Preventive Veterinary Medicine 134 (2016) 145–152

Contents lists available at ScienceDirect

Preventive Veterinary Medicine

journal homepage: www.elsevier.com/locate/prevetmed

Assessing the sensitivity of bovine tuberculosis surveillance in Canada's cattle population, 2009–2013

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ARTICLE INFO

Article history:
Received 7 June 2016
Received in revised form 12 October 2016
Accepted 17 October 2016

Keywords:
Bovine tuberculosis
Cattle
Scenario tree
Surveillance sensitivity

ABSTRACT

The objectives of this study were (1) to estimate the annual sensitivity of Canada's bTB surveillance system and its three system components (slaughter surveillance, export testing and disease investigation) using a scenario tree modelling approach, and (2) to identify key model parameters that influence the estimates of the surveillance system sensitivity (SSSe). To achieve these objectives, we designed stochastic scenario tree models for three surveillance system components included in the analysis. Demographic data, slaughter data, export testing data, and disease investigation data from 2009 to 2013 were extracted for input into the scenario trees. Sensitivity analysis was conducted to identify key influential parameters on SSSe estimates.

The median annual SSSe estimates generated from the study were very high, ranging from 0.95 (95% probability interval [PI]: 0.88–0.98) to 0.97 (95% PI: 0.93–0.99). Median annual sensitivity estimates for the slaughter surveillance component ranged from 0.95 (95% PI: 0.88–0.98) to 0.97 (95% PI: 0.93–0.99). This shows that slaughter surveillance to be the major contributor to overall surveillance system sensitivity with a high probability to detect *M. bovis* infection if present at a prevalence of 0.00028% or greater during the study period. The export testing and disease investigation components had extremely low component sensitivity estimates—the maximum median sensitivity estimates were 0.02 (95% PI: 0.014–0.023) and 0.0061 (95% PI: 0.0056–0.0066) respectively.

The three most influential input parameters on the model's output (SSSe) were the probability of a granuloma being detected at slaughter inspection, the probability of a granuloma being present in older animals (≥12 months of age), and the probability of a granuloma sample being submitted to the laboratory. Additional studies are required to reduce the levels of uncertainty and variability associated with these three parameters influencing the surveillance system sensitivity.

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1. Introduction

Bovine tuberculosis (bTB), caused by the bacterium *Mycobacterium bovis*, is a chronic infectious zoonotic disease that has a broad host range, including livestock, wildlife, and humans, and presents a significant threat to public and animal health as well as the economy. The main clinical signs in cattle are wasting, weight loss, and fever; however, infection frequently produces no clinical signs and infected animals may remain undetected for many years. Successful national surveillance programs have relied on a combination of ante-mortem testing and culling and post-mortem slaughter inspection to reduce the prevalence of disease. Although bTB is now largely controlled in the developed world, success has proven more difficult in countries with a wildlife reservoir of *M. bovis* and remains widely distributed throughout much of the developing world, where control strategies are unaffordable or socially unacceptable (Cousins, 2001).

Bovine tuberculosis was one of the first federally reportable diseases in Canada (Statutes of Canada, 1885) with a national eradication program initiated in the 1920s relying on regular tuberculin skin testing of all cattle with reactors removed to slaughter (Essey and Koller, 1994). This approach proved successful in reducing the estimated prevalence from greater than 4% to approximately 0.1% by the early 1960s (Harrington et al., 2014). With continued low prevalence but a lack of further progress towards eradication, the surveillance program shifted resources away from on-farm testing to slaughter inspection and trace-back investigation of cases in 1980. (Dukes and McAninch, 1992; Canadian Food Inspection

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http://dx.doi.org/10.1016/j.prevetmed.2016.10.012
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Agency, 2015). This shift, in combination with other program refinements made at the time, including greater emphasis on epidemiological tracing and a policy of whole-herd destruction for all bTB-affected herds, resulted in further progress towards eradication.

Today, all areas of Canada are considered officially free from bTB according to domestic criteria in the *Health of Animals Regulations* (Minister of Justice, 2015b), with only sporadic localized outbreaks detected over the past decade. The last detected case of bTB in Canadian domestic livestock occurred in 2011 and involved a single cattle herd in the province of British Columbia with no evidence of further spread (Appendix A1).

Canada's current national surveillance system for bTB is composed of multiple surveillance components: slaughter inspection of bTB-susceptible livestock; tuberculin testing performed for a variety of reasons (international export requirements, semen production centre requirements, in geographic areas considered at risk for transmission from endemically infected wildlife, and for outbreak associated herd investigations); and, because bTB is a mandatory reportable disease in Canada, the passive reporting of any suspect cases. A quantitative analysis to assess Canada's surveillance system for detecting bTB in Canada has not been undertaken previously. Therefore, assessing the sensitivity of Canada's surveillance system, and the relative contribution of individual surveillance components, is necessary for informed decision making related to the current program. The advent of modern epidemiological tools such as scenario tree modelling has facilitated this sort of assessment (Martin et al., 2007a,b; Wahlström et al., 2010; Welby et al., 2012; Calvo-Artavia et al., 2013; Rivière et al., 2015).

The objectives of this study were (1) to estimate the annual sensitivity of Canada's bTB surveillance system and its three system components (slaughter surveillance, export testing and disease investigation) using a scenario tree modelling approach, and (2) to identify key model parameters that influence the estimates of the surveillance system sensitivity.

2. Materials and methods

2.1. Target population and study period

The target population for this epidemiological analysis included all cows, bulls, steers, heifers, and calves in Canada for each year of the study period. For the purpose of this manuscript, "cattle" refers to bovines (genus *Bos*).

The study period was from 1 January 2009 to 31 December 2013. The bTB surveillance system sensitivity (SSSe) and component sensitivity (CSe) for the slaughter surveillance, export testing and disease investigation components with median and 95% probability interval (PI) were estimated on an annual basis for each year of the study period.

2.2. Case definition and data

According to Canadian Food Inspection Agency (CFIA) National Bovine Tuberculosis Eradication Program policy, the criteria for a confirmed case of bTB are the isolation and identification of *M. bovis* in tissues by bacterial culture and/or a positive polymerase chain reaction (PCR) assay performed on paraffin-embedded formalin-fixed tissue.

Data on live cattle demographics, slaughtered cattle population, exported cattle and cattle under disease investigation are described in Table 1 and Appendix A1.

2.3. Diagnostic testing scheme

2.3.1. Slaughter surveillance component

Inspection of cattle at slaughter for lesions compatible with bTB has served as the primary component of the bTB surveillance system since replacing on-farm tuberculin testing of cattle herds in 1980. Although both federal and provincial governments play a role in meat inspection, approximately 95% of all cattle slaughter in Canada occurs in federally registered establishments with inspection performed by the CFIA as the competent veterinary authority. Infection of cattle with *M. bovis* is characterized by slowly progressive clinical signs and pathological lesions consisting of small, rounded granulomas (tubercles). In mature cattle, inhalation is the primary route of infection, and lesions occur in the lung and dependent lymph nodes. This is in contrast to calves, where ingestion is the most common route, and lesions typically involve the mesenteric lymph nodes with possible spread to other organs. Any bTB-compatible lesion identified at slaughter as part of routine inspection procedures in Canada is required to be sampled and sent to a federal laboratory to meet requirements outlined in CFIA's Granuloma Submission Program.

Tissues from macroscopically visible lesions collected and submitted through the Granuloma Submission Program for histopathological examination are reported as "mycobacteriosis negative," "mycobacteriosis suspect," or "mycobacteriosis". If tissues are reported as "mycobacteriosis negative," the animal is classified as negative for bTB. Tissue samples confirmed as having a granulomatous lesion by histopathology, in the absence of acid-fast bacilli, are reported as "mycobacteriosis suspect" and tested by culture only. Results from tissue culture are reported as either positive or negative for *M. bovis*, and this diagnostic testing scheme is referred to as T_1. Granulomatous lesions in the presence of acid- fast bacilli are classified as "mycobacteriosis" and subject to both culture and paraffin-embedded formalin-fixed PCR (PEFF-PCR) testing in parallel, with the objective of maximizing unit-level diagnostic sensitivity (i.e. a positive result on either test is considered to be a confirmed case). The result of parallel testing by culture and PEFF-PCR is reported as either negative or positive (i.e. confirmed infected animal) and referred to as diagnostic testing scheme T_2.

2.3.2. Export testing surveillance component

A secondary surveillance system component, driven by testing of live cattle to meet international export requirements, relies on the measurement of delayed hypersensitivity responses following the intradermal injection of bovine purified protein derivative prepared from *M. bovis* (Monaghan et al., 1994). Caudal fold tuberculin (CFT) testing of cattle in order to meet conditions for export is performed by either CFIA inspectors or private veterinarians accredited by the CFIA, depending on the requirements of the importing country. Passive surveillance data collected via this component contribute to the bTB surveillance system. Animals classified as "reactors" to the CFT test are subject to ancillary testing by CFIA veterinary inspectors using the comparative cervical tuberculin (CCT) test– therefore a serial interpretation of CFT and CCT tests was applied. Animals with "positive" or "suspicious" CCT test results are ordered destroyed, and compensation is paid to owners as outlined in the *Compensation for Destroyed Animals Regulations* (Minister of Justice, 2015a). All cattle ordered destroyed on suspicion of bTB are subject to enhanced post-mortem inspection, during which samples from the retropharyngeal, caudal mediastinal, tracheobronchial, and cranial lymph nodes, as well as a node located near the ileocecal junction, and any suspect lesions observed are collected and submitted to a CFIA laboratory regardless of the presence or absence of gross visible lesions.

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