Spatiotemporal patterns, annual baseline and movement-related incidence of *Streptococcus agalactiae* infection in Danish dairy herds: 2000–2009

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**Abstract**

Several decades after the inception of the five-point plan for the control of contagious mastitis pathogens, *Streptococcus agalactiae* (*S. agalactiae*) persists as a fundamental threat to the dairy industry in many countries. A better understanding of the relative importance of within- and between-herd sources of new herd infections coupled with the spatiotemporal distribution of the infection, may aid in effective targeting of control efforts. Thus, the objectives of this study were: (1) to describe the spatiotemporal patterns of infection with *S. agalactiae* in the population of Danish dairy herds from 2000 to 2009 and (2) to estimate the annual herd-level baseline and movement-related incidence risks of *S. agalactiae* infection over the 10-year period.

The analysis involved registry data on bacteriological culture of all bulk tank milk samples collected as part of the mandatory Danish *S. agalactiae* surveillance scheme as well as live cattle movements into dairy herds during the specified 10-year period. The results indicated that the predicted risk of a herd becoming infected with *S. agalactiae* varied spatiotemporally; the risk being more homogeneous and higher in the period after 2005. Additionally, the annual baseline risks yielded significant yet distinctive patterns before and after 2005 – the risk of infection being higher in the latter phase. On the contrary, the annual movement-related risks revealed a non-significant pattern over the 10-year period. There was neither evidence for spatial clustering of cases relative to the population of herds at risk nor spatial dependency between herds. Nevertheless, the results signal a need to beef up within-herd biosecurity in order to reduce the risk of new herd infections.

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1. Introduction

*Streptococcus agalactiae* (*S. agalactiae*) is a contagious pathogen that exerts deleterious effects on bovine udder health, milk quality and productivity (Keefe, 1997). Consequently, in a quest to maintain production efficiency at the herd level, a justification for the deployment of resources aimed at preventing the introduction and subsequent within-herd spread of *S. agalactiae* is provided. In Denmark, a national surveillance and control scheme for *S. agalactiae* has been operational since 1966 (Anon., 1966). This was initiated against a backdrop of worrisome infection prevalences in the 1950s and 60s (Andersen et al., 2003). The control programme (with compulsory surveillance) entailed a rigorous combined application of within-herd sanitary and hygienic measures coupled with
a prohibition on the sale of cows and pregnant heifers from infected herds (Andersen et al., 2003). Thanks to these concerted efforts, the herd-level prevalence of S. agalactiae declined appreciably from 30 to 40% in 1950 (Anon., 1981) to approximately 2% in 1992, with a 1–2% incidence of herd infections (Anon., 1980–1992). However, since 2000 an increasing trend in both the herd-level prevalence and incidence of S. agalactiae has been reported suggesting a re-emergence of the pathogen in the Danish dairy herd population (Mweu et al., 2012a).

New herd infections with S. agalactiae can arise from internal (within-herd) and/or external (between-herd) factors. Of the internal factors, there is mounting evidence implicating humans as potential sources of infection for cattle (Jensen, 1982; Zadoks and Schukken, 2006; Zadoks et al., 2011). Notable personnel included in this internal category are farmers and relief milkers. Asymptomatic human carriage of S. agalactiae occurs in the urogenital and gastrointestinal tracts as well as the skin (Van der Mee-Marquet et al., 2008) and is frequent in young adults (20–40%) and the elderly (22%) (Manning et al., 2004, 2008; Edwards and Baker, 2005). A probable route of infection transfer to the cow is via hands during milking (Edmondson, 2011). Recently, work by Zadoks et al. (2011) involving multi-locus sequence typing of 111 isolates collected from a 2009 Danish bulk tank milk survey demonstrated the commonest S. agalactiae strains to be sequence types (ST) 1 (28%) and ST 23 (23%), which were previously primarily associated with human infections. Bovine strains are also recognisable, with introduction of new possibly infected animals into susceptible herds having been shown to constitute an external risk (Agger et al., 1994). This is particularly true for large herds with less stringent biosecurity measures whose pursuit for rapid expansion may favour acquisition as opposed to internal growth (Barkema et al., 2009). Spatially varying risk factors such as sharing of farm equipment may serve as additional avenues for the between-herd spread of S. agalactiae. Revisiting the human argument: dairy herds are visited by a variety of personnel who establish variable degrees of physical contact with cattle. Along with relief milkers (who likewise pose a within-herd risk), veterinarians and inseminators display varying geographical scales of operation stretching from local to regional, which in turn may influence the range of the spatial spread of S. agalactiae. Regrettably, movement patterns of these persons are seldom recorded precluding an evaluation of their relative roles in determining new herd infections. Importantly, unlike other streptococci, S. agalactiae is highly host-adapted and no environmental reservoirs have yet been identified (Keefe, 1997; Manning et al., 2010).

Even though the annual trend in the pooled herd-level incidence of S. agalactiae has been estimated (Mweu et al., 2012a), a supplementary undertaking seeking to disentangle the relative importance of within- and between-herd sources of new herd infections is worthwhile. In particular, availability of cattle movement data on individual herds can be critical in highlighting the possible role of animal introductions in driving S. agalactiae infections. Illustratively, by including exposure to animal introductions as a fixed effect in logistic regression analysis, the incidence risk attributable to these movements can be quantified. The risk in the unexposed herds is thus deemed representative of the ‘baseline’ risk in the general population of herds (Dohoo et al., 2009). In the absence of observable spatial dependency following semivariogram analysis of the logistic regression residuals, it is acknowledged that after accounting for the effects of known between-herd factors in the model, the source of the remaining risk rests in within-herd factors rather than in spatially-varying ones (Pfeiffer et al., 2008; Stevens et al., 2009). An understanding of the magnitude of the respective risks can be instrumental in guiding S. agalactiae policy formulation, thus ensuring effective targeting of control efforts.

A crucial step towards gaining insight into the epidemiology of a contagious pathogen involves investigating its geographical distribution – and if available data span a given time range – its associated temporal aspects. This serves the purpose of facilitating causal hypotheses generation, after which these can be formally tested (Berke, 2005). For instance, Fenton et al. (2009) investigated both large- and small-scale spatial and temporal patterns of infection in dairy herds with Salmonella enterica serovars. The number of cases arising within a defined distance and time period of an index case was found to be higher than expected. This provided evidence for spatiotemporal clustering suggesting the existence of either a contagious process or locally-acting environmental factors which increased the risk of infection. To date and to the best of our knowledge, there are no published studies examining the spatiotemporal epidemiology of S. agalactiae. Hence, the objectives of this study were: (1) to describe the spatiotemporal patterns of infection with S. agalactiae in the population of Danish dairy herds from 2000 to 2009 and (2) to estimate the annual herd-level baseline and movement-related incidence risks of S. agalactiae infection over the 10-year period.

2. Materials and methods

2.1. Data

Data for the present study comprised S. agalactiae surveillance and live cattle movement data extending over the period 1999–2009. The surveillance data were extracted from the Danish Cattle Database, which holds information on bacteriological culture of all bulk tank milk (BTM) samples collected as part of the mandatory Danish S. agalactiae surveillance scheme. The scheme entails an annual collection of BTM samples by truck drivers during milk collection, following which the samples are stored on ice. Within 24 h, they are sent to Eurofins laboratory (Holstebro, Denmark) for processing. Bacteriological culture of the samples follows the National Mastitis Council (1999) standards. Besides the test outcome, the herd-specific geo-coordinates (recorded as UTM EUREF89, zone 32 coordinates) and the test date are specified. The cattle movement data were extracted from the Central Herd Register (Danish Veterinary and Food Administration, Glostrup, Denmark). The register captures data on all daily cattle movements within the country. Each movement record details the unique identifier of the animal
involved, its movement date, the identity of the source and destination premises and type of the premises (i.e. beef, dairy, breeder, dealer, market, animal show, communal pasture and animal hospital). A description of the specific premise types is given elsewhere (Mweu et al., 2013).

With regards to the surveillance data, it is noteworthy that repeat testing was effected for selected herds in certain years especially if the first screening result was positive. Therefore, to ensure consistency with the rest of the data, only the initial test outcome for a given herd in a particular year was used to classify herds. By definition, a case was a herd from which S. agalactiae was cultured from its BTM sample; a non-case being otherwise defined. To generate an incidence dataset, cases were considered new in a given year only if they had been non-cases in the preceding year. As for the movement data, cattle translocations between source and destination premises in the year prior to each BTM survey were aggregated to give the number cattle transferred to specific premises. This was done to ensure a temporal sequence between any probable exposure associated with the importations and the risk of infection with the pathogen. Granted that the interest of the present study lay squarely in dairy herds, only movements to dairy herds were retained. Further, because movements between holdings that were registered under the same owner were also recorded, these were excluded since they were deemed not to pose an external risk. Subsequently, a single dataset combining the incidence and movement data was created.

2.2. Spatial and statistical analysis

For each herd in a given year, the time (in months) between screenings was computed and graphed to display the distribution of year-specific study periods.

2.2.1. Actual risk surfaces

In order to facilitate visualisation of the spatial distribution of cases and non-cases, a kernel smoothing technique was applied to the location of cases and non-cases in each year. Generation of the year-specific kernel density surfaces was based on the use of a quartic approximation of a true Gaussian kernel function and a common case-noncase fixed bandwidth, computed via a leave-one-out least squares cross-validation approach (Rudemo, 1982; Bowman, 1984) implemented in the sparr package (Davies et al., 2011) for R software (R Development Core Team, 2013). Arguably, the choice of the appropriate kernel function is comparably of less importance than the size of the bandwidth, with larger bandwidths yielding smoother surfaces (Berke, 2005). Considering that the computed bandwidths were year-specific, to permit temporal comparisons, a calculated median bandwidth value of 19 km was used. As there is not yet a mathematical algorithm developed to compute grid cell sizes, Pfeiffer et al. (2008) contend that the choice of an optimal grid cell size should instead stem from a presentational, biological and numerical perspective. Preferably, grid sizes ought to be larger than the geographical extent of the biological unit of interest. Given an average Danish farm size of 0.57 km² in 2004 (Levin et al., 2006), output grid cell sizes of 1 km² were utilised.

To correct for the spatial distribution of the underlying population of herds at risk, risk maps for each year were created by dividing the kernel density surfaces for cases and the population (given by summing case and non-case densities) in each year. The resulting risk surface provided an estimate of the probability of a herd contracting an infection with S. agalactiae at a specified location in a particular year (Bowman and Azzalini, 1997). The kernel density estimation was accomplished using the Spatial Analyst Extension available in ArcGIS 10.1 (ESRI, Redlands, CA, USA).

2.2.2. Spatial clustering

Evidence for spatial aggregation of cases over and above that of the population of all herds and scale of the distances over which clustering (if present) occurred, was investigated by means of the inhomogeneous K-function implemented in the spatstat package (Baddeley and Turner, 2005) for R software. The inhomogeneous K-function is a non-stationary analogue of the standard K-function (Ripley, 1976), which assesses the presence of clustering in spatial point processes after allowing for spatial heterogeneity in the underlying spatial distribution (Baddeley et al., 2000). Monte Carlo randomisation with 499 simulations was used to randomly permute the location of cases and the entire population of herds at risk in each year. The 95% confidence bounds of these permutations were plotted together with the observed difference functions.

2.2.3. Baseline and movement-related risks

Initially, herds were aggregated into four geographical regions comprising: the eastern Danish islands (including Bornholm, Zealand and Funen), South, Mid and North Jutland. In order to estimate the annual baseline and movement-related incidence risks, year-specific mixed-effects logistic regression models were fitted to the data. The primary fixed effect in the models was whether or not a movement had taken place prior to screening in a particular year. Moreover, as estimates of the annual baseline risks could differ by virtue of study period differences, to obtain 12-months equivalent baseline risks and hence allow for temporal comparability, the study period variable was included in the models centred at 12 months. The variable region was included in the models as a random effect to account for first-order (large-scale) spatial effects. First-order effects describe the variation in the mean value of a process in space (Ripley, 1981). The corresponding equation for the year-specific models can be expressed as follows:

$$\logit(P_i) = \beta_0(\text{intercept}) + \beta_i(\text{movement}) + \beta_i(\text{study period}) + \mu_{\text{region}(i)}$$

where $P_i$ is the probability of the ith herd becoming infected with S. agalactiae in a given year, $\beta_i$s are the regression coefficients associated with the fixed effect variables for the ith herd and $\mu_{\text{region}(i)}$ is the random effect of the region containing herd $i$, assumed to be $\mu_{\text{region}(i)} \sim N(0, \sigma_{\text{region}}^2)$. The baseline and movement-related risks were obtained
by conversion of the corresponding model intercepts and movement-associated coefficients as:

$$\text{Baseline risk} = \frac{\exp(\text{intercept})}{1 + \exp(\text{intercept})};$$

Movement-related risk

$$\exp(\text{intercept} + \text{logodds ratio[movement]}) = \frac{\exp(\text{intercept} + \logodds ratio[movement])}{1 + \exp(\text{intercept} + \logodds ratio[movement])}$$

where the movement-related risk is an attributable risk with a range of −1 to 1 (negative values denoting a protective exposure). Considering the pattern of the annual baseline risks hand in hand with the finding of a higher risk of infection after 2005 (Mweu et al., 2012a), we assessed whether this pattern corresponded to two distinctive risk profiles operating before and after 2005. This was originally undertaken by merging the year-specific data into a repeated measures dataset, and thereafter including the variables time (as binary) and herd (nested within region) as fixed and random effects respectively, in a mixed-effects logistic regression model.

To examine for the presence of any second-order (small-scale) spatial effects in the data, isotropic semivariograms of standardised Pearson residuals obtained from the year-specific models were plotted (Pfeiffer et al., 2008). Second-order effects result from the spatial correlation of a process and as such describe the tendency for deviation in values of the process from its mean to follow each other in neighbouring sites (Ripley, 1981). Accordingly, this analysis facilitated the investigation as to whether geographically close herds were more similar than those geographically distant and the extent to which this occurred. The 95% simulation envelopes of the semivariograms were based on 499 Monte Carlo permutations and were produced in R software using the geor package (Paulo et al., 2001). Additionally, anisotropic semivariograms at angles 0°, 45°, 90° and 135° (with tolerance of 22.5°) were graphed to assess whether any detectable spatial dependency varied with direction.

2.2.4. Predicted risk surfaces

Fitted risk values for the locations of all herds extracted from the year-specific mixed-effects logistic regression models were converted into continuous risk surfaces specific for each year by applying ordinary kriging. Kriging is an interpolation technique that predicts unknown values from data observed at known locations based on weights typically modelled by a semivariogram function (Bailey and Gatrell, 1995). The kriging weights in the present study were based on exponential models fitted to empirical semivariograms of the input data. As kriging holds a merit in allowing the errors of the imputed values to be estimated (Haining, 2003), standard error maps associated with the kriged surfaces were also produced. The analysis was carried out using the Geostatistical Analyst Extension in ArcGIS 10.1.

3. Results

An increasing trend in the pooled herd-level incidence risk of S. agalactiae was observed over the 10-year period, with the highest risk recorded in 2005 (Table 1). With the
exception of the year 2000, the proportion of herds with at least one animal imported was greater than 50%. The highest proportion was noted in 2005 at 60.16%. The temporal distribution of the study periods was uneven (Fig. 1); the median times between screenings being longest in 2001 and 2005 (Table 1). As indicated by the study period interquartile ranges in Table 1, the middle 50% of the herds were screened over longer time spans between 2000 and 2005 compared to the period extending from 2006 to 2009.

The actual risk of a herd becoming infected with *S. agalactiae* varied spatiotemporally (Fig. 2). For the period between 2000 and 2004, the risk was lower and more homogeneously distributed compared to the period spanning 2005–2009. In this latter period, foci of highest risk

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**Fig. 2.** Kernel density risk surfaces displaying the actual risk of a herd becoming infected with *Streptococcus agalactiae* in a given year during the period 2000 to 2009.
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Table 1
Annual pooled incidence risks, proportions of open herds and median study periods as well as the annual baseline and movement-related incidence risks derived from year-specific mixed-effects logistic regression models during the period 2000 to 2009.

<table>
<thead>
<tr>
<th>Year</th>
<th>Incidence</th>
<th>Population at risk</th>
<th>Pooled incidence risk</th>
<th>Proportion of open herds</th>
<th>Median study period (interquartile range)</th>
<th>Baseline incidence risk (95% CI)</th>
<th>Movement-related incidence risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2000</td>
<td>65</td>
<td>9138</td>
<td>0.71</td>
<td>46.34</td>
<td>11.60 (2.70)</td>
<td>0.88 (0.65–1.19)</td>
<td>−0.33 (−0.41–0.05)</td>
</tr>
<tr>
<td>2001</td>
<td>78</td>
<td>8076</td>
<td>0.97</td>
<td>52.17</td>
<td>18.47 (5.10)</td>
<td>0.50 (0.24–1.02)</td>
<td>−0.02 (−0.10–0.49)</td>
</tr>
<tr>
<td>2002</td>
<td>73</td>
<td>7068</td>
<td>1.03</td>
<td>50.42</td>
<td>11.20 (1.63)</td>
<td>0.87 (0.56–1.34)</td>
<td>0.05 (0.19–0.90)</td>
</tr>
<tr>
<td>2003</td>
<td>87</td>
<td>6924</td>
<td>1.26</td>
<td>59.06</td>
<td>11.00 (6.77)</td>
<td>0.86 (0.53–1.36)</td>
<td>0.60 (0.04–2.26)</td>
</tr>
<tr>
<td>2004</td>
<td>56</td>
<td>6416</td>
<td>0.87</td>
<td>57.90</td>
<td>10.83 (10.23)</td>
<td>0.69 (0.44–1.08)</td>
<td>0.28 (−0.08–1.54)</td>
</tr>
<tr>
<td>2005</td>
<td>127</td>
<td>5246</td>
<td>2.42</td>
<td>60.16</td>
<td>15.20 (7.40)</td>
<td>1.70 (1.00–2.89)</td>
<td>0.47 (−0.12–2.36)</td>
</tr>
<tr>
<td>2006</td>
<td>80</td>
<td>4873</td>
<td>1.64</td>
<td>55.30</td>
<td>9.30 (0.67)</td>
<td>2.27 (1.28–3.99)</td>
<td>0.14 (−0.41–2.47)</td>
</tr>
<tr>
<td>2007</td>
<td>96</td>
<td>4495</td>
<td>2.14</td>
<td>55.88</td>
<td>13.10 (0.97)</td>
<td>2.07 (1.48–2.89)</td>
<td>0.65 (−0.19–2.75)</td>
</tr>
<tr>
<td>2008</td>
<td>101</td>
<td>4201</td>
<td>2.40</td>
<td>56.82</td>
<td>12.47 (0.53)</td>
<td>2.80 (2.07–3.77)</td>
<td>0.04 (−0.66–1.85)</td>
</tr>
<tr>
<td>2009</td>
<td>91</td>
<td>4015</td>
<td>2.27</td>
<td>54.35</td>
<td>12.50 (0.50)</td>
<td>1.72 (1.06–2.78)</td>
<td>0.95 (0.01–3.74)</td>
</tr>
</tbody>
</table>

a. Expressed as a percentage.
b. Proportion of herds with at least one animal moved in.
c. Expressed in months.

(0.21–1) were noted in eastern Zealand, with other relatively smaller pockets observable in northern Funen and the western part of Zealand (see area references in the top left map of Fig. 2). However, owing to the low density of dairy herds in Zealand, the uncertainty around the computed kernel density risk estimates for this region is expected to be high.

After accounting for spatial heterogeneity in the underlying population at risk in each year, the year-specific observed difference K-functions showed no evidence for spatial clustering of cases relative to the population of herds at risk in each year (Fig. 3).

The annual movement-related incidence risks revealed a non-significant pattern \((P>0.05)\) over the 10-year span (Fig. 4). Contrastingly, the annual baseline incidence risks demonstrated two characteristic patterns \((P<0.001)\) before and after 2005; the risk being higher for the latter period. Notably, the annual baseline risks were higher than the

![Fig. 3. Observed difference K-functions (with 95% simulation envelopes denoted by black dashed lines) for cases and the population of Danish dairy herds during the period 2000 to 2009.](image-url)
Fig. 4. Plot of the annual baseline and movement-related incidence risks of *Streptococcus agalactiae* in Danish dairy herds during the period 2000 to 2009.

Fig. 5. Empirical semivariograms (with 95% simulation envelopes denoted by black dot–dashed lines) of the residuals of the year-specific mixed-effects logistic regression models during the period 2000 to 2009.
movement-related risks. The year-specific semivariograms of the model residuals demonstrated no evidence for the existence of significant spatial dependency (Fig. 5) i.e. geographically close herds were no different with respect to their status compared to those distant. Moreover, the anisotropic semivariograms established that the spatial distribution of the residuals did not vary with direction. As was the case with the actual risks, the predicted risk of a herd becoming infected with S. agalactiae varied spatiotemporally (Fig. 6). Two patterns of risk were
distinguishable in the period before and after 2005. For the former period, the risk was rather inhomogeneously distributed (though lower than the latter phase), with herds located in certain areas of Jutland (and partly Funen) being at greater risk. In the latter period, the probability of a herd contracting *S. agalactiae* was reasonably uniform throughout the country. The range of the standard error values associated with the predicted risk values was 0.0003–0.03.

The error values were highest in 2008 and 2009 owing to the comparatively few numbers of herds in those years (Fig. 7).

4. Discussion

Analysis of the longitudinal data has demonstrated a spatiotemporal evolution of the predicted risk of infection

![Fig. 7. Standard error maps associated with the predicted risk of a herd becoming infected with *Streptococcus agalactiae* in a given year during the period 2000 to 2009 (as displayed in Fig. 6).](image_url)
with *S. agalactiae*; the risk of a herd becoming infected being more homogeneous and higher during the period following 2005. In the same vein, the annual baseline incidence risks exhibited two distinctive patterns before and after 2005; the latter phase corresponding to the greater risk. However, the analysis neither showed evidence for both spatial clustering and dependency between herds nor any significant role played by acquisition of animals in inducing new infections with the pathogen. The absence of spatial aggregation of infected herds during the 10-year period suggests that after adjusting for the effects of known covariates (in this case region and animal introductions) on the risk of infection, the source of the remaining risk in the year-specific models may reside in within-herd characteristics as opposed to spatially varying factors such as sharing of farm equipment, veterinarians, inseminators, relief milkers, or local trade in animals (*Benschop et al., 2006; Pfeiffer et al., 2008*). This within-herd risk is exemplified by the pattern of the annual baseline risks observed in this study whose key source is largely ascribed to the within-herd human factor (*Jensen, 1985; Zadoks et al., 2011*). Conceivably, farmers and within-herd based relief milkers share a sizeable part of the blame in view of the amount of contact time spent with the milking herd. In one Danish study, ribotyping of isolates derived from dairy workers and bovine milk samples revealed ribotype similarities suggesting the existence of a common origin (*Jensen and Aarestrup, 1996*) whereas in a separate one, 5% (4/77) of interviewed owners of infected herds reported having undergone medical treatment (*Katholm, 2010*). It is however noteworthy that in both studies, a temporal sequence of the infection events was not established. Considering the commonness of the human element within the population of herds, it would be generally expected that the probability of herds acquiring *S. agalactiae* infection would be rather uniformly distributed in space as was witnessed after 2005 in the present study. Therefore, any spatial variation in risk could be presumed to be correlated to the degree of exposure to within-herd personnel, which indirectly relates to the level of biosecurity (*Villarroel et al., 2007*). In Denmark, the number of dairy herds has been on the decline from 9886 to 4258 in the course of the period 2000 to 2009 (*Mweu et al., 2012a*), although accompanied by gradually increasing herd sizes. This growth pattern may heighten the demands for human labour bringing about temporal variations in risk.

The characteristic change observed in 2005 coincides with a repeal in the *S. agalactiae* control policy effected in the same year that saw the earlier ban on movements from *S. agalactiae* infected herds lifted paving way for trade from the affected herds (*Anon., 2005*). Although this shift in policy is evidently supported by the finding that new receipts of animals played no significant role in determining incidence, a presumable consequence of this move could well have been the implied perception by farmers that *S. agalactiae* was under control prompting their adoption of a more relaxed approach to biosecurity that would catalyse the 2005 surge in baseline incidence. Such opportunities for ‘lowering the guard’ may be readily seized especially when farmers fail to grasp the value of maintaining costly preventive strategies (*Hujips et al., 2008*). The finding that the movement-related risks remained stable following the reversal of the movement ban may connote that, relative to the human strains of *S. agalactiae*, bovine strains are supposedly less resistant and thus more amenable to existing management measures. As a case in point, *Dogan et al. (2005)* carried out a comparative study on the phenotypic and genotypic characteristics of 52 human and 83 bovine *S. agalactiae* isolates and demonstrated that resistance to tetracycline and erythromycin was more common among human (84.6% and 26.9%, respectively) than bovine (14.5% and 3.6%, respectively) isolates. If indeed the occurrence of *S. agalactiae* in predominantly naïve herds is as a result of spilt over of human *S. agalactiae*, *Zadoks et al. (2011)* contend that eradication of the pathogen may be infeasible. Nonetheless, this work signifies the need for bolstering biosecurity measures.

In a bid to minimise the risk of introducing *S. agalactiae* into susceptible herds, the pressing call for strengthening within- and between-herd biosecurity measures cannot be overemphasised. With regards to within-herd biosecurity, granted the potential risk of infection transmission from humans to cows, it is advisable for owners of herds in high risk regions to consider reducing the number of relief milkers and barring external personnel from handling cows in parlours (*Barkema et al., 2009*). As supplementary measures, education of milking personnel on personal hygiene and mastitis prevention, together with provision of gloves and hand-washing facilities should be prioritised (*Villarroel et al., 2007*). In fact, gloving has been shown to reduce the bacterial load on milkers’ hands by 75%, and if the gloves are disinfected prior to being worn, the load decreases by 98% (*Olde Riekerink et al., 2008*). Despite the insignificant threat of importing *S. agalactiae* from new animal acquisitions realised from the current study, it would still be preferable that herds remain closed to ensure between-herd biosecurity. However, owing to superseding interests in fulfilling herd genetic improvements and expansion goals, purchase of animals may be necessary. In such cases, it has been recommended that both the history of the herd of origin and the animal to be purchased be established (*Keefe, 2012*). In Denmark, farmers can readily retrieve this information from a public database (the B-register) that stores data on all *S. agalactiae* culture-positive herds (*Katholm et al., 2012*). *Barkema et al. (2009)* offer useful guidelines that could facilitate the acquisition process: importantly, (1) the herd of origin should have a geometric mean BTM somatic cell count of less than 200,000 cells/mL for at least one year and it should not have tested positive for *S. agalactiae* in the last two years and (2) prepartum heifers without udder, teats and milk abnormalities should provide optimal candidates.

There are a couple of limitations inherent to the present study. The presence of *S. agalactiae* in the BTM is often construed as a direct reflection of infected udder quarters in a typical herd (*Keefe, 1997*). However, potential cross-contamination arising either during milk collection associated with residual milk from previously sampled infected herds or during processing at laboratories is possible (*Andersen et al., 2003*). As this study is not immune to the effects of potential cross-contamination, it is plausible that some herds were positively misclassified and
consequently, the computed incidence risks would be over-estimates of the actual risks. Bacteriological culture of BTM has been shown to have an estimated sensitivity and specificity of 68.0% and 99.7%, respectively (Mweu et al., 2012b). Since the spatial algorithms employed in the study could not permit incorporation of the test’s characteristics, the resulting estimates are liable to non-differential misclassification. As such, the estimates should only be viewed as apparent. An obvious drawback afforded by the use of interval-censored data is the inability to determine the exact time that events occur, which therefore impedes the estimation of relevant risk periods (Dohoo et al., 2009). In light of this, the computed study periods should be viewed as proxies for the corresponding risk periods. Edge effects are seen as challenges to spatial analysis. They arise as a result of data locations at the periphery of a study area having fewer neighbours than those at the centre of the study area (Pfeiffer et al., 2008). Considering the robustness of the available data, the main patterns identified in the study are unlikely to have been substantially influenced by potential edge effects.

As an adjunct to the present study, a prospective research area that could prove promising with the advent of molecular sequence data is the investigation of S. agalactiae strain-specific transmission dynamics. This could provide a useful understanding of their transmission potentials and in turn the determination of their threshold levels for control. Furthermore, this work paves way for risk factor studies that could elucidate potential sources of within-herd risk.

5. Conclusion

Analysis of the data spanning the period 2000 to 2009 has demonstrated that the predicted risk of a herd becoming infected with S. agalactiae varied spatiotemporally; the risk being more homogeneous and higher in the period after 2005. Moreover, the annual baseline incidence risks indicated significant but distinctive patterns before and after 2005, where the risk of infection was higher in the latter phase. Contrastingly, the annual movement-related risks revealed a non-significant pattern over the 10-year period. There was neither evidence for spatial clustering of cases relative to the population of herds at risk nor spatial dependency between herds. Notwithstanding this, there is need to step up within-herd biosecurity to minimise the risk of introducing S. agalactiae into naïve herds.

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