, T., Fretin, D., Godfroid, J., Sattorov, N., Boqvist, S., . . . Magnusson, U. (2017). Detection and characterization of *Brucella* spp. in bovine milk in small-scale urban and peri-urban farming in Tajikistan. PLOS Neglected Tropical Diseases, 11, e0005367. doi:10.1371/journal.pntd.0005367

Lopes, L. B., Nicolino, R., & Haddad, J. P. A. (2010). Brucellosis - risk factors and prevalence: A review. The Open Veterinary Science Journal, 4(1), 72-84. doi:10.2174/1874318801004010072

McDermott, J. J., Grace, D., & Zinsstag, J. (2013). Economics of brucellosis impact and control in low-income countries. Revue Scientifique et Technique de l'OIE, 32, 249-261. doi:10.20506/rst.32.1.2197

Mekonnen, H., Kalayou, S., & Kyule, M. (2010). Serological survey of bovine brucellosis in barka and arado breeds (Bos indicus) of Western Tigray, Ethiopia. Preventive Veterinary Medicine, 94(1), 28-35. doi:10.1016/j.prevetmed.2009.12.001

More, S. J., Radunz, B., & Glanville, R. J. (2015). Lessons learned during the successful eradication of bovine tuberculosis from Australia. Veterinary Record, 177, 224-232. doi:10.1136/vr.103163

Moreno, E. (2002). Brucellosis in central America. Veterinary Microbiology, 90(1-4), 31-38. doi:10.1016/s0378-1135(02)00242-0

OIE. (2014). World organisation for animal health. Final reports of the general sessions on the World assembly of the delegates of the OIE. Final Report 2014, 82nd General Session, Paris 2014. Retrieved from http://www.oie.int/fileadmin/Home/eng/About_us/docs/pdf/A_FR_2014_public.pdf

OIE. (2017a). World organisation for animal health. 2017. Handistatus interface: Animal Health Data (prior to 2005). Retrieved from http://web.oie.int/hs2/report.asp?lang=en

OIE. (2017b). World organisation for animal health. 2017. World animal health information database (WAHIS) interface. Retrieved from https://www.oie.int/wahis/

OIE. (2017c). World animal health information database (WAHID). Animal population. Retrieved from http://www.oie.int/wahis_2/wah/health_v7_es.php

OIE. (2017d). World organisation for animal health. Terrestrial manual. Brucellosis (*Brucella abortus, B. melitensis* and *B. suis*) (infection with *B. abortus, B. melitensis* and *B. suis*). Retrieved from www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.04_BRUCELLOSIS.pdf

OIE. (2017e). World organisation for animal health. Active search for non-official animal health information. Retrieved from http://www.oie.int/en/animal-health-in-the-world/the-world-animal-health-information-system/active-search/

Pavade, G., Awada, L., Hamilton, K., & Swayne, D. E. (2011). The influence of economic indicators, poultry density and the performance of veterinary services on the control of high-pathogenicity avian influenza in poultry. Rev Sci Tech, 30, 661-671.

Quantum GIS Development Team. (2017). Quantum GIS geographic information system, open source geospatial foundation project. Retrieved from http://qgis.osgeo.org

R Development Core Team. (2017). R: A language and environment for statistical computing. Vienna: R Foundation for Statistical Computing.

Radunz, B. (2006). Surveillance and risk management during the latter stages of eradication: Experiences from Australia. Veterinary Microbiology, 112, 283-290. doi:10.1016/j.vetmic.2005.11.017

Ragan, V. E. (2002). The animal and plant health inspection service (APHIS) brucellosis eradication program in the United States. Veterinary Microbiology, 90(1-4), 11-18. doi:10.1016/s0378-1135(02)00240-7

Santos, R. L., Martins, T. M., Borges, Á. M., & Paixão, T. A. (2013). Economic losses due to bovine brucellosis in Brazil. Pesquisa Veterinária Brasileira, 33, 759-764. doi:10.1590/s0100-736x2013000600012

Schumaker, B. (2013). Risks of *Brucella abortus* spillover in the Greater Yellowstone Area. Revue Scientifique et Technique de l'OIE, 32(1), 71-77. doi:10.20506/rst.32.1.2185

Seleem, M. N., Boyle, S. M., & Sriranganathan, N. (2010). Brucellosis: A re-emerging zoonosis. Veterinary Microbiology, 140, 392-398. doi:10.1016/j.vetmic.2009.06.021

Shepherd, A. A., Simpson, B. H., & Davidson, R. M. (1980). An economic evaluation of the New Zealand bovine brucellosis eradication scheme. Paper presented at the Second International Symposium on Veterinary Epidemiology and Economics, Canberra.

Singh, B. B., Dhand, N. K., & Gill, J. P. S. (2015). Economic losses occurring due to brucellosis in Indian livestock populations. Preventive Veterinary Medicine, 119, 211-215. doi:10.1016/j.prevetmed.2015.03.013

Stärk, K. D. C., & Häsler, B. (2015). The value of information: Current challenges in surveillance implementation. Preventive Veterinary Medicine, 122, 229-234. doi:10.1016/j.prevetmed.2015.05.002

Taleski, V., Zerva, L., Kantardjiev, T., Cvetnic, Z., Erski-Biljic, M., Nikolovski, B., . . . Kirandziski, T. (2002). An overview of the epidemiology and epizootology of brucellosis in selected countries of Central and Southeast Europe. Veterinary Microbiology, 90(1-4), 147-155. doi:10.1016/s0378-1135(02)00250-x

Terefe, Y., Girma, S., Mekonnen, N., & Asrade, B. (2017). Brucellosis and associated risk factors in dairy cattle of eastern Ethiopia. Tropical Animal Health and Production, 49, 599-606. doi:10.1007/s11250-017-1242-7

The World Bank (WB). (2017). World dev. indic. GDP per capita (current US$). Retrieved from http://data.worldbank.org/indicator/NY.GDP.PCAP.CD

Thiermann, A. B. (2005). Globalization, international trade and animal health: The new roles of OIE. Preventive Veterinary Medicine, 67(2-3), 101-108. doi:10.1016/j.prevetmed.2004.11.009

Tweddle, N. E., & Livingstone, P. (1994). Bovine tuberculosis control and eradication programs in Australia and New Zealand. Veterinary Microbiology, 40(1-2), 23-39. doi:10.1016/0378-1135(94)90044-2

United Nations. (2017). List of UN members states. Retrieved from http://www.un.org/en/member-states/index.html

World Health Organization (WHO). (2015). Estimates of the global burden of foodborne diseases. Retrieved from http://www.who.int/foodsafety/publications/foodborne_disease/fergreport/en/

Yoon, H., Moon, O. K., Her, M., Carpenter, T. E., Kim, Y. J., Jung, S., & Lee, S. J. (2010). Impact of bovine brucellosis eradication programs in the Republic of Korea. Preventive Veterinary Medicine, 95, 288-291. doi:10.1016/j.prevetmed.2010.04.004

Tables

Table 1. Distribution of category of countries at the continental level (n=156).

	Africa	America	Asia	Europe	Oceania	World
Enzootic*	34	22	31	18	0	105
Non-Enzootic**	4	1	6	10	0	21
Free***	4	2	3	17	4	30

*Enzootic: countries infected, which may have been free of brucellosis, but for periods less than 3 years. **Non-enzootic: countries where the disease was present one or more years, but there was at least a 3-year period without the disease. ***Free: countries where the disease remained absent during the whole period.

Table 2. Results of the GLM for the presence of the disease and the application of surveillance and control programmes in Enzootic and Non-enzootic countries and year

Dependent variable	**Independent Variable**	**Beta**	**SE (beta)**	**OR (95% CI)**	**p-value**	
Presence of the disease	Enzootic			1		
	Non-Enzootic	-2.40	0.13	0.09 (0.07 - 0.12)	<0.001	***
	Year	-0.08	0.01	0.92 (0.90 - 0.94)	<0.001	***
Application of Surveillance	Enzootic			1		
	Free	0.07	0.13	1.07 (0.83 - 1.39)	0.598	NS
	Non-Enzootic	-0.01	0.15	0.99 (0.74 - 1.33)	0.935	NS
	Year	0.12	0.01	1.12 (1.10 - 1.15)	<0.001	***
Application of Control Policies	Enzootic			1		
	Free	-1.05	0.10	0.35 (0.29 - 0.43)	<0.001	***
	Non-Enzootic	-0.71	0.12	0.49 (0.39 - 0.62)	<0.001	***
	Year	0.02	0.01	1.02 (1.00 - 1.04)	0.011	*

NS = Not significant (p>0.05); * = Significant (p<0.05); ** = Very significant (p<0.01); *** = Highly significant (p<0.001).

See footnote, description of countries in Figure 1.

Figure legends

Fig. 1. Distribution of bovine brucellosis in countries based on their health situation from 1996 to 2014.

Enzootic: countries infected, which may have been free of brucellosis, but for periods less than 3 years. Non-enzootic: countries where the disease was present for one or more years, but there was at least a 3-year period without the disease. Free: countries where the disease remained absent during the whole period.

Fig. 2. GDP values per health situation.

See footnote, description of countries in Figure 1.

Fig. 3. Bovine population in the three groups according to the health situation.

See footnote, description of countries in Figure 1.

Fig. 4. Evolution of the percentage of Enzootic and Non-Enzootic countries that declared the disease present each year between 1996 and 2014.

See footnote, description of countries in Figure 1.

Fig. 5. Evolution of the percentage of Enzootic, Non-Enzootic and Free countries applying Surveillance programmes between 1996 and 2014.

See footnote, description of countries in Figure 1.

Fig. 6. Evolution of the percentage of Enzootic (dotted line) and Non-Enzootic (plain line) countries with implementing control policies between 1996 and 2014.

See footnote, description of countries in Figure 1.

Fig. 7. The number of changes in the implementation of surveillance programmes between 1996 and 2014 per category of countries.

See footnote, description of countries in Figure 1.

Fig. 8. The number of changes in the implementation of control policies between 1996 and 2014 per category of countries.

See footnote, description of countries in Figure 1.