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Use of partial budgeting to determine the economic benefits of antibiotic treatment of chronic subclinical mastitis caused by *Streptococcus uberis* or *Streptococcus dysgalactiae*

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The economic effect of lactational antibiotic treatment of chronic subclinical intramammary infections due to *Streptococcus uberis* or *Streptococcus dysgalactiae* was explored by means of partial budgeting. Effects at cow level and herd level were modelled, including prevention of clinical mastitis episodes and the prevention of transmission of infections. Input variables for our deterministic model were derived from literature or based on 2002/2003 dairy prices and farming conditions in The Netherlands. Sensitivity analysis was used to examine the effect of uncertainty around input variables or changes in price estimates. On farms where pathogen transmission was prevented through proper udder health management, 3-d antibiotic treatment during lactation resulted in an average net profit of €+11·62 over no treatment while 8-d antibiotic treatment had an average negative net result of €−21·83. Sensitivity analysis showed that profitability depends on the probability of treatment-induced cure, pathogen transmission rates, culling rate, retention pay-off, and costs of antibiotic treatment. Three-day antibiotic treatment of chronic subclinical streptococcal mastitis is economically profitable over a range of input values for cure probabilities, transmission rates and losses due to culling. In contrast, 8-d lactational treatment is only profitable for very valuable animals, on farms where the risk of pathogen transmission is high and/or when the farmer is likely to cull a high percentage of cows with subclinical mastitis. Because bacterial flora, cow characteristics and management differ widely between farms, the economic outcome of lactational treatment of chronic subclinical streptococcal mastitis may be highly farm-dependent.

Keywords: Economics, antibiotic treatment, subclinical mastitis, *Streptococcus uberis*, *Streptococcus dysgalactiae*.

Mastitis is the most costly disease in dairy cattle in developed countries (Smith & Hogan, 2001). Costs are mainly due to milk production losses, culling, treatment and milk discarded because of antibiotic residues (Craven, 1987; Esslemont & Kossaibati, 1997; Hortet & Seegers, 1998). Additional costs include decreased fertility (Schrick et al. 2001), changed composition of milk (Hortet & Seegers, 1998), and risk of violation of bulk tank limits or loss of premium for low bulk tank somatic cell count (BTSCC) (Allore et al. 1998; Hogeveen, 2003). In cases of clinical mastitis, farmers are usually willing to treat animals because the animals are diseased, milk is visibly abnormal, and/or milk production has decreased dramatically. Treatment of clinical mastitis is not only a matter of cost *v.* benefit. Legal, ethical and animal welfare arguments also need to be considered in treatment decisions. For example, according to Milk Hygiene directive 92/46 EEC it is not allowed to deliver milk from cows suffering from recognizable inflammation of the udder.

In cases of subclinical mastitis, animals are not clinically diseased and milk is not visibly abnormal. Therefore, inflammation is not recognizable without additional testing and treatment may not seem necessary. Subclinical mastitis, like clinical mastitis, affects milk quality and quantity, and is associated with economic losses as described

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above. Furthermore, cows with subclinical infections may act as a source of infection for other animals, resulting in spread of a mastitis problem in the herd. If benefits of treatment of subclinical mastitis outweigh the costs, treatment may be economically viable, especially when milk quality is a significant component of price (Hillerton & Berry, 2003) or when clinical cases (St. Rose et al. 2003) or infection transmission (Zadoks et al. 2002) can be prevented.

Treatment of subclinical mastitis is often deferred until the dry period (Hillerton & Berry, 2003). However, treatment of subclinical *Streptococcus agalactiae* infections during lactation is economically profitable (Yamagata et al. 1987). The success of treatment programmes for *Str. agalactiae* is partly due to the high proportion of quarters cured after treatment, and to the prevention of disease transmission that is achieved through cure of infected animals (Loeffler et al. 1995). Reported cure proportions for *Streptococcus uberis* and *Streptococcus dysgalactiae* are high too, ranging from 50% to 100% (Bramley, 1984; Owens et al. 1997; McDougall, 1998). Recent studies have shown that treatment of subclinical infections with non-agalactiae streptococci may contribute to prevention of clinical mastitis (St. Rose et al. 2003) and to prevention of streptococcal transmission (Zadoks et al. 2001a, 2003). The cost-benefit ratio of antibiotic treatment of subclinical *Str. uberis* and *Str. dysgalactiae* infections during lactation has not been determined.

The purpose of this paper is to explore the economic benefit of antibiotic treatment of chronic subclinical *Str. uberis* and *Str. dysgalactiae* infections during lactation by means of partial budgeting. In this analysis, effects at the cow level, such as bacteriological cure and prevention of clinical mastitis, and effects at herd level, such as reduced transmission potential, will be taken into account.

Material and Methods

Partial budgeting was used for the development of a deterministic simulation model to estimate the net cost or benefit of lactational treatment of subclinical streptococcal mastitis with antibiotics. The model was specifically adapted for two mastitis-causing agents, *Str. uberis* and *Str. dysgalactiae*, because they are highly prevalent pathogens in many dairy countries but, unlike for *Str. agalactiae*, the economic feasibility of treatment of infections has not been explored. Input variables for the model were based on literature, if available, or on the 2002/2003 dairy situation and prices in the Netherlands. Costs and benefits were calculated at the cow level during one lactation. Three treatment scenarios were explored: no treatment, 3-d treatment (St. Rose et al. 2003), and 8-d treatment (DeLuyker et al. 2001). The choice of treatment duration was based on common practice and availability of registered antibiotics for parenteral (3-d) or intramammary (8-d) treatment of subclinical mastitis in the Netherlands. For each of the three treatment scenarios, a sensitivity analysis was performed to determine the impact of input variables, including the probability of cow-to-cow transmission of mastitis pathogens. Four scenarios were analysed, i.e., 3-d treatment and 8-d treatment, combined with the transmission scenario with low risk of contagious transmission ($R < 1$, specifically $R = 0{\cdot}21$) or high risk of contagious transmission ($R > 1$, specifically, $R = 1{\cdot}4$). In each scenario, sensitivity analysis was performed for all input variables that are listed in Table 1.

A schematic outline of the deterministic model is depicted in Fig. 1, and details of input variables and model assumptions are presented below.

Model Inputs

Probability of Cure. Under Dutch farming and screening conditions, subclinical mastitis is suspected if two out of three consecutive milk samples taken at 3-week or 4-week intervals have somatic cell counts (SCC) >250 000 cells/ml. Thus, a subclinical streptococcal infection would have been present for at least 3 or 4 weeks before it was eligible for treatment. Usually, a decision to treat will be preceded by milk sample collection and bacteriological culture, adding to the duration of infection before treatment, if any, is initiated. The probability of spontaneous bacteriological cure for chronic subclinical streptococcal infections was estimated to be between 0% (St. Rose et al. 2003) and 20·5% (DeLuyker et al. 2001: 25% for *Str. uberis*, 16% for *Str. dysgalactiae*). The arithmetic average, i.e. 10%, was used in our model (Fig. 1). After 2-d or 3-d treatment with intramammary or parenteral antibiotics, cure probabilities have been reported to be 82·6% for *Str. uberis* (McDougall, 1998), 58·6% for both species combined (St. Rose et al. 2003), and 33·5% for *Str. uberis* and 73·5% *for Str. dysgalactiae* (DeLuyker et al. 2001). The arithmetic average, 62%, was used as the estimated probability of cure after 3-d treatment in our model (Fig. 1). After 8-d treatment, the probability of cure is 75% for *Str. uberis* and 100% for *Str. dysgalactiae* (DeLuyker et al. 2001). The average, 87·5%, was used as the estimated probability of cure after 8-d treatment in our model (Fig. 1). Chronic subclinical infections that do not cure may remain subclinical or develop into clinical flare-ups. The probability of clinical flare-ups is estimated at 19·3% (average of Lam, 1996: 27·5%; St. Rose et al. 2003: 16·7%; Zadoks et al. 2003: 13·8%) (Fig. 1).

Probability of transmission. Cows with chronic streptococcal mastitis and continued bacterial shedding cause extended exposure of the whole herd to pathogenic bacteria which may result in infection of other cows in a herd (Zadoks et al. 2001a; Hillerton & Berry, 2003). The extent to which transmission to other cows occurs is species dependent and is higher for *Str. agalactiae* than for non-agalactiae streptococci, and higher for *Str. dysgalactiae* than for *Str. uberis* (Neave et al. 1969; Fox &

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Table 1. Partial Budgeting: calculation of net profit (€) of 3-d or 8-d lactational treatment *v.* no treatment of chronic subclinical mastitis due to *Streptococcus uberis* or *Streptococus dysgalactiae*. Net profit is calculated as (extra revenue + reduced costs) minus (reduced revenue + extra costs)

Contribution to Economic Effect	Reference	Treatment	
		3-d	8-d
Extra revenue			
Increase in milk production after cure, kg milk	McDermott, 1983 St. Rose, 2003	0	0
Total extra revenue	Calculated	0	0
Reduced costs			
Reduction in probability of clinical mastitis after treatment, %	St. Rose, 2003 Calculated	12·3%	17·3%
Costs of clinical flare-up of pre-existing subclinical mastitis	De Vos & Dijkhuizen,1998	117	117
Reduced costs due to prevention of clinical flare-ups, €	Calculated	14·39	20·24
Reduction in probability of persistent subclinical mastitis, %	Calculated	43·7%	61·7%
Number of new infections that is prevented	This paper	0·15	0·15
Probability that new infection results in spontaneous cure, %	McDougall, 1998 Zadoks, 2003 Smith, 1985 Wilson, 1996, 1999	38%	38%
Probability that new infection results in clinical mastitis, %	Jayarao, 1999 Lam, 1996 Zadoks, 2003	30%	30%
Probability that new infection results in chronic subclinical mastitis, %	This paper	32%	32%
Costs of spontaneous cure, €	This paper	5	5
Cost of clinical mastitis, €	De Vos & Dijkhuizen,1998	209	209
Costs of subclinical mastitis, €	This paper	122·80	122·80
Reduced costs due to prevented transmission, €		6·81	9·62
Reduction in probability of persistent subclinical mastitis, %		43·7%	61·7%
Retention pay-off, €	De Vos & Dijkhuizen,1998	526	526
Culled animals, %	Esslemont & Kossaibati, 1997 Whitaker, 2001 NRS, 1998 This paper	12%	12%
Reduced costs due to prevented culling, €		27·58	38·95
Reduced costs due to prevented penalties for high SCC		0	0
Reduced costs due to prevention of decreased fertility		0	0
Total reduced costs, €		48·78	68·80
Reduced revenue			
Milk discard because of antibiotic residue, kg/d	NRS, 1998	24·2	24·2
Duration of milk withhold, d	This paper	6	11
Total discarded milk, kg		145·2	266·2
Balanced profit milk, €/kg		0·07	0·07
Total reduced revenue, €		10·16	18·63
Extra costs			
Antibiotics, €	This paper	27	72
Labour, €	This paper	0	0
Costs penalties antibiotic residues in milk, €		0	0
Total extra costs, €		27	72
Net profit, €		+11·62	−21·83

Gay, 1993). The infectiousness of a pathogen can be expressed in the transmission parameter, β, i.e., the average number of new infections caused by an infectious individual per unit of time. For mastitis, this would translate into the number of new infections caused per day by an infected cow (Zadoks et al. 2001a). The total number of new infections caused by an infected individual also depends on the duration, τ, of the infection in that individual. The combined effect of infectiousness and duration is represented by the reproductive ratio, R, which is the total number of new infections caused by an infected individual during its infectious lifetime. R is commonly represented as β/α, where α is the cure rate. The cure rate is equivalent to $1/\tau$, i.e., the inverse of duration.

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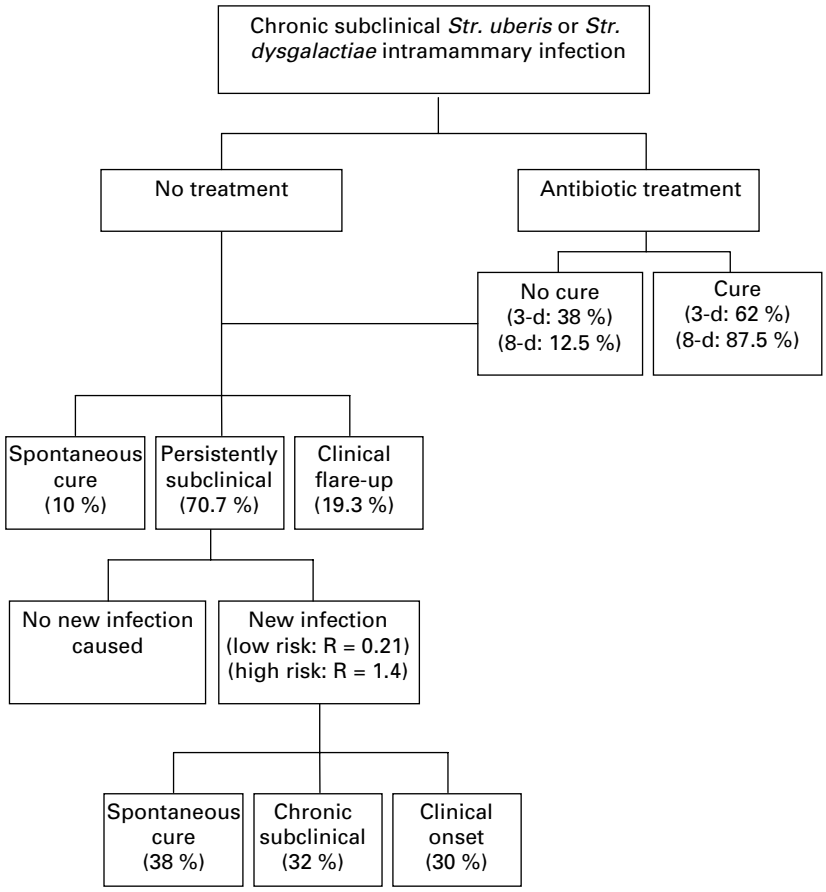

Fig. 1. Deterministic model for the effect of 3-d or 8-d antibiotic treatment or no treatment of chronic subclinical intramammary infections with *Streptococcus uberis* or *Streptococcus dysgalactiae*. Flow through diagram is from top to bottom, not in reverse. R = reproductive ratio, i.e., the total number of new infections caused by an infected individual during its infectious lifetime (Zadoks et al. 2001a).

The duration of non-agalactiae streptococcal infections has been described in several studies, and ranges from 1 d to a full lactation (Todhunter et al. 1995; Zadoks et al. 2003). Median duration has been estimated at 42 d for *Str. uberis* (Zadoks et al. 2003), while mean durations have been estimated at 13 d for environmental streptococci (Todhunter et al. 1995), at 67 d for *Str. uberis* (Zadoks et al. 2003), at 56–96 d for *Str. uberis* (Lam et al. 1997), and at 34–81 d for *Str. dysgalactiae* (Lam et al. 1997). Because duration of infection is not normally distributed, the median (42 d) is probably a more appropriate measure of duration than the mean. Therefore, we assumed $\tau = 42$ d or $\alpha = 0{\cdot}024$ as the most likely scenario. For those animals that are eligible for and/or subjected to treatment, there is left and right censoring of the duration of infection. Animals are not considered eligible for treatment until they have been infected for at least 3–4 weeks (minimum duration for detection of two subsequent SCC values $>250\,000$ cells/ml, plus time needed for diagnosis and treatment decision). This censoring excludes infections of less than approximately 30 d of duration. Animals that receive treatment will cure in a large proportion of cases, resulting in right censoring of the duration of infection. Because diagnosis, treatment decision and treatment usually take several days or even weeks, the maximum duration of infection would be around 50 d for such animals. Hence, 42 d seems a reasonable estimate for duration of infection both for untreated and for treated animals.

Estimates for the transmission parameter of mastitis causing bacteria are scarce owing to the labour-intensive nature of studies needed to generate them (Lam, 1996; Zadoks et al. 2001a, 2002). The transmission parameter for *Str. uberis* has been estimated from field data as 0·033 during an outbreak of *Str. uberis* mastitis, while it was much lower, 0·005, during a non-outbreak situation, as described in detail elsewhere (Zadoks et al. 2001a). Briefly, an outbreak is where many new infections occur over a short period, probably as a result of contagious transmission, while a non-outbreak is where contagious transmission is controlled and new infections originate predominantly from the environment (Zadoks et al. 2001a, 2003). In our economic model, 0·005 was used as baseline estimate for β while 0·033 was considered a worst-case

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scenario. Estimates were originally based on udder quarter as the unit of analysis, but were used as cow-level estimates in our economic model, for lack of a better approximation. For *Str. dysgalactiae*, no estimates of the transmission parameter are available, and values for *Str. uberis* were also applied to *Str. dysgalactiae*. Based on our estimates for duration ($\tau = 42$) and the transmission parameter ($\beta = 0{\cdot}005$ with good control of contagious transmission; $\beta = 0{\cdot}033$ with poor control of contagious transmission), the reproductive ratio, R, is calculated to be 0·21 or 1·4 for scenarios with good and poor control of contagious transmission, respectively (Fig. 1).

Treatment of chronic subclinical mastitis reduces the duration of infection and therefore the chance of transmission to other cows. For *Str. uberis* infections that last longer than 42 d, median duration is 72 d (original data from Zadoks et al. 2003). According to Lam et al. (1997), duration is similar for *Str. uberis* and *Str. dysgalactiae*, so one estimate for both species was used. As a result, prevented duration of infection by treatment is calculated as 30 d and hence prevented contagious transmission is estimated at $0{\cdot}005 \times 30 = 0{\cdot}15$ new infections under good herd management (Table 1), and $0{\cdot}033 \times 30 = 1$ new infection under poor herd management.

When transmission of infection occurs, the new infection may be clinical or subclinical. For *Str. uberis*, the probability that a new infection is clinical has been reported as 48% in seven Dutch herds with annual BTSCC < 150 000 cells/ml (Lam, 1996), as 15% in two Dutch herds with annual BTSCC between 200 000 cells/ml and 300 000 cells/ml (Zadoks et al. 2003), and as 5% in one research herd in the USA (Jayarao et al. 1999). For *Str. dysgalactiae*, 51% of infections were reported to have clinical onset (Lam, 1996). The arithmetic average probability that a new infection with either species has clinical onset is 30% (Fig. 1). The remaining 70% of new infections have subclinical onset. The infections with subclinical onset may cure within a month, or become chronic so that they would be detected under the Dutch 3–4-weekly sampling scheme. During the first month of subclinical infection, spontaneous cure was observed for *Str. uberis* in 73·2% of cases in New Zealand (McDougall, 1998), and 37·5% of cases in The Netherlands (original data from Zadoks et al. 2003), and for non-agalactiae streptococci in 38·5%, 60% or 59% of cases (Smith et al. 1985, Wilson et al. 1996, Wilson et al. 1999, respectively). The arithmetic average probability of spontaneous cure based on those estimates is 54%. Thus, of all new infections, 30% are assumed to be clinical at onset, 54% of the remaining 70%, i.e., 38%, are assumed to be subclinical in onset followed by spontaneous cure within a month, and the remaining 32% of new infections are expected to become subclinical and chronic (Fig. 1). Flare-ups of chronic subclinical infections to clinical cases are incorporated in the cost calculations, but remission of clinical cases to subclinical infections is not included in the model.

Economic calculations

To enable calculation of economic effects, the input variables are divided into four parts: extra revenue, reduced costs, reduced revenue and extra costs. If the sum of extra revenue and reduced costs is larger than the sum of reduced revenue and extra costs, the net result is positive. A positive net result means treatment is economically profitable. A negative net result means treatment is not economically profitable (Dijkhuizen & Morris, 1996). Input variables used for calculation of economic effect are listed in Table 1.

Extra revenue. Increase in milk production resulting from treatment would be extra revenue. This increase was assumed to be zero based on results from McDermott et al. (1983) and St. Rose et al. (2003) who found no increase in milk production after bacteriological cure of subclinical mastitis (Table 1).

Reduced costs. Successful treatment of chronic subclinical mastitis may prevent other costs. Costs can be reduced by (1) prevention of clinical mastitis (St. Rose et al. 2003), (2) prevention of transmission of infection to other cows (Zadoks et al. 2001a), (3) prevention of culling (Esslemont & Koissabati, 1997), (4) prevention of penalties for high SCC (Allore et al. 1998; Hoogeveen, 2003), and (5) prevention of losses due to poor fertility (Schrick et al. 2001).

The estimated reduced cost due to prevention of clinical mastitis is based on results from the Netherlands as reported by De Vos & Dijkhuizen (1998), who considered clinical cases that were new infections and clinical cases that were flare-ups of pre-existing subclinical infections. For streptococci, cost of new clinical mastitis cases was calculated as €209 while the cost of clinical flare-ups of subclinical infections was calculated as €117 (De Vos & Dijkhuizen, 1998) (Table1). For both situations, costs of premature culling, antibiotic treatment and discarded milk were included in the cost estimate, while milk loss is only attributed to the clinical mastitis if it is a new infection, but not when it is part of a pre-existing infection. Without treatment, the probability of clinical flare-up is 19·3% (Fig. 1). With treatment, clinical flare-up only happens in non-cured cases (Fig. 1), i.e., in 19·3% of 38% or 7% of treated cases for 3-d treatment, and in 19·3% of 12·5% or 2% of treated cases for 8-d treatment. Thus, the reduction in probability of clinical flare-up is 19·3% −7% = 12·3% and 19·3% −2% = 17·3% for 3-d and 8-d treatment, respectively (Table 1). The estimated reduced cost due to prevention of subclinical mastitis can be attributed to reduced probability of persistent subclinical mastitis, to prevention of new infections, prevention of culling, and prevention of elevated BTSCC. The probability of persistent subclinical mastitis is 70·7% without treatment (Fig. 1). After treatment, 38% or 12·5% of cases do not cure

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(Fig. 1), and 70·7% of these non-cured cases will persist as subclinical infections. Thus, 70·7% of 38%, i.e., 27%, or 70·7% of 12·5%, i.e., 9% of treated cases will persist as chronic subclinical infection after 3-d and 8-d treatment, respectively. This results in a reduction of chronic subclinical infections of 70·7% −27% = 43·7% and [70·7% −9·0% = 61·7%] for 3-d and 8-d treatment, respectively (Table 1). When new subclinical infections are prevented, the milk production losses and probability of culling, clinical flare-up and transmission associated with such infections are prevented, resulting in reduced costs. Milk production losses of a cow with SCC of 50 000 cells/ml are assumed to be zero, while there is a decrease in milk production of 0·4 kg/d for heifers and 0·6 kg/d for a multiparous cow for every doubling of the cow-level SCC (Hortet & Seegers, 1998). The average SCC is $10^{6.34}$ cells/ml for quarters infected with *Str. dysgalactiae* and $10^{6.72}$ cells/ml for quarters infected with *Str. uberis* (Schepers et al. 1997). When using the geometric average for SCC of *Str. dysgalactiae* or *Str. uberis* infected quarters, and assuming that the average cow has one infected quarter (SCC = $10^{6.53}$ cells/ml) and three non-infected quarters (SCC = 50 000 cells/ml) with equal milk production per quarter, the SCC of an infected cow can be calculated to be $10^{5.95}$ cells/ml or 884 610 cells/ml, implying a greater than 16-fold increase in SCC, or a loss of 1·6 kg/d for heifers and 2·4 kg/d for multiparous cows. We assumed that the probability of a new infection was independent of stage of lactation (Zadoks et al. 2001b) and that, on average, intramammary infection starts at 150 d from calving. Under that assumption, production loss was calculated as 150 × 1·6 kg/d = 240 kg/heifer per lactation and 150 × 2·4 kg/d = 360 kg/cow per lactation, with an arithmetic average of 300 kg. This calculation does not take into account that older cows are more likely to get new infections than heifers (Zadoks et al. 2001b), that herds are usually composed of < 50% heifers, or that infection and production losses may occur in more than one quarter per cow. The importance of errors in estimated production losses were evaluated as part of the sensitivity analysis.

A spontaneous cure of a new subclinical infection is still considered to result in production loss because we assumed the cow had been infected for a short period (approximately 30 d). This production loss is then calculated as 30 d × 1·6 kg/d = 48 kg, or 30 d × 2·4 kg/d = 72 kg. The costs of spontaneous cure are assumed to be 72 × 0·07 = €5 (Table 1). The total costs of a new subclinical infection include milk production loss, premature culling and transmission to other cows and were calculated to be €122·80 (Table 1).

Prevention of culling is another reduced cost that results from prevention of new subclinical infections. Culling due to mastitis was 10·1% and 16·3% of the total number of cows culled per year among 50 and 340 herds, respectively, in the UK (Esslemont & Kossaibati, 1997; Whitaker et al. 2001). The latter value is close to the average culling percentage (17·6% of culled cows was culled because of mastitis) reported for a limited number of research herds in the Netherlands (Smolders et al. 1994). For our model, we used an estimated culling percentage due to udder health of 15% of the total number of cows culled per year. Of the culling due to mastitis, 50–65% was attributed to subclinical mastitis. On average, 34% of cows are culled annually on Dutch farms (NRS data, 1998), so that 3% (50–65% of 15% of 34%) of the total number of cows would be culled due to subclinical mastitis. When assuming that on average approximately 25% of animals are subclinically infected in a herd with BTSCC of 200 000–300 000 cells/ml (Eberhart et al. 1982), the probability of an already subclinically infected animal being culled is 12%. For the average value of an animal we used the retention pay-off of €526 (De Vos & Dijkhuizen, 1998). In this retention pay-off, salvage value has been allowed for.

Other reduced costs, such as prevention of impaired fertility or prevention of penalties for high SCC were not considered in the current model, although it is acknowledged that penalties and bonuses in particular may be important factors in the economics of mastitis (Allore et al. 1998).

Reduced revenue. Reduced revenue of treatment is the discarded milk due to antibiotic residues resulting from treatment. Average milk production was assumed to be 24·2 kg (8073 kg in 334 d of lactation) (NRS, 1998) (Table 1). The average milk-withholding period is assumed to be 6 d for 3-d treatment and 11 d for 8-d treatment, equivalent to the duration of treatment plus an extra 3 d of milk withhold (six milkings when milking twice a day).

Extra costs. The extra costs for treatment include costs of diagnostic testing, antibiotics, and extra labour. In addition, there is a risk of penalties for antibiotic residues in the milk when cows are treated. Diagnostic testing can be done at quarter, cow or herd level, through evaluation of SCC patterns, or through culture of milk samples from individual quarters, cows, clinical cases, or bulk tank milk. Because of the variability of methods and associated cost, we did not include the cost of diagnostic testing in our model.

Costs of antibiotic treatment depend on the treatment regimen, i.e., choice of drug, dosage, route of administration, and treatment duration. In 2002/2003, the farmers' price in an average Dutch veterinary practice for a 3-d treatment was estimated to be €27 and for an 8-d treatment to be €72 (Table 1).

Labour for treatment has to be taken into account if the farmer can economically use the time that is saved by not treating the animal. Since this is not likely, we have assumed the labour costs to be zero. Extra costs due to penalties for antibiotic residues in milk are also neglected, because they can be prevented through good management (Table 1).

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Table 2. Sensitivity analysis: Effect on net profit of the five most influential input variables (proportional change in output higher than proportional change in input) in the scenario of 3-d or 8-d treatment on a farm with a low probability of contagious transmission of *Streptococcus uberis* or *Streptococcus dysgalactiae*

	Net profit 3-d treatment, €	Net profit 8-d treatment, €
Bacteriological cure, %		
21 (DeLuyker et al. 2001)	−20·56	−74·03
39 (DeLuyker et al. 2001)	−6·82	−60·29
50 (DeLuyker et al. 2001)	1·81	−51·66
59 (St. Rose et al. 2003)	8·88	−44·59
69 (DeLuyker et al. 2001)	16·73	−36·74
75 (DeLuyker et al. 2001)	21·04	−32·43
82 (McDougall, 1998)	27·32	−26·15
90 (Owens et al. 1997)	33·21	−20·26
100 (DeLuyker et al. 2001)	41·06	−12·41
Number of new infections caused by an existing infection, R		
0·21 (low risk of contagious transmission) (Zadoks et al. 2001a)	11·62	−21·83
1·4 (high risk of contagious transmission) (Zadoks et al, 2001a)	68·60	58·62
Proportion of cows with subclinical mastitis that is culled, %		
0	−15·96	−60·78
12 (this paper)	11·62	−21·83
20	30·01	4·13
Retention pay-off, €		
0	−15·96	−60·78
526 (De Vos & Dijkhuizen, 1998)	11·62	−21·83
1200	46,97	28·07
Antibiotic costs, €		
15	23·62	35·17
27 (this paper; 3-d treatment)	11·62	23·17
38	0·62	10·93
50	−11·38	0·17
72 (this paper; 8-d treatment)	−33·38	−21·83

Sensitivity Analysis

Sensitivity analysis is used to calculate what happens to the net result if one input variable at a time is changed from the average situation. Input variables that have a strong effect on the return on investment need to be estimated in a herd-specific manner to give adequate economic prognoses for antibiotic treatment in specific herds. When estimates for input variables that have a strong impact on economic outcome are scarce or vary widely among sources, need for further research into the value of that parameter may be indicated.

We present two treatment scenarios, i.e., 3-d treatment and 8-d treatment, combined with the transmission scenario without contagious transmission ($R < 1$, specifically $R = 0{\cdot}21$). In each scenario, sensitivity analysis was performed for all input variables that are listed in Table 1.

Results

The average economic benefit of treatment of chronic subclinical infection with *Str. uberis* or *Str. dysgalactiae* during lactation after 3-d or 8-d treatment on farms where the probability of transmission to other cows is low is shown in Table 1. The average net profit of 3-d treatment or 8-d treatment is €+11·62 and €−21·83, respectively. On farms where the probability of transmission is high, the average net profit of 3-d treatment or 8-d treatment is €68·60 and €58·62, respectively. All other scenarios yielded profits or losses in between these extremes.

Results of sensitivity analyses for the two treatment scenarios with low risk of transmission are shown in Table 2. The table lists the five input variables that had the strongest impact on economic return. This impact was based on the relative effect on economic return when compared with the relative change of the input variable. For example, if the input variable was changed by 10% and as a result, the economic return changed by more than 10%, the input variable was classified as being influential. Of all the input variables shown in Table 1, the influential input variables are (1) the probabilities of bacteriological cure and transmission (R), (2) the probability of culling together with the retention pay-off, and (3) the cost of antibiotics used for treatment. Changes in milk production

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losses did not have much impact on economic returns. The same variables were influential in sensitivity analysis of the treatment scenarios under high risk of transmission (results not shown).

Results for 3-d treatment in a herd where contagious transmission is unlikely indicate a net profit for most input variable values explored in the sensitivity analysis, provided that the bacteriological cure is at least 45–50% and the combined cost of diagnosis and treatment does not exceed €38. When contagious transmission is unlikely, 8-d treatment is not economically profitable, except for very valuable animals with a high retention pay-off, on farms where the probability of culling due to subclinical mastitis exceeds approximately 20% or when the combined costs of diagnosis and antibiotic treatment remains below €50 (Table 2).

When contagious transmission of streptococci is likely, the net result of treatment would nearly always be positive according to our sensitivity analysis, irrespective of the level of other input variables. Note that this result is based on sensitivity analysis for one input variable at a time. If multiple input variables are changed together, all in a direction of strong negative influence on economic profit, treatment may not be advantageous.

Discussion

In Europe, where acceptable maximum levels for bulk milk SCC are much lower than in the USA (400 000 cells/ml *v.* 750 000 cells/ml) and where milk quotas are in place in many countries, antibiotics for treatment of subclinical mastitis during lactation are currently being marketed. The availability of these products, combined with results from recent research prompted us to re-examine the long-held view that treatment of *Str. agalactiae* mastitis during lactation is profitable (Yagamata et al. 1997), but that lactational treatment of subclinical mastitis caused by non-agalactiae streptococci is not economically justified (Craven, 1987; Wilson et al. 1999). We show that lactational treatment of chronic subclinical mastitis caused by *Str. dysgalactiae* or *Str. uberis* may also be economically beneficial.

Factors that we took into account and that have not been considered in previous economic calculations include the prevention of clinical flare-ups of subclinical infections (St. Rose et al. 2003) and the prevention of contagious transmission. Although non-agalactiae streptococci are often termed ''environmental streptococci'', *Str. dysgalactiae* is widely considered to be a contagious pathogen (Neave et al. 1969; Fox & Gay, 1993; Wang et al. 1999). *Str. uberis* does often have an environmental source (Wang et al.1999; Phuektes et al. 2001; Zadoks et al., 2003), but it may also spread from cow to cow (Phuektes et al. 2001; Zadoks et al. 2003). Measures that prevent contagious transmission reduce the prevalence of both *Str. dysgalactiae* and *Str. uberis* (Neave et al. 1969) and failure to treat infected animals or to use post-milking teat disinfection has been associated with outbreaks of *Str. uberis* mastitis (Cattell, 1996; Zadoks et al. 2001a, 2003). Strain typing is widely used in research to determine whether contagious transmission plays a role in a specific herd (Wang et al. 1999; Phuektes et al. 2001). As technology becomes cheaper, strain typing may become available for diagnostic purposes. Its use may improve insight in herd-specific epidemiology and assist in sound economic decision-making with respect to treatment of subclinical mastitis.

There is uncertainty and variability in many input parameters in our model. Sensitivity analysis indicated that the most important factors affecting the outcome of our economic analysis could be associated with the biology of mastitis and its causative agents, herd management, and economic factors such as retention pay-off or cost of antibiotics. Some of these factors, e.g., the probability of cure, may be strain-dependent or cow-dependent. For example, for *Staphylococcus aureus* it has been shown that some strains are more likely to cure than others (Sol et al. 2000), and also that some cows are more likely to cure than others, be it with (Sol et al. 1997, 2000) or without treatment (Schukken et al. 1999). Some *Str. uberis* strains are more likely to cause chronic infections than others (Zadoks et al. 2003), but strain- or cow-specific factors that affect the probability of cure after treatment have not been determined. Further research on those topics is desirable for *Str. uberis* and *Str. dysgalactiae*.

Other factors, e.g., the probability of contagious transmission, may be strain dependent as well, as shown for *Staph. aureus* (Middleton et al. 2002) and *Str. uberis* (Zadoks et al. 2003), or management dependent, again as shown for *Staph. aureus* (Zadoks et al., 2002) and *Str. uberis* (Zadoks et al., 2001a). Because bacterial flora, cow characteristics and management differ widely between farms, the economic outcome of lactational treatment of chronic subclinical streptococcal mastitis may be highly farm-dependent.

Several of the factors that have an important impact on model outcome may differ between the two bacterial species we considered, *Str. dysgalactiae* and *Str. uberis*. On average, cure probabilities are higher for *Str. dysgalactiae* than for *Str. uberis* (DeLuyker et al. 2001) making a positive economic outcome more likely for treatment of *Str. dysgalactiae* mastitis. *Str. dysgalactiae* and *Str. uberis* also differ in contagiousness (Neave et al. 1969). Because contagiousness contributes to the profitability of economic treatment, as reflected in well-accepted feasibility of lactational treatment of the highly contagious *Str. agalactiae*, lactational treatment is again more likely to be profitable for *Str. dysgalactiae* than for *Str. uberis*. Data on *Str. dysgalactiae* are relatively scarce in the mastitis literature and its epidemiology is not entirely clear. The lack of information on *Str. uberis* and even more so for *Str. dysgalactiae* hampers an objective and detailed comparison

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of the two pathogens. As a generalization, epidemiology and response to treatment seem to favour treatment of *Str. dysgalactiae* over treatment of *Str. uberis* although management and strain differences between herds may make treatment economically (un) feasible for either species. Sensitivity analysis showed that 3-d treatment is profitable as long as combined costs of diagnosis and treatment does not exceed €38, and provided that at least 45–50% of treatments result in bacteriological cure. Thus, costs of culture (€3·95/sample, Animal Health Service, The Netherlands, data from 2003) and 3-d treatment (€27) would, on average, be offset by treatment revenues. Further analysis would be necessary to determine which specific diagnostic strategy (SCC-based or culture-based, at quarter, cow or herd level) would be economically most advantageous under various management conditions.

In contrast to 3-d treatment, 8-d treatment of chronic subclinical mastitis caused by *Str. dysgalactiae* or *Str. uberis* is, on average, not economically feasible, even if the prevention of clinical flare-ups and the costs that are prevented through prevention of new infections are considered. The higher costs of antibiotics and stronger reduction in profits due to milk withdrawal are not compensated for by the reduced costs due to a higher probability of bacteriological cure in comparison with 3-d treatment. Sensitivity analysis shows that 8-d treatment is profitable only for very valuable cows, when costs of diagnosis and treatment do not exceed €50 (which is well below the average retail price at the time this paper was written), or during an outbreak. Even then, it does not compare favourably with 3-d treatment. Treatment alone should never be considered the solution to an outbreak. Identification and removal of sources, be it infected animals or environmental sources, and management changes, must also be considered.

In this study, we assumed the costs of penalties due to high BTSCC, costs of other diseases resulting from mastitis, impact on fertility, and costs due to antibiotic residues in milk all to be zero. All these costs can be substantial on specific farms, but were considered to be of minor importance on an average farm and for the average cow. If any of these costs were included in the model, the economic benefit of lactational treatment of chronic subclinical streptococcal mastitis would increase.

Another factor that has not been incorporated in our model but which must be considered is the risk of development of antimicrobial resistance when antimicrobials are used for treatment of subclinical streptococcal infections other than *Str. agalactiae*. Traditionally, antimicrobials were not used for this purpose, and the introduction of this usage may appear to lead to increased use of such products and hence an increased risk of contributing to the development of, or selection for, antimicrobial resistance. The main difference between our model, which predicts an economic benefit for the use of antimicrobials, and older models that did not predict such a benefit, is that we considered prevention of clinical flare-ups and transmission of infections to other animals. Both clinical flare-ups and infections in other animals, which could also be clinical, would be reasons for antimicrobial treatment under current management practices. If the increased use of antimicrobials for treatment of subclinical cases is offset by a decreased use of antimicrobials for new clinical cases, there may not be a net increase in use of antimicrobials. In fact, some models predict a decrease in mastitis prevalence and treatments in the long term when subclinical mastitis is treated with antibiotics (Zadoks et al. 2002). The hypothesis that lactational treatment of subclinical mastitis may improve udder health and reduce the net use of antibiotics in the long term is currently being tested in commercial dairy herds. Monitoring of antimicrobial resistance levels among streptococci is part of this study and should continue to be a concern when lactational treatment of clinical or subclinical mastitis is applied in dairy practice.

Partial budgeting is a relatively simple method to assess economic profitability of the treatment of mastitis. It is particularly useful for relatively small changes on a farm, such as treatment *v.* no treatment of animals. However, as for any simple model, assumptions are relatively crude when compared with the complexity of reality. To address simplifications and assumptions like the ones used in our model and our sensitivity analysis, and to obtain more accurate estimates of the range of economic effects and the probability of specific outcomes within that range, a stochastic model would need to be developed to assess the profitability of treatment of subclinical mastitis due to non-agalactiae streptococci.

In conclusion, depending on circumstances such as prevailing bacterial flora, farm management and economic conditions, lactational treatment of chronic subclinical mastitis caused by *Str. dysgalactiae* or *Str. uberis* with antibiotics may or may not be economically beneficial. On farms where the probability of contagious transmission of causative agents is low, 3-d treatment is, on average, profitable but 8-d treatment is not (net profit +€11·62 and −€21·83 respectively). During outbreaks or in herds where contagious transmission is likely, both 3-d and 8-d treatments are profitable. In this situation, 3-d treatment is on average more profitable than 8-d treatment and 8-d treatment should probably only be considered for very valuable cows where the extra cost of antibiotics and discarded milk is offset by the higher probability of cure and the higher retention value of the cow. Identification of cow factors and bacterial strain characteristics associated with cure and/or transmission would improve the cow- and herd-specific estimates of the economic outcome of antibiotic treatment. Stochastic modelling will be needed to perform more accurate calculations of the range and probabilities of potential economic outcomes of lactational treatment of chronic subclinical *Str. dysgalactiae* and *Str. uberis* mastitis. Prudent use of antibiotics may favour treatment of subclinical infections when there is

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a net-reduction of antibiotic usage in the long term, but development of antimicrobial resistance should be monitored, whether treatment is used for subclinical mastitis, clinical mastitis, or both.

References

Allore HG & Erb HN 1998 Partial budget of the discounted annual benefit of mastitis control strategies. *Journal of Dairy Science* **81** 2280–2292

Bramley AJ 1984 *Streptococcus uberis* udder infection – a major barrier to reducing mastitis incidence. *British Veterinary Journal* **140** 328–335

Craven N 1987 Efficacy and financial value of antibiotic treatment of bovine clinical mastitis during lactation – a review. *British Veterinary Journal* **143** 410–422

Catell MB 1996 An outbreak of *Streptococcus uberis* as a consequence of adopting a protocol of no antibiotic therapy for clinical mastitis. *Proceedings 35th National Mastitis Council Annual Meeting, Nashville TN USA* pp. 123–130. Arlington VA USA: National Mastitis Council Inc

DeLuyker HA, Michanek P, Wuyts N, Van Oye SN & Chester ST 2001 We treat sick cows don't we? The case of subclinical mastitis. *Proceedings National Mastitis Council Annual Meeting* pp. 170–174. Arlington VA USA: National Mastitis Council Inc

De Vos CJ & Dijkhuizen AA 1998 [Economical aspects of udder health]. *Proceedings wetenschappelijke vergadering van de Groep geneeskunde van het rund Rheden 27 mei* 1998. pp. 7–9

Dijkhuizen AA & Morris RS 1996 *Animal Health Economics. Principles and Application*. University of Sydney Australia: Post Graduate Foundation in Veterinary Science. pp. 28–29

Eberhart RJ, Hutchinson LJ & Spencer SB 1982 Relationships of bulk tank somatic cell counts to prevalence of intramammary infection to indices of herd production. *Journal of Food Protection* **45** 1125–1128

Esslemont RJ & Kossaibati MA 1997 Culling in 50 dairy herds in England. *Veterinary Record* **140** 36–39

Fox LK & Gay JM 1993 Contagious mastitis. *Veterinary Clinics of North America Food Animal Practice* **9** 475–487

Hillerton JE & Berry EA 2003 The management and treatment of environmental streptococcal mastitis. *Veterinary Clinics of North America Food Animal Practice* **19** 157–169

Hogeveen H 2003 Mastitis control in The Netherlands. *IDF Mastitis Newsletter* **24** 25–28

Hortet P & Seegers H 1998 Calculated milk production losses associated with elevated somatic cell counts in dairy cows: review and critical discussion. *Veterinary Research* **29** 497–510

Jayarao BM, Gillespie BE, Lewis MJ, Dowlen HH & Oliver SP 1999 Epidemiology of *Streptococcus uberis* intramammary infections in a dairy herd. *Zentralblatt für Veterinarmedizin [B]* **46** 433–442

Lam TJGM 1996 Dynamics of bovine mastitis: a field study in low somatic cell count herds. PhD Dissertation, Utrecht University, The Netherlands

Lam TJGM, Schukken YH, van Vliet JH, Grommers FJ, Tielen MJM & Brand A 1997 Effect of natural infection with minor pathogens on susceptibility to natural infection with major pathogens in the bovine mammary gland. *American Journal of Veterinary Research* **58** 17–22

Loeffler SH, Lam TJGM, Barkema HW, Scholten D, Hessels AL & van Gestel AM 1995 [The dairying veterinary approach to a high bulk milk cell count caused by *Streptococcus agalactiae]. Tijdschrift voor Diergeneeskunde* **120** 458–463

McDermott MP, Erb HN, Natzke RP, Barnes FD & Bray D 1983 Cost benefit analysis of lactation therapy with somatic cell counts as indications for treatment. *Journal of Dairy Science* **66** 1198–1203

McDougall S 1998 Efficacy of two antibiotic treatments in curing clinical and subclinical mastitis in lactating dairy cows. *New Zealand Veterinary Journal* **46** 226–232

Middleton JR, Fox LK, Gay JM, Tyler JW & Besser TE 2002 Use of pulsed-field gel electrophoresis for detecting differences in *Staphylococcus aureus* strain populations between dairy herds with different cattle importation practices. *Epidemiology and Infection* **129** 387–395

Neave FK, Dodd FH, Kingwill RG & Westgarth DR 1969 Control of mastitis in the dairy herd by hygiene and management. *Journal of Dairy Science* **52** 696–707

NRS [Nederlands Rundvee Syndicaat] 1998 Annual Statistics CR-Delta, Arnhem, The Netherlands

Owens WE, Ray CH, Watts JL & Yancey RJ 1997 Comparison of success of antibiotic therapy during lactation and results of antimicrobial susceptibility tests for bovine mastitis. *Journal of Dairy Science* **80** 313–317

Phuektes P, Mansell PD, Dyson RS, Hooper ND, Dick JS & Browning GF 2001 Molecular epidemiology of *Streptococcus uberis* isolates from dairy cows with mastitis. *Journal of Clinical Microbiology* **39** 1460–1466

Schepers AJ, Lam TJGM, Schukken YH, Wilmink JBM & Hanekamp WJA 1997 Estimation of variance components for somatic cell counts to determine thresholds for uninfected quarters. *Journal of Dairy Science* **80** 1833–1840

Schrick FN, Hockett ME, Saxton AM, Lewis MJ, Dowlen HH & Oliver SP 2001 Influence of subclinical mastitis during early lactation on reproductive parameters. *Journal of Dairy Science* **84** 1407–1412

Schukken YH, Leslie KE, Barnum DA, Mallard BA, Lumsden JH, Dick PC, Vessie GH & Kehrli ME 1999 Experimental *Staphylococcus aureus* intramammary challenge in late lactation dairy cows: quarter and cow effects determining the probability of infection. *Journal of Dairy Science* **82** 2393–2401

Smith KL, Todhunter DA & Schoenberger PS 1985 Environmental mastitis: cause, prevalence, prevention. *Journal of Dairy Science* **68** 1531–1553

Smith KL & Hogan JS 2001 The world of mastitis. In *Proceedings of the National Mastitis Council's 2nd International Symposium on Mastitis & Milk Quality, Vancouver, BC, Canada*. Madison, WI, USA: National Mastitis Council, Inc. pp. 1–12

Smolders H 1994 Fertility and production, important culling reasons. *Praktijkonderzoek* **1** 20–22

Sol J, Sampimon OC, Snoep JJ & Schukken YH 1997 Factors associated with bacteriological cure during lactation after therapy for subclinical mastitis caused by *Staphylococcus aureus*. *Journal of Dairy Science* **80** 2803–2808

Sol J, Sampimon OC, Barkema HW & Schukken YH 2000 Factors associated with cure after therapy of clinical mastitis caused by *Staphylococcus aureus*. *Journal of Dairy Science* **83** 278–284

St. Rose SG, Swinkels JM, Kremer WDJ, Kruitwagen CLJJ & Zadoks RN 2003 The effect of penethamate hydriodide treatment on bacteriological cure, somatic cell count and milk production of quarters with *Streptococcus uberis* or *Streptococcus dysgalactiae* chronic subclinical infection. *Journal of Dairy Research* **70** 1–8

Todhunter DA, Smith KL & Hogan JS 1995 Environmental streptococcal intramammary infections of the bovine mammary gland. *Journal of Dairy Science* **78** 2366–2374

Wang SM, Deighton MA, Capstick JA & Gerraty N 1999 Epidemiological typing of bovine streptococci by pulsed-field gel electrophoresis. *Epidemiology and Infection* **123** 317–324

Whitaker DA, Kelly JM & Smith S 2000 Disposal and disease rates in 340 British dairy herds. *Veterinary Record* **146** 363–367

Wilson DJ 1996 Factors influencing therapy decisions in clinical cases of Gram-positive mastitis. *Bovine Practice* **28** 90–93

Wilson DJ, Gonzalez RN, Case KL, Garrison LL & Gröhn YT 1999 Comparison of seven antibiotic treatments with no treatment for bacteriological efficacy against bovine mastitis pathogens. *Journal of Dairy Science* **82** 1664–1670

Yamagata M, Goodger WJ, Weaver L & Franti C 1987 The economic benefit of treating subclinical *Streptococcus agalactiae* mastitis in lactating cows. *Journal of American Veterinary Medical Association* **191** 1556–1560

Zadoks RN, Allore HG, Barkema HW, Sampimon OC, Gröhn YT & Schukken YH 2001a Analysis of an outbreak of *Streptococcus uberis* mastitis. *Journal of Dairy Science* **84** 590–599

Zadoks RN, Allore HG, Barkema HW, Sampimon OC, Wellenberg GJ, Gröhn YT & Schukken YH 2001b Cow and quarter level risk factors for *Streptococcus uberis* and *Staphylococcus aureus* mastitis. *Journal of Dairy Science* **84** 2649–2663

Zadoks RN, Allore HG, Hagenaars TJ, Barkema HW & Schukken YH 2002 A mathematical model of *Staphylococcus aureus* control in dairy herds. *Epidemiology and Infection* **129** 397–416

Zadoks RN, Gillespie BE, Barkema HW, Sampimon OC, Oliver SP & Schukken YH 2003 Clinical, epidemiological and molecular characteristics of *Streptococcus uberis* infections in dairy herds. *Epidemiology and Infection* **130** 335–349

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