# Risk Analysis and Bovine Tuberculosis, a Re-emerging Zoonosis

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**ABSTRACT: The widespread of immunodeficiency with AIDS, the consequence of poverty on sanitary protection and information at both individual and state levels lead control of tuberculosis (TB) to be one of the priorities of World Health Organization programs. The impact of bovine tuberculosis (BTB) on humans is poorly documented. However, BTB remains a major problem for livestock in developing countries particularly in Africa and wildlife is responsible for the failure of TB eradication programs. In Africa, the consumption of raw milk and raw meat, and the development of bushmeat consumption as a cheap source of proteins, represent one of the principal routes for human contaminations with BTB. The exploration of these different pathways using tools as participatory epidemiology allows the risk analysis of the impact of BTB on human health in Africa. This analysis represents a management support and decision tool in the study and the control of zoonotic BTB.**

**KEYWORDS: bovine tuberculosis; risk analysis; participatory epidemiology; zoonosis; bushmeat**

## INTRODUCTION

Human tuberculosis (TB) of animal origin (zoonotic TB) is an important public health concern in developing countries. African nations pose a particular challenge in TB control, because of deficiencies in public health control measures for cattle and animal products, coupled with a high prevalence and incidence of HIV in the human population. Risk analysis is an important tool in defining the public health danger posed by zoonotic TB in Africa. Using risk analysis, two potential pathways are proposed as comprehensive models

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when considering different routes of human infection: (*a*) from domestic and wild animals; and (*b*) from animal products including milk and bushmeat.

Globally, wildlife reservoirs threaten the success of TB eradication programs (e.g., badgers in the United Kingdom;[1] however, according to Donnelly *et al*.,[2] the presence of badgers seems actually to keep transmission of TB down in cattle, possums in New Zealand, white-tailed deer in Michigan, USA, wild boar and deer in Spain and France). In Africa, little is known about wildlife reservoir, but in southern Africa (mainly South Africa), in the Kruger National Park, 15 years of studies clearly indicate that the African buffalo (*Syncerus caffer*) is the main reservoir of the pathogen agent, with other species like the greater kudu (*Tragelaphus strepsiceros*) and common warthog (*Phacochoerus africanus*) having a potential role in the continued prevalence of the disease.[3] Depending on the specific ecosystem with respect to species abundance, diversity, and anthropic factors, such as habitat impact and wildlife management, wildlife species seem to be more or less susceptible to the *Mycobacterium* spp. and therefore, the disease dynamics and the role of species have been varying accordingly.

The purpose of this article is to examine the impact of bovine tuberculosis (BTB) on human health in Africa and to propose an approach for its study and its control using risk analysis.

## ECOLOGY, EPIDEMIOLOGY, AND ZOONOTIC ASPECTS OF BTB IN AFRICA

In Africa, BTB primarily affects cattle.[4–9] However, infection in other farm and domestic animals are sometimes reported. *Mycobacterium bovis* has a broad host range as the principal cause of TB in free-living wildlife, captive wildlife, domestic livestock, and non-human primates.[10] Wild ruminants and carnivores, such as African buffalo, lion, cheetah, greater kudu, leopard, warthog, and eland, can be infected.[11–13] Scavengers (hyenas, genet) and Chacma baboons in Kenya became infected through the ingestion of abattoir wastes.[14] Most of the time, BTB transmission is considered as passing from livestock to wildlife. In wild ruminants, the disease has been documented worldwide, and lesions and symptoms are very similar to those of domestic ruminants.[15]

Depending on the susceptibility of a species to, and on the prevalence of BTB, these animals could act as reservoirs or spill-over hosts to other species.[13–16] In reservoir or maintenance hosts, infection can persist through horizontal transfer in the absence of any other source of *M. bovis* and may well be transmitted to other susceptible hosts. Only a limited number of species act as maintenance or reservoir hosts of TB, which include brush-tailed possum (*Trichosurus vulpecula*), European badgers (*Meles meles*), bison (*Bison bison*), African buffalo

**TABLE 1. Worldwide TB Figures (WHO 2002)**

| | | |
|---|---|---|
| World population | | 6 219 000 000 |
| TB-infected people | | 2 073 000 000 |
| Estimated incidence | Tuberculosis | 8 797 000 |
| | Pulmonary TB (Smear-positive cases) | 3 887 000 |
| Deaths due to TB | | 1 800 000 |
| TB cases due to HIV | | 9% |
| Deaths of TB patients due to HIV | | 12% |

(*Syncerus cafer*), and white-tailed deer (*Odocoileus virginianus*). In contrast, spill-over hosts become infected with *M. bovis*, but the infection only occurs sporadically, or persists within these populations if a true maintenance host is present in the ecosystem. In the case of high density populations, spill-over hosts can act as reservoir hosts of *M. bovis*.[17]

In Africa, TB infection in humans is principally caused by *Mycobacterium tuberculosis.* However, human TB of animal origin caused by *M. bovis* is becoming increasingly prevalent in developing countries[18] due to the lack of both control and diagnostic measures and pasteurization of milk.[19,20] Concomitantly, TB is a major opportunistic infection in HIV-infected persons, and the World Health Organization (WHO) estimated that 70% (6 million) of the people co-infected with TB and HIV live in Sub-Saharan Africa.[19] The prevalence, incidence, and deaths caused by TB, reported in 2002 by WHO, are given in TABLE 1. Every year, there are 8–10 million new cases of TB reported, and 2–3 million deaths attributed to TB,[21] but the exact percentage of TB that may be caused by *M. bovis* is not known. Global prevalence of human TB due to *M. bovis* is estimated at 3.1% of all human TB cases, of which 2.1% are pulmonary infections, and 9.4% extra pulmonary.[19] However, the proportion of *M. Bovis* in Africa and within the TB–HIV complex is unknown.

Information regarding human disease due to *M. bovis* is rare. In Africa, where *M. bovis* is present in animal species, there is substantial lack of knowledge about the distribution, epidemiological patterns, and transmission dynamics of this important zoonosis. The fact that 50% of total African cattle happen to be in countries without any control measures for BTB[22] is a matter of concern. Results from several studies conducted in different African countries have clearly established the importance of BTB as a major public health problem. In Malawi, a survey of human sputum cultures from human TB patients revealed that 42.8% of the culture-positive specimens were *M. bovis* (Ministry of Health, 1985, cited by Wedlock *et al*.[20]). In Egypt, a study reported that 9 out of 20 randomly selected patients with TB peritonitis were infected with *M. bovis.*[23] Jiwa *et al*.,[4] in Tanzania, suggested that the presence of BTB in cattle necessitates further investigation into the role of animal-derived BTB in human health. In Burkina Faso, the Ministry of Health reported 1,334 human

cases of zoonotic TB.[24] Ameni *et al*.[25] reported high occurrences of BTB in cattle and cattle owners, respectively, in central Ethiopia, and pointed out the need to assess and evaluate the impact of zoonotic TB on human populations in order to design cost-effective control methods throughout the country. The risk of contracting TB is 20–50 times greater in Africa than in Europe.[18]

The importance of *M. bovis* in human TB cases is not mentioned in any of the national reports submitted to OIE (World Organization of Animal Health) and WHO by African member states. Cases of *M. bovis* infection in humans are underreported as a result of diagnostic limitations and non-adapting sampling for searching extra pulmonary TB.[19]

TB infection may occur via contaminated materials (fomites), aerosolization (human to human), and predation, or by vertical and/or horizontal transmission in humans.[15] Zoonotic TB caused by *M. bovis* could be acquired by humans through the inhalation of cough sprayed from infected cattle, or from handling or consumption of milk contaminated with the organism.[20] BTB in humans affects young individuals and causes cervical lymphadenopathy, intestinal lesions, chronic skin TB (*Lupus vulgaris*), and other non-pulmonary forms.[19] If *M. bovis* is acquired by inhalation, humans typically develop pulmonary TB.[19]

Another factor which increases the risk of acquiring zoonotic TB in Sub-Saharan Africa is the active competition in all Sub-Saharan African countries between large-scale commercial food enterprises and smaller, less-regulated farmers who frequently ignore safety standards for hygiene and product quality. These smaller farmers sell directly to final consumers and contribute to the spread of TB.[19] Furthermore, 90% of the total milk produced by these countries and consumed by people is either fresh or soured, and not pasteurized (Walshe *et al*., 1991, cited by Cosivi *et al*.[19]

Finally, we can underline that the recent development of wildlife activities, such as game tourism, farming, and hunting to develop the peripheral zones of protected areas contributes to the exposure of specific persons to *Mycobacterium* spp.

## RESEARCH QUESTION, TOOLS, AND METHODOLOGIES

Efficient risk analysis could become an important tool in assessing and overcoming the public health danger posed by zoonotic TB. Risk analysis is a relatively new research tool that encompasses qualitative, deterministic, and probabilistic health assessment. This tool requires interdisciplinary collaborations to satisfy the demands for high quality characterization of risk. Risk could be defined as the likelihood of occurrence of an adverse event and the severity of the consequences if the result does occur.[26] MacDiarmid and Pharo[27] defined risk analysis as a tool intended to provide decision-makers with an objective, repeatable, and documented appraisal of the risk posed by a particular action.

Based on the OIE (World Organization for Animal Health) code, risk analysis constitutes four steps: (1) hazard identification; (2) risk assessment; (3) risk management; and (4) risk communication.[28] Risk assessment evaluates the probability of entry, the establishment or spread of a disease under existing conditions, predetermined control measures, and the associated potential biological and economic consequences of establishment of the disease. In the case of zoonotic TB, it consists of the identification, estimation of statistical probabilities, and evaluation of the consequences of all risks associated with the transmission of BTB from animals to humans. Release assessment is the probability of releasing viable *M. bovis* to bordering communities from (*a*) cattle; (*b*) contaminated carcasses and meat; (*c*) contaminated milk; and (*d*) bushmeat. Exposure assessment is the probability of being exposed to viable *M. bovis*. Factors involved in this assessment are: (*a*) rural and peri-urban populations; and (*b*) abattoir workers, farm workers, and people with a high degree of contact with animals (e.g., game farm workers, rangers, wildlife vets). Consumption of contaminated food and hunting habits are also exposure variables. Consequence assessment is the probability of becoming infected, diseased, or of dying. Consequences of human BTB are sickness, death, as well as the potential for one group to be the release source for human-to-human transmission. Risk analysis can be quantitative providing a numeric, or qualitative estimate, when a descriptive approach is used.[29] Both types of assessments are equally valid if they are based on good quality data and concentrate on all the defined stages of the infective process.[29] Some of the inputs and variables of this model are unknown, which requires that we incorporate uncertainty and variability into the model. These variations are modeled using Monte-Carlo simulation technique, a stochastic iterative approach.[30] Input parameters should be defined through the collection of existing data, expert opinions, and the use of field surveys including participatory epidemiology (PE).

PE is an emerging field based on epidemiological technique using participatory methods to collect epidemiological data by the widely accepted methods of Rapid Rural Appraisal and Participatory Rural Appraisal. PE relies on observation, existing veterinary knowledge of traditional livestock owners, and oral history from the local communities. PE is based on the principle of flexibility with the use of iterative analysis and on the principle of triangulation which is the cross-checking of information gained from several intentionally different perspectives. A wide range of PE tools are available and can be categorized into three main groups, complemented with secondary sources and direct observation in the field: informal interviews of key informants, visualization methods, and ranking or scoring methods. Information derived from all these sources is then combined and cross-checked to build a picture of the issues under investigation. Use of conventional veterinary diagnostic tools is an integral part of, and in some cases overlaps with PE methods. PE can make use of quantitative information coming from previous formal epidemiological surveys, and uses qualitative intelligence to fill the gaps between

available data.[31] Examples of PE used in veterinary research include: basic research on the epidemiology of endemic and epizootic diseases, used with Orma communities in Kenya for the Bovine Trypanosomiasis,[32] participatory disease searching which is a widely applied method of assessing Rinderpest risk, verifying eradication, and substantiating disease-free herd status,[33] disease modeling done on the construction of a model of the contagious bovine pleuropneumonia (CBPP) transmission in transhuman production systems.[34] PE methods augment the capacities of conventional epidemiological methods to provide reliable and fast epidemiological information on complex disease concerns. For risk factor identification and assessment of the local epidemiological situation of BTB, qualitative and semi-qualitative data are needed. The use of PE methods could provide guidance on local attitudes and behavior with regard to: animal husbandry practices, social and cultural habits (e.g., milk processing, milk consumption, and hunting and consumption of bushmeat).[35]

Risk assessment for *M. bovis* human infection is exemplified using one scenario pathway model: the milk pathway. This pathway determines an orderly series of events which would ultimately lead to the acquisition of BTB by humans in Uganda. The pathway looks at the probability that an individual is infected with *M. bovis* at the source.

Proposals will be based on the milk and meat pathways in African countries.

## FRAMEWORK PROPOSED FOR RISK ANALYSIS OF ZOONOTIC BTB IN AFRICA MILK PATHWAY

In Uganda, as in most Sub-Saharan countries, human TB has a high prevalence. The Ugandan Ministry of Health reported in 1995 a mean annual incidence rate of human TB of 1.34/1000 person-years, and the role of BTB is unknown.[9] The same authors, using intradermal TB-skin testing, reported a 74% prevalence of TB reactors among cattle herds, 6% of individual-animals, and a within-herd range of 1–50% that could be 100% if suspicious reactors were included.[9] A regular high prevalence of BTB in cattle can be correlated with the isolation of *M. bovis* in milk samples. Vekemans *et al*.[36] reported isolation of *Mycobacteria* in 26% of 60 retailed milk samples collected from markets in Burkina Faso.

The high prevalence of BTB in Ugandan cattle could have public health implications; however, there is no information about the risk of zoonotic infections of BTB to humans. Because of this unknown transmission potential, we are proposing a BTB risk analysis in order to make recommendations to public health agencies for prevention and control of the disease. During their 6 years of study in the region, CIRAD (*Centre de Coopération Internationale en Recherche Agronomique pour le Développement*) established a series of comprehensive social and political networks. The public health authorities are aware of CIRAD's study and wish to understand the risk presented by

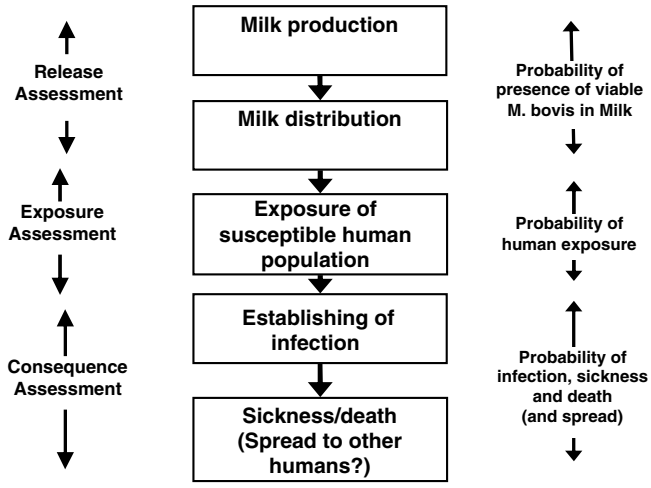


**FIGURE 1.** Risk assessment for the milk pathway.

zoonotic TB. CIRAD has proposed a basis for a comprehensive quantitative risk analysis (FIG. 1) with evidence of a potential risk, thorough knowledge of the structure of the culture, networks within the population and the dairy production industry, links to public health authorities and agencies, and organizing efficient field investigation capabilities. Risk hazard identification for zoonotic TB is currently based on a cross-sectional study with TB patients of the Mbarara Hospital in Uganda, in order to determine the risk factors for TB caused by *M. bovis*. A laboratory study component includes bacterial isolation of *Mycoplasma* spp. and characterization of *M. bovis* using molecular techniques. Risk factors are being categorized using a questionnaire that accounts for general information about the patients and their medical history, occupational information, household information, habits of milk consumption, habits of meat consumption, and knowledge of TB transmission routes (including the zoonotic aspects).

## MEAT PATHWAYS WITH WILDLIFE AND DOMESTIC ANIMALS APPROACH

Eating raw or undercooked meat is one of the ways of contracting BTB. Because of local habits concomitant with a high prevalence of BTB in cattle, some countries present a real zoonotic risk of BTB transmission. Ameni *et al*. showed 99% of either raw meat or raw and cooked meat consumption versus 1% of only cooked meat consumption in Central Ethiopia.[25] The same study showed herd and individual animal prevalences of BTB of 42.6% and 7.9%, respectively. At the end, 24.5% of the interviewed households had

experienced at least one human TB case in the family. In Ethiopia, BTB prevalence is a major concern for veterinary services ranging from 3.4% in smallholder production systems to 87% in intensive farms.[37,38] Because of the lack of sensibility of the routine post-mortem examination in the abattoirs and because of the high proportion of backyard slaughtering, this problem is in reality a public health problem.

The bushmeat trade and meat consumption have been increasing at an alarming rate in Sub-Saharan Africa, particularly in the forested areas of West and Central Africa.[39] Its relative importance as a source of proteins as compared to domestic animals and fish varies between 6% (southern Africa) and 55% (Central Africa) of total protein consumption.[40] This practice has demonstrated that in areas where bushmeat is important, hunters and persons involved in the bushmeat trade are exposed to the transmission of several wildlife diseases.[41,42] Despite the possibilities of human TB infection through bushmeat, these protein products have rarely been considered as a source of TB. In order to assess the risk of BTB infection from wildlife to humans, we need to investigate the problem at different levels. Data on BTB in wildlife in most of West and Central African countries are scarce or nonexistent. Proteins come from both wildlife hunted in the neighboring forests, and from cattle herds arriving from pastoral regions in several areas of Sub-Saharan Africa, such as the Central African Republic and Cameroon. Because prevalence of TB is important in transhuman herds,[43] there is a risk of transmission from cattle to wildlife as described in literature when wild and domesticated animals share the same territory.[11,17,19,44,45] A surveillance of BTB in bushmeat markets can be a method to monitor the presence of *M. bovis* in wildlife species. An advantage for sampling wildlife carcasses is that in bushmeat markets in West and Central Africa, a variety of species are available. The choice of species to be examined will depend on the likely prevalence of *M. bovis* within each species, their abundance, and the ease of sampling different hosts.[17] In some cases, spill-over species such as carnivores and other species at the top of the food chain have become useful sentinel species for the detection of BTB in other wildlife animals.[46] The level of detection of BTB in wildlife species will also depend on the kind of diagnosis used to test for the presence of the organism. In infected white-tailed deer in Michigan, it has been demonstrated that acid fast staining histopathology and PCR methods can underestimate the prevalence of BTB as compared to culture methods.[47] The chances of detecting *M. bovis* in a diseased carcass are also variable depending on the anatomical site used for screening the carcasses. The body parts harboring the most infectiveness will depend on the pathogenesis of *M. bovis* in the species being tested. Most wild ruminants present with gross lesions in the lymph nodes of the head,[48] while mesenteric lymph nodes lesions are more common in carnivores or scavengers.[17]

The risks of TB transmission from wildlife to humans have been insufficiently studied in Sub-Saharan areas where bushmeat consumption prevails. Indeed, in those areas, contact with wildlife carcasses from a wide variety

of species is probably more widespread and common than in southern Africa. There, the most likely source of infection might be the cutaneous route, because slaughtering is performed in open areas. On the other hand, overcooking meat is a common measure used to prevent gastro-intestinal infections in African countries, and venison is seldom consumed insufficiently cooked. However, socioeconomic conditions, such as a lack of hygiene, informal trade, lack of veterinary inspection and food safety services, lack of disease awareness, and not using gloves, can be considered as risk factors for bushmeat traders, butchers, hunters, and middlemen to become infected via the cutaneous route, particularly when they cut themselves while dressing the carcass, or when they dress an unprotected, open wound or abrasion on their arms or forearms.[49]

Consequences for humans infected with *M. bovis* through bushmeat pathways are probably very similar to those assessed for milk consumers. The difference might be that the most exposed persons are adults, but with milk consumers, children are also exposed. Women are usually involved in the bushmeat trade and marketing, while men are more involved in hunting activities. Dressing carcasses is more commonly done in the field by men, who deal with heavy species (e.g., antelopes, bushpigs), while small species, such as primates, rodents, and reptiles are more likely to be dressed by women in the markets.

In addition, some molecular characterization techniques—for example, spacer oligonucleotide typing,[50] Single-step DNA-based assay[51] RFLP[52]—if tested specifically for *M. bovis* in multi-species model could permit, if successful, to introduce an idea of the historical contingency of disease strains in wildlife and domestic populations and at their interface. From these links, hypothetical pathways can be proposed and tested.

Last, the understanding of BTB dynamics in and between wildlife and domestic reservoirs is an important issue to be looked at. Pathogens' dynamics between the wildlife and domestic reservoirs in some areas will explain the incidence of the disease in cattle and therefore, will have an impact on the risk assessment in humans. Later in the analysis, risk management can take into account wildlife reservoir management options, inducing a change in prevalence in the domestic reservoir and changing the risk exposure of human population at a higher level.

## CONCLUSION

Despite the lack of study coverage related to the impact of BTB in human TB cases, one can hypothesize that immunodepressed HIV patients would be more susceptible to BTB contamination when a specific threshold of risk factors is encountered. Contamination from human to human of *M. bovis* is usually considered as a rare event. But in the context of high HIV prevalence and the presence of many risk factors, the epidemiology of the disease in the

human host could be changed and human-to-human transmission could be more common.[43]

The increase of population in Africa is leading to the use of more and more marginal lands by pastoral societies and agricultural "colons." These marginal lands correspond to areas where the remaining population of wildlife has been pushed by land-use pressure. Most of the national parks in Africa are based in these areas. Therefore, one can observe an increased contact between livestock production systems and wildlife ecosystems, leading to the potential for pathogen transmission in both ways. Another consequence linked to the political agenda trying to integrate development and conservation issues in the areas surrounding the national parks is the development sustainable activities, including game hunting and sustainable natural resources harvest. These activities also constitute new risk factors for the transmission of pathogens. Thus, contamination from buffalo and other wildlife species to humans has to be taken into account in terms of bushmeat consumption, as also including game hunting and traditional hunting. Other potential pathways should be studied and included as direct transmission from livestock. Modeling of the interface between wild and domestic animals will also help in building up comprehensive risk assessment models.

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