A systematic review on the relationship between periparturient management, prevalence of MAP and preventable economic losses in UK dairy herds

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Executive Summary

Johne's disease (JD) is an infectious, progressive, gastrointestinal disease affecting ruminants. Calves are mostly infected in their first six months of life, or in utero. We investigated the impact of specific periparturient management practices on within-herd JD prevalence and economic losses foregone in UK dairy herds by means of data synthesis (systematic appraisal of published evidence and expert elicitation) and use of a pre-existing simulation model. Our results show the scarcity of accurate estimates of the impact of specific periparturient management practices on within-herd JD prevalence, which could, in part, be explained by challenges associated with the chronic nature of JD. Management practices aiming to limit the faecal-oral transmission route of *Mycobacterium avium* subspecies *paratuberculosis* (MAP) were found to be most effective at reducing within-herd prevalence of JD. Practices aiming to limit MAP transmission via colostrum and milk were found to be less effective. Losses foregone for a hypothetical herd of 200 milking cows were considerable; based on the assumptions, it is reasonable to expect between £7000 and £11,000 of losses foregone when management practices are implemented as a package of measures. The findings of this study are envisaged to enable farmers and veterinarians to make more informed decisions on changes to periparturient management to control JD.

Introduction

Johne's disease (JD) is an infectious, progressive, inflammatory gastrointestinal disease affecting ruminants (Harris and Barletta, 2001). The causative bacterium: *Mycobacterium avium* subspecies *paratuberculosis* (MAP) commonly infects dairy cattle; a survey carried out in 2009 estimated that between 27.6% and 42.5% (95% Confidence Interval [C.I.]) of UK dairy herds are MAP-infected (DEFRA, 2009). If unaddressed, JD hampers welfare, productivity and profitability (Richardson and More, 2009). Controls via periparturient management practices have proven effective, economical and practical (Groenendaal et al., 2002). The aim of this study is to estimate the two main desirable outcomes of implementing specific periparturient management practices to control JD in UK dairy farms, namely: the reduction in within-herd prevalence of infection and the economic losses foregone.

MAP infections occur most often during the first 6 months of life due to an incomplete immune system (Whittington and Windsor, 2009; Cocito et al., 1994); infection in adulthood, unlike calfhood, rarely develops into clinical disease (Rankin, 1962). Hence management practices, specific to the periparturient stage are the subject of this study. Infections occur primarily via the faecal-oral route but also via intrauterine transmission or consumption of infected colostrum or milk (Clarke, 1997). Management practices directly address faecal-oral, colostral and milk infection routes; following their implementation, intrauterine transmission would lower in the long-term as the percentage of infected cows in the herd is reduced. Infected ruminants shed MAP primarily in faeces: MAP shed in a day can be enough to potentially infect up to 50,000 calves (Mackenzie, 2011). MAP is also shed in milk and colostrum (Stabel, 2008). Faecal shedding is greater in clinically-infected animals;furthermore, heavy faecal shedders are more likely to shed MAP in colostrum (Streeter et al., 1995).

JD hampers production and profitability prior to clinical signs (Johnson-Ifearulundu et al., 2000). Richardson and More (2009) estimated that decreased feed efficiency in infected cows in Ireland, lowers milk yield by approximately 10% (~1259.3 kg per lactation). DEFRA (2005) estimated JD to cost the UK economy £13 million. Additionally, premature culling incurs costs of replacement stock and is a loss of valuable animals and genetics (Sorge et al., 2010); slaughter value of clinically-infected cows depreciates by 20-30% (National Research Council [U.S.], 2003). Carcasses with significant clinical pathology may not enter the food chain (Herenda et al., 2000). Granulomatous inflammation on the ileal wall can bring about a negative energy balance, initiating an anovulatory state thus incurring reproduction losses and increased culling rate (Wettemann et al., 2003). A study estimated that MAP-positive cows were more likely to be lame (5x), and develop mastitis (2x), digestive disease (1.83x) and respiratory disease (1.25x) (Villarino and Jordan, 2005). One can appreciate the effect of JD on herd health, production and profitability. It was deduced by theoretical research that firstly, improved farm management is the most economically attractive JD control strategy and that a test-and-cull strategy would not eradicate JD within 20 years of implementation; (Norton et al., 2005; Groenendaal et al., 2003). Despite this, a Canadian JD-control survey reported farmers were uncomfortable estimating monetary expenses of management changes (Sorge et al., 2010).

Periparturient management practices can be conveniently grouped into four categories based on the transmission pathway of MAP that they address. These categories are: firstly, faecal-oral (others), whereby faeces originate from other cows in the herd, secondly, faecal-oral (own dam), whereby faeces originate from the calf's own dam, thirdly, colostral and finally, milk transmission pathways. It is well established that "strict calf hygiene" is the most effective, economical and practical JD control strategy (Groenendaal and Galligan, 2003; Dorshorst et al.,2006; Kudahl et al., 2007), however this is a non-specific term. This study will examine various specific management practices to achieve this ideal, thus translating this idea into actions that vets and farmers are able to take. For significant progress in controlling JD, management practices are most often delivered as a package of measures as opposed to individual practices, however, this study will address each management practice individually. Rossiter and Burhans (1996) had identified the need for implementation at the individual farm-level to be prioritized as opposed to generic management strategies. Due to the heterogeneity of farm objectives, management and constraints, a unique set of management practices will suit each scenario. Defining the individual benefits of each management practice will enable farms to “pick, choose and prioritize” a package of management practices that suit their needs.

The study presented here combined firstly, a systematic review of the literature and secondly, information systematically gathered via a questionnaire from the international JD research body. The findings were incorporated into a “Delphi panel” methodology for expert elicitation to assess the likely impact of specific management practices on within-herd prevalence of JD in the context of UK dairy farms. The impact of management practices on within-herd JD prevalence was then used as an input into a previously developed economic model to estimate losses foregone attributable to specific management practices. The findings will be of use to farmers, vets and epidemiologists by enabling them to make informed decisions for the purpose of reducing JD in endemic UK dairy herds.

Methods

Systematic review

A systematic search of relevant evidence published in the scientific literature was carried out, firstly, by applying nineteen search terms to a comprehensive database of published research, namely PUBMED (http://www.ncbi.nlm.nih.gov/pubmed/) during October 2011. Inclusion search terms encompassed the population, location, intervention, measurement and outcome of the study question and were applied to the title and abstract of the papers. Exclusion search terms encompassed species not of interest, type of study not of interest (e.g. review papers) and unrelated terms commonly arising in test searches and were applied to the title only. Inclusion terms within each component were linked using "OR" whilst exclusion terms were linked using “NOT”. Whole components were linked using “AND”. Two filters were applied: papers published in English and papers with abstracts.

Secondly, the proceedings of the International Association of Paratuberculosis conferences (1991-2011) were hand searched (http://www.paratuberculosis.org/pubs/index.htm) for relevant studies. Finally, as part of the expert-opinion questionnaire described below, respondents were asked to suggest any published or unpublished studies that they were aware of which were relevant to this systematic review.

Relevance screening was conducted on papers identified by the systematic search. Research was to be primary in nature, furthermore, studies based on generating outcomes using computer simulations and other forms of theoretical research were rejected. Studies had to contain data relevant to the study question. Relevant papers were then subject to quality assessment. Part 1 of quality assessment involved the rejection of field studies where the JD culling policy was intensified in conjunction with management practices as this would shroud the true impact of management practices. Part 2 involved the completion of a quality assessment form concerning methodology of studies and the soundness and credibility of the results and conclusions; this was completed independently by two assessors. Data was extracted from all studies using a standardized form. Management practices were classified by the transmission pathway of MAP that they aimed to limit: faecal-oral (others), faecal-oral (own dam), colostrum and milk. Associations where deemed statistically significant when $P<0.05$ throughout the study.

International-opinion questionnaire

All members of the International Association of Paratuberculosis (153) and all contactable authors of papers contributing to the systematic review (32) were approached to complete an online questionnaire including fifteen questions of a variety of formats and based on the preliminary findings of the systematic review. Following some initial questions concerning the respondents' background, the main body of the questionnaire gathered their views on the impact of various periparturient management practices by means of scenario-based questions. If a participant had particularly low confidence (i.e. guessing) about an answer to a question, they were asked to indicate this in the comments box provided for each question; these answers were rejected.

Expert elicitation (Delphi panel method)

Expert elicitation was conducted at a Johne's Disease workshop at the Royal Veterinary College on 21st November 2011. Fifteen people attended and formed the "Delphi panel". Experts were mostly experienced large animal UK vets with expertise in designing/implementing JD control programs and academics specialising in JD/MAP were also present. The background and experience of the panel in relation to JD was established via a series of questions. The workshop included two sessions. During the morning session, eight questions were posed, each regarding the impact of maximally implementing a specific management practice on reducing within-herd JD prevalence after 5 years. Five options of reductions in within-herd prevalence could have been selected for each question. Participants did not debate or confer before answering. Questions were posed in the context of a theoretical farm typical of the UK (baseline within-herd JD prevalence of 10% and 200 milking cows). Each question was followed with a “confidence question” whereby participants ranked their confidence from 1 (not very confident) to 4 (very confident) regarding their previous answer. During the afternoon session, key findings from the systematic review and expert-opinion questionnaire and the panels’ grouped responses to the morning session were presented to the panel.The questions of the morning session (with “confidence questions”) were re-posed to the panel. However, during the afternoon session debate was permitted in light of the opinions of others, review and questionnaire findings and a discussion facilitated by a moderator. The responses to the afternoon round of questioning were used for further analysis.

To determine the distribution of the most likely impact of periparturient management practices on within-herd JD prevalence in the context of UK farms, responses from all participants were weighted assuming discrete distributions and considering both i. prevalence reduction following implementation of management practices, and ii. participants’ confidence levels for that answer. For a reduction in within-herd prevalence of less than 25%, it was assumed that such reduction would be 12.5% (halfway), for the rest of possible answers, the same value was considered (100%, 75%, 50% and 25%) and for confidence, the ranking selected (between 1 and 4) was input. Monte Carlo simulations were run ten thousand times to arrive at the mean most likely impact of a management practice on within-herd JD prevalence although the distribution of the impact was used as an input for the economic model described below. Simulations were carried out using @RISK version 4.5 throughout study (Palisade, USA).

Economic model

An economic modelling framework developed by the University of Wisconsin to assess economics of JD in US dairy herds was used to estimate the annual economic losses foregone, attributable to the specific management practices in the same context as for determining the within-herd JD prevalence reduction (http://www.johnes.org/handouts/files/CostofJD_IDEXX%20booklet.pdf). The model was used to estimate losses foregone as a result of implementing specific practices, using stochastic inputs appropriate for UK dairy farms. The outcome was obtained as the minimum, 25% quartile, median, 75% quartile and maximum. Monte Carlo simulation and probability distributions were used to account for variability and uncertainty and run one thousand times.

All fixed inputs were derived from DairyCo data where possible or the theoretical farm posed to the Delphi panel. Exceptions to this are percentage reduction in milk production and slaughter value for clinically-infected cows (10% and 31%) (Richardson and More, 2009; Kudahl and Nielsen, 2009).

The distribution of the most likely impact for each periparturient management practice on within-herd JD prevalence (the response variate) was converted into the variable input required in the model: number of clinically infected cows. The conversion was based on the assumption that out of all MAP-infected cows present in the herd, the clinically infected were those that were in their third parity or higher and also shedding MAP in faeces and/or milk. Firstly, to determine the most likely number of cows in the herd which were in their third parity or higher (45%); a binomial distribution was assumed. Secondly, the number of these cows was multiplied by the resulting within-herd JD prevalence distribution following the implementation of the management practice; a binomial distribution was assumed. Finally, the number of these cows was multiplied by the probability of shedding MAP in faeces and/or milk (0.7 and 0.95) (Nielsen et al., 2002; Nielsen and Ersboll, 2006;Nielsen and Toft, 2006); a uniform distribution was assumed.

Results

Systematic review

A total of twelve papers contributed to the systematic review. Seven papers were identified by the systematic search on PUBMED, four from conference proceedings and one from suggestions by experts who completed the questionnaire. The majority of the studies (n=10) were observational although two were randomized controlled trials concerning preventing colostral MAP-transmission. Furthermore, most observational studies were retrospective (n=7) whilst three were prospective. For three studies, the study unit was the individual animal as opposed tothe herd. The duration of most studies (n=9) was a few years however three were carried out at one point in time. Most studies were conducted in the USA. Mean within-herd JD prevalence of participating herds ranged from 2.7% to 8% whilst mean prevalence of infected herds ranged from 17% to 61%. Most studies relied solely on ELISA for diagnosis.

Management practices aiming to limit faecal-oral (others) MAP transmission were assessed 28 times over ten studies. “High usage of the calving area” (more than 90% of calvings taking place here) was more common in seropositive than seronegative herds (Muskens et al., 2003). However, the association with MAP-infection was only marginally significant (P=0.08). An observational study carried out to inform the New York State paratuberculosis control program found that the odds of MAP-seropositive status where calves (aged 0-6 weeks) had been exposed to adult manure was 30 times higher than in herds where this had not occurred (95% C.I.:1.2-808.7) (Obasanjo et al., 1997). Exposure to other adult cows and multiple animal use of calving area were significant risk factors for infection in other studies (Pillars et al., 2001; Muskens et al., 2003).

Management practices aiming to limit faecal-oral (own dam) transmission were assessed 10 times over seven studies. Only one of five studies assessing the influence of calf time spent with its dam and MAP-infection found a significant association (OR=1.27, P<0.0001) (Pillars et al., 2011). Two of the three management practices concerning udder hygiene were found to be significantly associated with MAP-infection although they were conflicting practices: firstly, soiled udders and legs (OR=1.22) and secondly, washing of cows’ udders prior to parturition (OR=8.66, multivariable) (Pillars et al., 2011; Johnson-Ifearulundu et al., 1998). The latter was supported by the finding that udder washing was not associated with lower MAP-infection (Cavirani et al., 2005).

Management practices aiming to limit colostral MAP-transmission were assessed 8 times over seven studies. Only one of the three studies investigating only feeding colostrum to a calf from its own dam found this to be a significant factor (OR=1.21) (Pillars et al., 2011). Colostrum replacement over maternal colostrum was significantly associated with reduced MAP infection (RR=0.559) (Pithua et al., 2011). Feeding colostrum from one cow to multiple calves as opposed to only feeding colostrum to the dams’ own calves was significantly associated with MAP-infection (OR=1.1) (Pillars et al., 2011).

There were six studies between which management practices were assessed 6 times aiming to limit milk MAP-transmission. Two studies found use of only milk replacer rather than farm milk to be practiced by a greater percentage of MAP-seropositive herds than MAP-seronegative herds although results were not significant (van Weering et al., 2005; Muskens et al., 2003).

Expert-opinion questionnaire

There were 31 respondents to the questionnaire, however, not all responded to each question. Over half of the respondents had experience with the epidemiology of JD. Forty-five percent were involved with implementing JD control programs. Most respondents were working in academia and also government and research institutes. The vast majority were based in North America or Europe. Nineteen respondents were involved with field research. The mode herd size interval in respondents' areas was between 100-199 and 60-99 adult milking cows. Around half of the respondents' indicated that the approximate proportion of adult cows seropositive to MAP in their area was between 2% and 5%.

Collectively respondents ranked the targeting of the four MAP-transmission pathways in the same order (faecal-oral [others], faecal-oral [own dam], colostral and milk) for effectiveness, extent to which the pathway is currently being addressed and cost-effectiveness of targeting it. Although, notably a contradictory comment was left: "Farmers adhere easily to milk and colostrum management, our survey showed that faecal-oral is hardest to deal with" (Academia, Denmark). To limit faecal-oral (others) transmission, respondents viewed separation of feed and water sources to be the most effective measure when compared to appropriate cleaning of calf pens after use and using different equipment to clean adult cow and calf housing, although none of these differences were significant.

Eleven of eighteen respondents recommended calves are removed from their dam immediately or within one hour of birth, the majority of whom were influenced by limiting faecal-oral (own dam) transmission as well as limiting colostral transmission, however no respondent was influenced by limiting solely colostral transmission. Furthermore, the majority of respondents (19/22) considered hygienic collection of colostrum as very important or important. Regarding best practice, twelve respondents favoured maternal colostrum whilst ten favoured colostrum replacement. When asked to prioritize one of the two practices of firstly, pasteurizing milk for calves and secondly, ceasing the pooling of milk, equal numbers of respondents (11) selected each.

Expert elicitation

The mean expected percentage reduction in within-herd JD prevalence achievable by fully implementing specific management practices is shown in Figure 1.The impact of management practices addressing faecal-oral (others) MAP-transmission route (shaded blue) was considered relatively high; participants selecting greater prevalence reductions tended to have higher confidences regarding these answers than participants selecting smaller prevalence reductions. The two management practices addressing faecal-oral (own dam) transmission (shaded green) were perceived very differently: reducing time spent with dam was viewed to have relatively high impact whilst cleanliness of dams' udders and legs was viewed upon as relatively ineffective. Management practices to reduce colostrum (shaded red) and milk transmission (shaded yellow) were not seen as particularly effective, nearly all participants felt implementing these would reduce within-herd JD prevalence by 25% or less than 25%; furthermore, confidences regarding these answers were particularly high.

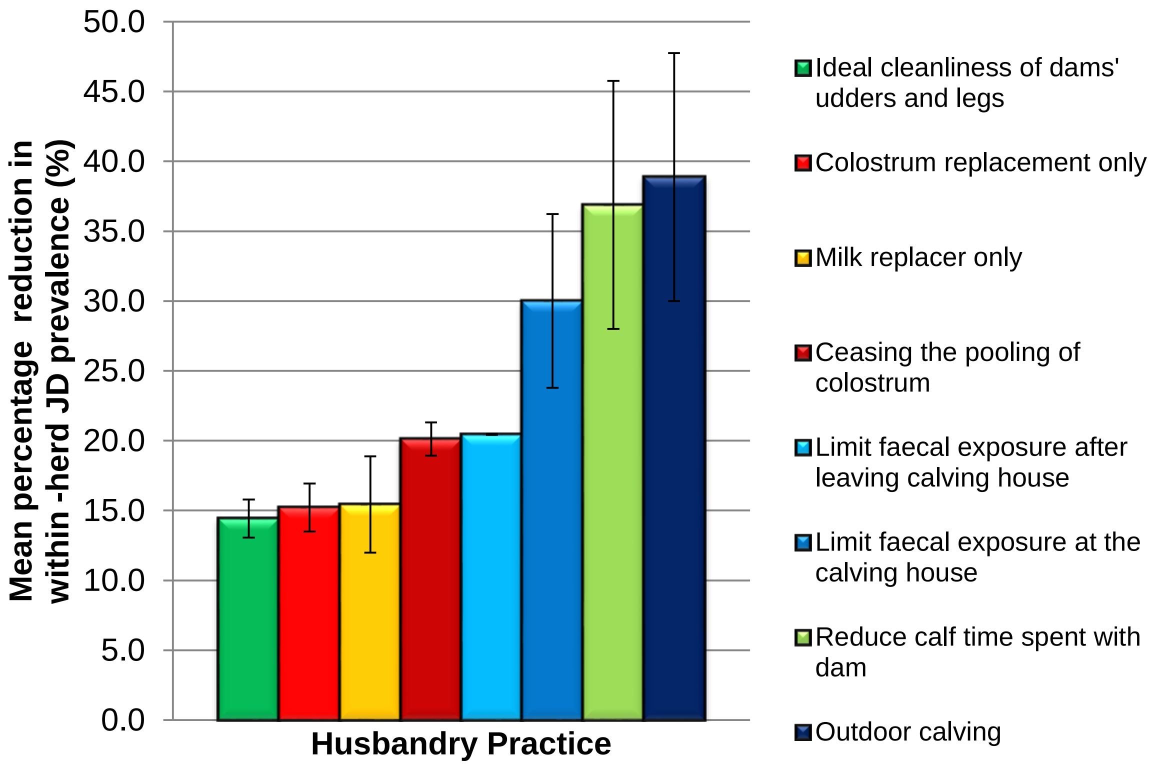

Figure 1.Mean percentage reduction in within-herd JD prevalence attributable to implementation of eight management practices.

Economic losses foregone

Estimates of the economic losses foregone attributable to specific management practices are presented in Figure 2.Reducing use of the calving house was found to confer the greatest savings annually (median: £4184). Addressing faecal-oral (others), tended to be economically attractive, whilst addressing faceal-oral (own dam) tended to give mixed results depending on the management practice. The median economic benefit of using colostrum replacement only and milk replacer only was similar: £1692 and £1700 respectively, these tended to be less effective in terms of foregoing economic losses.

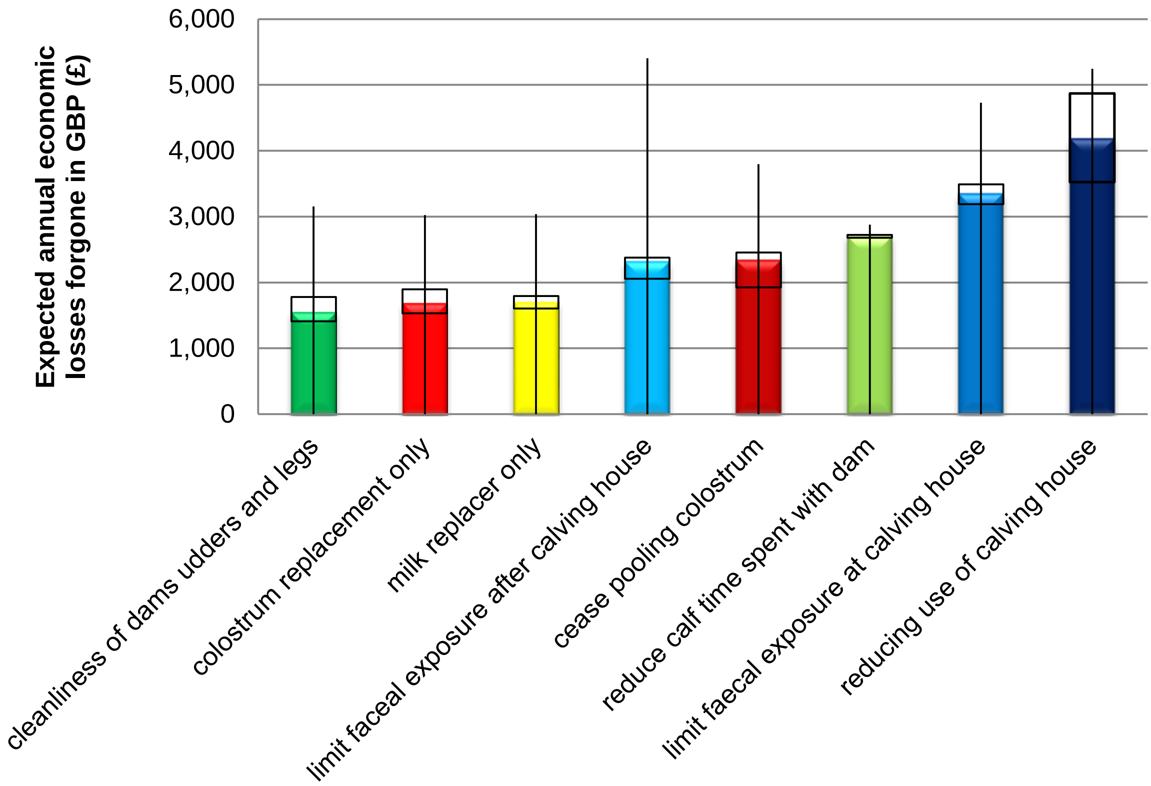

Figure 2. Expected annual losses foregone in GBP (£) attributable to full implementation of specific management practices. Losses foregone are presented as lowest, 25% quartile, median, 75% quartile and greatest loss foregone. The plot shows the median (tip of the coloured bar within the box), 25th and 75th percentiles (black outline box) and 10th and 90th percentiles (ends of the vertical black line).

Discussion

Johne's disease hampers animal welfare and productivity and is of national and international significance. This study aimed to investigate the impact of specific periparturient management practices on within-herd JD prevalence and economic losses foregone. To our knowledge, this is the first study to characterise individual management practices in this context, by means of data synthesis and theoretical research, specifically: appraisal of published evidence, expert elicitation and use of a simulation model.

The systematic review highlighted the lack of field studies regarding the impact of specific management practices on within-herd JD prevalence. A reason for this is the lack of empirical evidence is probably the chronic nature of the infection, which requires lengthyfollow-upof individual animals to assess the relationship between exposure at early stages of life and infection. Lack of reliable diagnostic tests is another reason that may have contributed to the scarcity of field observational studies (Behr and Collins, 2010). Nevertheless, this was surprising as periparturient management is assumed to be a keystone for farm-level JD control and numerous control programs include guidelines on specific periparturient management strategies(Groenendaal and Galligan, 2003; Dorshorst et al.,2006; Kudahl et al., 2007).

Addressing faecal-oral MAP transmission routes were regarded as relatively effectivein comparison to colostral and milk MAP-transmission routes; this was directly expressed by questionnaire respondents and there was a consensus amongst systematic review findings of the association of calf exposure to adult cows with MAP-infection. This latter is in agreement with the findings of a theoretical study conducted for the Netherlands JD control program where prevention of calf exposure to adult cows significantly reduced within-herd JD prevalence (Groenendaal et al., 2003). This is likely due to the significance of adult cows in spreading MAP through the herd (Nielsen et al., 2002). The probability of shedding by these older, infected cows is higher and the concentration of MAP shed can be up to 10^8 cells per gram of faeces (Chiodini et al., 1984); MAP shed in a day can be enough to potentially infect up to 50,000 calves (Mackenzie, 2011).

Similarly, the impact of management practices addressing the faecal-oral MAP transmission routes were deemed effectiveby expert elicitation, particularly, outdoor calving. Outdoor calving diminishes, or at least dampens MAP-transmission associated with the calving house due to availability of space outdoors, less exposure to adult cows and lower faecal contamination density. The advantages of outdoor calving overlap with preventing calf exposure to adult cows, the latter was identified as effective by the systematic review. Outdoor calving also diminishes the need for calving house provisions and was cited as the gold standard for animal health by Dairy Group's Guide to Calving Hygiene (Pocknee, 2011). Obviously, practicalities such as weather conditions and supervision levels do need considering for such a practice.

An exception to the favourability of addressing faecal-oral MAP transmission was practicing cleaning of dams' udders and legs prior to parturition, which was deemed relatively ineffective. Studies have found this practice to be associated with MAP-infection citing negative causality whereby farms with poor hygiene in general attempt to compensate by practicing this (Johnson-Ifearulundu et al., 1998; Wells and Wagner, 2002). The experts may have held a similar view that hygiene measures should be an on-going process aiming to limit faecal-contamination closer to its source rather than "last-minute" measures. An alternative suggestion is that washing udders and legs may truly increase MAP-transmission as the moistening of dried faecal matter in this area may enhance teat contamination. This theory is supported by the importance placed on hygienic methods of colostrum collectionby respondents to the online-questionnaire.

Estimates of the economic losses foregone, attributable to specific management practices were naturally a reflection of their impact on within-herd JD prevalence, as this was the variable input in the economic model. Outdoor calving conferred the greatest JD-associated median losses foregone (£4184); in general, management practices addressing faecal-oral (others) were economically favourable. Cleanliness of dams' udders and legs conferred the least median losses foregone (£1551). Losses foregone were considerable, particularly when it is considered that management practices are implemented as a package of measures, for example using model data it can be estimated that implementing at least one management practice addressing each MAP-transmission route could lead to the foregoing of between £7,000 and £11,000.

Losses associated with JD infectionforegoneas a result of implementing specific management practices have not been previously determined, however Pillars and associates (2009) estimated JD control programs in general to save $79/cow/year. This is roughly £50 (2012), applying this estimate to a 200 cow herd would lead to £10,000 losses foregone –a comparable result to our findings. These estimates support the views of industry as expressed in a recent article in Farmers Weekly (Spackman, 2011).

This study has encompassed the review of published field studies, an expert-opinion questionnaire, expert-elicitation and simulation to determine the impact of specific periparturient management practices implemented on UK dairy herds on within-herd JD prevalence and economic losses foregone. Our results should be interpreted with caution, as they are entirely based on estimates obtained by previous field studies and the opinion of experts. However, the findings have implications for JD control strategies, agricultural policy and understanding of the economic impact of JD and are envisaged to serve as a tool for UK farmers, veterinarians and epidemiologists to tailor JD control programs for different scenarios.

Conclusion

Longitudinal field studies of UK dairy herds are needed to generate estimates under local conditions that could be used in more detailed and realistic economic models. In the absence of such estimates, several useful conclusions can be drawn from this study, firstly, estimates of the impact of specific periparturient management practices on within-herd JD prevalence are scarce and further field studies are required. Secondly, management practices addressing the faecal-oral route of transmission, (whereby faeces originate from the calves' own dams and other adult cows), have a greater impact on reducing within-herd JD prevalence and the foregoing of the economic losses than management practices addressing colostral and milk transmission routes. Where practiced, outdoor calving is an effective strategy to reduce MAP-transmission and to forgo the greatest economic losses.

AHDB Dairy
Agriculture and Horticulture Development Board
Stoneleigh Park
Kenilworth
Warwickshire
CV8 2TL

T: 024 7647 8702
E: dairy.info@ahdb.org.uk
W: dairy.ahdb.org.uk

AHDB Dairy is a division of the Agriculture and Horticulture Development Board (AHDB).