ECONOMICS OF TREATING CHRONIC SUBCLINICAL *STREPTOCOCCUS UBERIS* CASES

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Mastitis is generally regarded as the most costly disease in dairy cattle in developed countries Costs are mainly due to milk production losses, culling, treatment and discarded milk due to antibiotic residues. Additional costs include decreased fertility, changed composition of milk and risk of violation of bulk tank limits or loss of premium for low bulk milk somatic cell count. 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. 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. Treatment of subclinical mastitis is often deferred until the dry period. However, subclinical mastitis, like clinical mastitis, affects milk quality and quantity, and is associated with economic losses as described 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. However, treatment of subclinical *Streptococcus agalactiae* infections during lactation is economically profitable (Yamagata et al. 1987). The success of treatment programs for *S. 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. Reported cure proportions for *Streptococcus uberis* 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. 2001, 2003). The cost-benefit ratio of antibiotic treatment of subclinical *S. uberis* infections during lactation has not been determined.

The purpose of this paper is to explore the economic benefit of antibiotic treatment of chronic subclinical *S. uberis* infections during lactation, including the indirect effects of treatment, prevention of clinical mastitis and prevention of transmission.

A Deterministic Simulation Model

Partial budgeting was used for the development of a deterministic simulation model to estimate the net cost or benefit of lactational treatment of subclinical *S. uberis* mastitis with antibiotics. Input variables for the model were based on literature, if available, and the 2003/2004 dairy situation and prices in the Netherlands. The model works at cow level with a time horizon of one lactation. A schematic outline of the deterministic model is depicted in Figure 1.

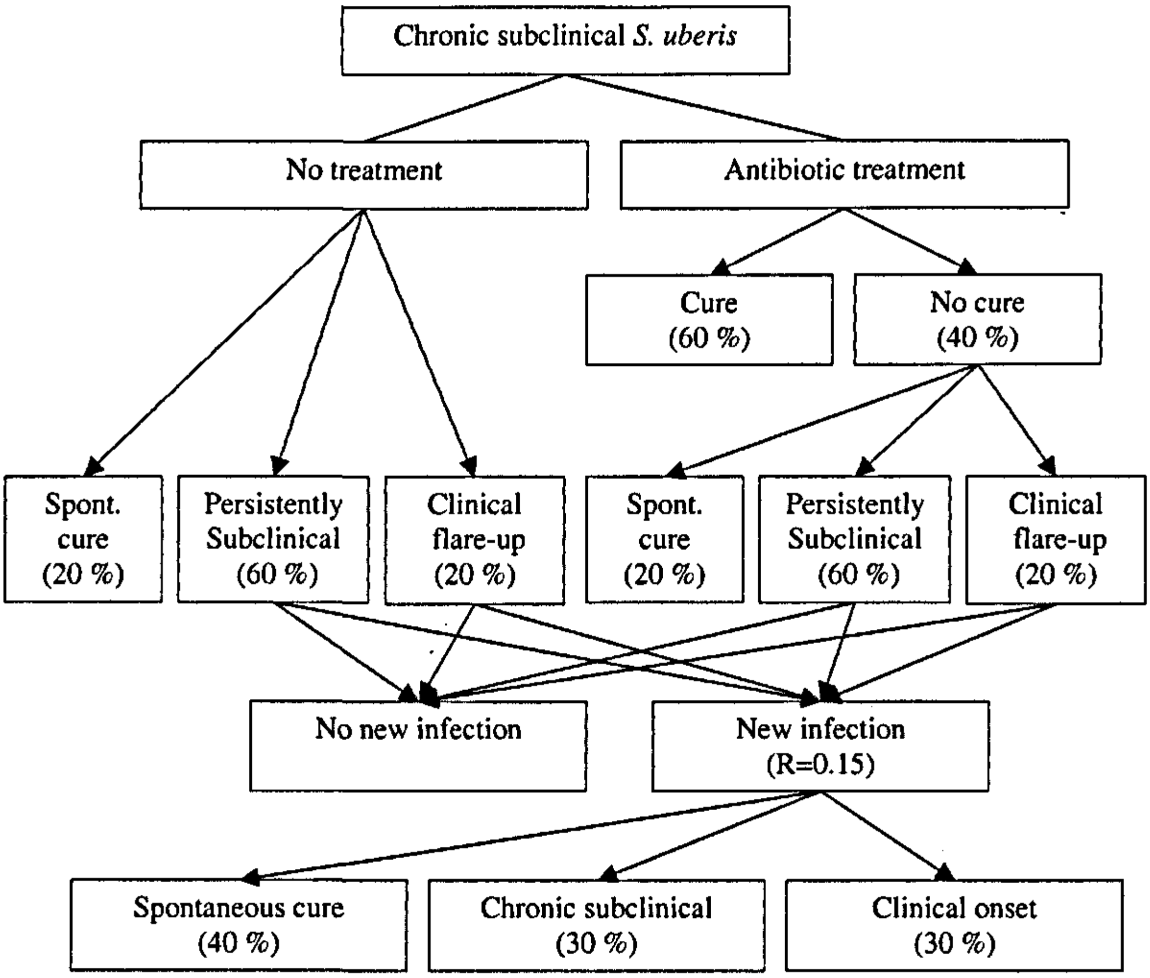

Figure 1. The deterministic model for effect of antibiotic treatment versus no treatment of chronic subclinical intramammary infections with *S. uberis*.

The starting point for decisions on lactation treatment is the moment of detection of a chronic case of subclinical mastitis, which is after a minimum of two consecutive test days with an increased SCC. Bacteriological examination has taken place to confirm an infection with *S. uberis*. Antibiotic treatment can lead to cure or no cure. The consequences of the latter are the same (also in probabilities) as giving no treatment. When not treated or not cured after treatment, a cow may cure spontaneously, my get a so-called clinical flare-up or may maintain subclinical. When a cow is not cured (due to treatment or spontaneously), she is infectious and thus may infect other cows, depending on the transmission rate (R) of that specific strain of *S. uberis* and herd management (Zadoks et al., 2001). A newly infected cow may cure spontaneously, become clinical or become a chronic subclinical mastitis case.

The following parameters are used in the model (including assumptions and used references for the default value of the parameter). The basic treatment is a short, 3-day treatment with intramammary or parenteral antibiotics. The probability of cure after treatment is 60 % (McDougall, 1998; St. Rose et al. 2003; DeLuyker et al. 2001). The probability of spontaneous cure is 20 % (St. Rose et al. 2003; DeLuyker et al. 2001). The probability of clinical flare-ups is estimated at 20 % (Lam, 1996; Zadoks et al. 2003). Given the probability of spontaneous cure and clinical flare-ups, the probability of remaining subclinical is 60 %. The probability that a cow with a persistent subclinical mastitis is infecting other cows is represented by the reproduction ratio (R). This parameter represents the total number of new infections that is caused by an infected animal and is based upon the infectiousness of *S. uberis* (transmission parameter β) and the duration of the infection (τ). In a field study, β was found to be 0.033 during an epidemic outbreak of *S. uberis* mastitis, while it was much lower, 0.005, during a non-outbreak situation (Zadoks et al. 2001). The duration of a non-cured *S. uberis* infection, after detection, is estimated to be 30 days on average. For the purpose of this study, treatment of chronic *S. uberis* infections, R is estimated to be between 0 and 1. As default value R = 0.15 is used. When transmission of infection occurs, the new infection can be clinical or subclinical. For *S. uberis*, the probability that a new infection is clinical is estimated to be 30 % (Lam, 1996; Zadoks et al. 2003; Jayarao et al. 1999), 40 % is assumed to cure within a few weeks and 30 % is assumed to become chronic subclinical mastitis cases.

Economic effects of treatment of chronic subclinical mastitis caused by *S. uberis* are calculated by means of partial budgeting. A partial budget can be used to estimate the change that will occur in farm profit from some change in the management, by considering only those items of returns and costs that change. The format of a partial budget is made up of four sections: additional returns, reduced costs, returns forgone and extra costs (Dijkhuizen and Morris, 1997). In this study, the basic situation is a chronic subclinical *S. uberis* infection which is not treated. The change in management is treatment of this infection. The additional returns are a possible increase of milk production when the subclinical mastitis case is cured. Reduced costs consist of a reduced probability of clinical mastitis, a reduction of costs associated with persistent subclinical mastitis and a reduction of mastitis (either clinical or subclinical) in other cows due to infectiousness of the current mastitis case. Moreover, reduced costs consist of a reduction in culled animals (calculated by the retention pay-off), reduced number of penalties for increased bulk milk SCC and reduced costs of decreased fertility (the latter two are expected to be minimal for the Dutch circumstances). Returns forgone consist of discarded milk because of the withdrawal period of milk after antibiotic treatment. Extra costs consist of the antibiotics and labor necessary to carry out the treatment. In Table 1, the input values to calculate the partial budget are given. The assumptions behind these input variables can be found in Swinkels et al., 2005.

Table 1. Input parameters used in the partial budget to estimate the costs and benefits of treatment of chronic subclinical *S. uberis* mastitis. Basic situation is no treatment. Cost estimates are given in Euro (in December 2004 € 1.- ≈ $ US 1.25)

Parameter	Value
Treatment and cure	
Duration treatment (days)	3
Costs antibiotics (€)	27
Withdrawal period (after end of treatment; days)	3
Cost of labor (€/hour)	0[1]
Milk production	
Milk production at treatment (kg/day)	25
Cost of discarded milk (€/kg)[2]	0.14[3]
Increase of production after cure (kg/lactation)	0
Production decrease of spontaneously cured new mastitis case (kg/lactation)	72
Production decrease of new chronic subclinical mastitis case (kg/lactation)	300
Cost of decreased milk production (€/kg)[2]	0.07[4]
Mastitis	
Cost of new case of clinical mastitis (€)	209[5]
Cost of clinical flare-up (€)	163[5]
Culling	
Probability of culling	12 %
Retention pay-off (€)	506[6]
Other factors	
Reduced fertility due to mastitis	0
Probability milk payment penalty BMSCC when cow is not cured	0
Milk payment penalties due to increased bulk milk SCC (€)	335
Probability milk payment penalty antibiotics	0
Milk payment penalties due to antibiotic residues in milk (€)	385

[1]On a family farm there is no alternative use of labor. Therefore, the economic value of labor is regarded to be € 0.-

[2]Under a situation with milk quota and no alternative use for farm labor and barn

[3]≈ € 0.53/US Gallon

[4]≈ € 0.26/US Gallon

[5]Based on de Vos and Dijkhuizen (1998). A large component of the cost for clinical mastitis is made up by milk production losses (€ 92.-). In the case of clinical flare-up, a large part of the milk production losses already occurred during the subclinical phase. Therefore, the damage for milk production losses has been adjusted in case of a clinical flare-up.

[6]The retention pay-off differs from cow to cow (Dijkhuizen and Morris 1998). In this case an average cow in parity 2, 7 months in lactation and 2 months pregnant under Dutch 2004 market situation is taken.

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. Four groups of input variables have been adjusted: cure rates and clinical flare-ups, infectiousness of persistent subclinical cases, production effects and economic parameters. When estimates for input variables that have a strong impact on economic outcome are scarce or vary widely among sources, further research into the value of that parameter may be indicated.

Besides a sensitivity analysis, where variables are adjusted one at each run, an economic model can also be used to carry out scenario studies. In a scenario study, multiple variables are changed at the same time, representing a possible scenario. In this study only one scenario has been calculated: a longer treatment as proposed by DeLuyker et al. (2001). In this scenario, due to a longer treatment (8 days instead of 3 days), the cure rate will increase to 90 %. On the other hand the costs for treatment and milk withdrawal will also increase.

Results

Under the basic situation described in this paper, the average economic benefit of treatment of chronic subclinical infection with *S. uberis* is given in Table 2. The costs and benefits are almost equal around € 48, and the net result of treatment is € 0.55. The most important beneficial factors of treatment are less culling (45 %) and a reduced risk of clinical mastitis (40 %). Under the basic circumstances the prevention of new infections denotes 15 % of the benefits. Costs are due to withheld milk and, of course, the used antibiotics.

Table 2. Costs and benefits (€; in December 2004 € 1.- ≈ $ US 1.25) of antibiotic treatment of chronic subclinical *S. uberis* mastitis under the basic assumptions.

Benefits		Costs	
Extra revenues		*Reduced revenues*	
Milk production increase	0	Withheld milk	21
Reduced costs		*Extra costs*	
Reduced clinical mastitis	19.56	Antibiotics	27
Less new infections	7.13	Labor	0
Less culling	21.86	More penalties due to antibiotics	0
Less BMSCC penalties	0		
Total	48.55	Total	48
	Net result:	0.55	

Results of sensitivity analysis are shown in Table 3. The most important parameters to determine the effect of treatment of chronic subclinical *S. uberis* are: cure rate after treatment, the infectiousness (α) of the pathogen involved (to a lesser extend the infectious period), risk of a penalty for a high BMSCC, costs of antibiotics, value of a decreased milk production (and thus also the value of discarded milk) and the risk and cost of culling. Parameters such as spontaneous cure, production changes and costs of clinical mastitis had less effect.

Table 3. Results (€; in December 2004 € 1.- ≈ $US 1.25) of the sensitivity analysis for treatment of chronic subclinical *S. uberis* mastitis.

Factor	Original value	Costs	Benefits	Net result
Basic		48	48.55	0.55
Cure rates and clinical flare-ups				
Cure after treatment 50 %	60%	48	40.46	-7.54
Cure after treatment 70 %	60%	48	56.64	8.64
Spontaneous cure 10 %	20%	48	53.08	5.08
Spontaneous cure 30 %	20%	48	44.01	-3.99
Spontaneous cure after treatment 10 %	20%	48	45.53	-2.47
Spontaneous cure after treatment 30 %	20%	48	51.57	3.57
Clinical flare-ups 10 %	20%	48	42.06	-5.94
Clinical flare-ups 30 %	20%	48	55.04	7.04
Infectiousness				
Duration of infection (t) 20 days	30 days	48	46.17	-1.83
Duration of infection (t) 40 days	30 days	48	50.92	2.92
Duration of infection (t) 60 days	30 days	48	55.68	7.68
Infectiousness of pathogen (a) 0	0.005	48	41.42	-6.58
Infectiousness of pathogen (a) 0.0025	0.005	48	44.98	-3.02
Infectiousness of pathogen (a) 0.015	0.005	48	62.81	14.81
Infectiousness of pathogen (a) 0.033	0.005	48	88.47	40.47
Production effects				
Recovery of milk production after cure 25 %	0%	48	51.07	3.07
Recovery of milk production after cure 50 %	0%	48	53.59	5.59
Production decrease subclin. mastitis 200 kg	300 kg	48	48.4	0.40
Production decrease subclin. mastitis 400 kg	300 kg	48	48.7	0.70
Risk of culling 6%	12%	48	36.96	-11.04
Risk of culling 18 %	12%	48	60.13	12.13
Risk of penalty due to high BMSCC 5 %	0%	48	54.58	6.58
Risk of penalty due to high BMSCC 10 %	0%	48	60.61	12.61
Economic factors				
Costs antibiotics € 17	€27	38	48.55	10.55
Costs antibiotics € 37	€27	58	48.55	-9.45
Value milk production decrease middle	Low	58.5	49.15	-9.35
Value milk prod. decrease high (no quotum)	Low	72	49.92	-22.08
Costs clinical mastitis € 168	€206	48	42.57	-5.43
Costs clinical mastitis € 250	€206	48	54.53	6.53
Retention pay-off € 250	€506	48	37.24	-10.76
Retention pay-off € 750	€506	48	59.72	11.72

The scenario with a longer treatment gave a net result of - € 41.53. The benefits of a higher cure rate were less than the increased costs due to more expenses on antibiotics and a large amount of discarded milk.

Discussion

In Europe, where acceptable maximum levels for bulk milk somatic cell count are much lower than in the USA (400.000 cells/ml vs. 750.000 cells/ml, respectively) 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 position that lactational treatment of subclinical mastitis caused by non-agalactiae streptococci is not economically justified (Wilson et al. 1999). Results of this study show that, for an average situation, the benefits of treatment of chronic subclinical *S. uberis* mastitis equal the costs. In a comparable study where the same techniques have been applied on treatment of chronic subclinical mastitis caused by *S. uberis* or *S. dysgalactiae*, the benefits were higher (net result € 11.62) (Swinkels et al., 2005). There were some differences in assumptions but an important difference was the spontaneous cure rate. Swinkels and co-workers averaged estimates for *S. uberis* and *S. dysgalactiae*, where *S. dysgalactiae* has a higher spontaneous cure rate than *S. uberis*.

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 *S. uberis* infections often have an environmental source (Phuektes et al. 2001; Wang et al.1999; Zadoks et al., 2003), they may also spread from cow to cow (Phuektes et al. 2001; Zadoks et al. 2003).

There is uncertainty about 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 *S. 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). These types of factors have not been determined for *S. uberis*. 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.

In this study, we assumed the costs of penalties due to antibiotic residues in the milk, costs of other diseases resulting from mastitis and impact on fertility 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. Moreover, these costs are very difficult to quantify in a relatively simple model such as described in this paper.

Partial budgeting is a relatively simple method to assess economic profitability of the treatment of mastitis. It is particularly useful for relative small changes on a farm, such as treatment vs. no treatment of animals. However, as for any simple model, model assumptions are relatively coarse when compared to 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 caused by *S. uberis*. Such a model is currently under development and factors which are getting specific interest in this study are: moment of decision (days in lactation), uncertainty about the infectiousness of the causative pathogen and production characteristics of the treated cow.

In conclusion, depending on circumstances such as prevailing bacterial flora, farm management and economic conditions, lactational treatment of chronic subclinical mastitis caused by *S. dysgalactiae* or *S. uberis* with antibiotics may or may not be economically beneficial. 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 *S. uberis* mastitis.

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