Economic optimization of antibiotic treatment for clinical mastitis

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Abstract

Most clinical mastitis (CM) cases are treated in the same way, following a farm-specific treatment protocol. Cure rates, however, are strongly influenced by several cow factors. Therefore each CM case should be treated in the most appropriate way, based on those specific cow factors. The objective of this research was to develop a simulation model to determine the optimal treatment for each CM case in terms of total costs. Total costs of 4 different antibiotic treatment regimes (standard intramammary, extended intramammary, combination intramammary + parenterally, and combination extended intramammary + parenterally) were compared by simulating 5,000 CM cases. All input for the model was based on literature information and authors' knowledge. Bacteriological cure for each individual cow depended on the choice of treatment, the causal pathogen and the cow factors parity, SCC and CM history. Total costs for each individual case were dependent on treatment costs, milk production losses and costs for culling. Mean total costs for the 4 treatments were €170, €189, €190 and €209, respectively. For 65% of CM cases the 3-day intramammary antibiotic treatment had the lowest costs and was defined as optimal. For 23% of the cases an extended intramammary treatment was optimal, while for 10% and 1% of the cases the combination intramammary + parenterally and the combination extended intramammary + parenterally were optimal, respectively. For 1% of the CM cases, immediate culling was optimal. For cows producing more than 35 kg, for cows which had previous CM cases and for cows in the first months of

lactation, the more intensive antibiotic treatments became more advantageous. The results show the potential of a cow-specific treatment of CM.

Introduction

Most clinical mastitis (CM) cases are treated in the same way, following a farm-specific treatment protocol. It is, however, known that the cure rate of CM is highly cow dependent (Bradley and Green, 2009). By taking into account cow factors, it is possible to optimize the choice and duration of treatment. For instance, it is likely that a heifer with a low SCC and no CM history will cure by using a standard antibiotic treatment, while an older cow with a high SCC and a history of CM might need an extended antibiotic treatment to cure.

Optimizing the choice of treatment for each CM case, which also includes the option to cull a cow with CM immediately (Bar et al., 2008b), can result in more prudent use of antibiotics. The optimal treatment of CM is often measured in terms of clinical or bacteriological cure. Dairy farming is, however, an economic enterprise, and it could be argued that the real measure of cure should be the cost-benefit of treatment (Barkema et al., 2006).

In the current study, a stochastic Monte Carlo model was developed to simulate CM cases treated with one of four different antibiotic treatment regimes or immediately culled. Subsequently, this model was used to determine for which cows which option for CM is optimal in terms of total costs.

Material and Methods

Model development

The model described in this paper was built using Microsoft Excel with @Risk add-in software (Palisade, 2002). All discrete events and variability at the cow level were triggered stochastically, using random numbers drawn from distributions. Input for these distributions was based on knowledge of the model domain, information from literature and expertise of the authors.

Model outcomes were generated in 3 steps. First, every iteration (5,000 in total) during the simulation process gave a specific cow with CM caused by streptococci, *Staphylococcus aureus* or *Escherichia coli*. In the second step the follow up of this CM case for each of the five treatments (4 different antibiotic treatment regimes and immediate culling) were simulated. The third step involved calculation of the associated costs for each of the five treatments for this case. Finally, for each simulated CM case, the optimal treatment was defined as the option with the lowest total costs.

Simulation of CM cases

By using a discrete probability distribution, for each CM case the causal pathogen was simulated (streptococci (40%), *S. aureus* (30%) or *E. coli* (30%)). Subsequently, for each cow with CM, the parity, the day in milk, the most recent SCC, the 305-day milk production, the calving interval and whether it was a repeated CM case or not (Döpfer et al., 1999; Swinkels et al., 2005a; Swinkels et al., 2005b) were determined. Daily milk production at day of CM and the remaining milk production during the rest of lactation were estimated by Wood’s lactation curve (Wood, 1967).

Simulation of effect of treatment of a CM case

Four different treatment regimes were defined, differing in route of application, duration, costs, treatment time, days of milk withdrawal and bacteriological cure rate (Table 1).

Table 1. Characteristics of the four defined antibiotic treatment regimes.

	Antibiotic treatment regime			
	INT1	INT2	INT_PAR1	INT_PAR2
Application (number)	Intramammary (3)	Intramammary (5)	Intramammary (3) + parenterally (3)	Intramammary (5) + parenterally (3)
Total costs antibiotics (€)	15	25	45	55
# days milk withdrawal	5	7	5	7
Total treatment time (minutes)	42	62	45	65
Bacteriological cure (%)[1]				
Streptococci	75	80	80	85
S. aureus	40	50	60	70
E. coli	80	85	85	90

[1] Bacteriological cure rates assumed for heifers, with somatic cell count <200,000 cells/mL and no clinical mastitis before.

For each CM case, treated with the four defined antibiotic regimes, it was determined whether it was cured bacteriologically or not. If the cow was not cured bacteriologically, the cow had an 80% probability to be clinically cured. All non-clinically cured CM cases were treated again with the same antibiotic treatment. If after retreatment no clinical cure had occurred, the cow had a 5% chance of dying and a 95% probability that the infected quarter would be dried-off. Cows with dried-off quarters had a probability of being culled during the remainder of the lactation of 33%. All completely cured CM cases had a probability varying between 5 and 25%, depending on the number of CM cases, of being culled during the remainder of the lactation. All non-bacteriologically cured CM cases had a probability of having a clinical flare-up later in lactation of 10%, 12% and 5% for streptococci, *S. aureus* and *E. coli*, respectively (Döpfer et al., 1999; Swinkels et al., 2005a; Swinkels et al., 2005b). Additionally, cows not cured bacteriologically had a probability of being culled during the remainder of lactation. This probability was 16% for cows with 1 previous CM case and 20% for cows with 2 previous CM cases. If an antibiotic treatment of the second clinical flare-up did not result in bacteriological cure, the cow was culled immediately (Table 2 + Figure 1).

Bacteriological cure rates from literature were used (Bradley and Green, 2009; McDougall et al., 1998; McDougall et al., 2003; McDougall et al., 2007; Sol et al., 2000) as basis for the success rate of the four defined antibiotic regimes. Based on those cure rates, the maximum bacteriological cure for CM cases caused by streptococci, *S. aureus* and *E. coli* was determined based on expertise of the authors for all four antibiotic regimes. The maximum cure was assumed for heifers with a SCC below 200,000 cells/mL and no CM case before (Table 1). Thereafter, that maximum bacteriological cure rate was adapted, based on the literature (Barkema et al., 2006; Bradley and Green, 2009) and expertise of the authors, for the parity of the cow, the most recent SCC and whether it was a repeated case or not. In comparison with the maximum, for CM cases in older cows the cure rate was reduced by 10%, for CM cases after a SCC between 200,000 and 500,000 cells/mL the cure rate was reduced by 10%, for CM cases after a SCC above 500,000 cells/mL the cure rate was reduced by 15% and for repeated CM cases the cure rate was divided by two.

Costs of CM

The costs for CM included costs for antibiotics (Table 1), costs for discarded milk (€0.17 per kg), labour (hourly rate of €18), costs for milk production losses (€0.12 per kg) and costs for culling.

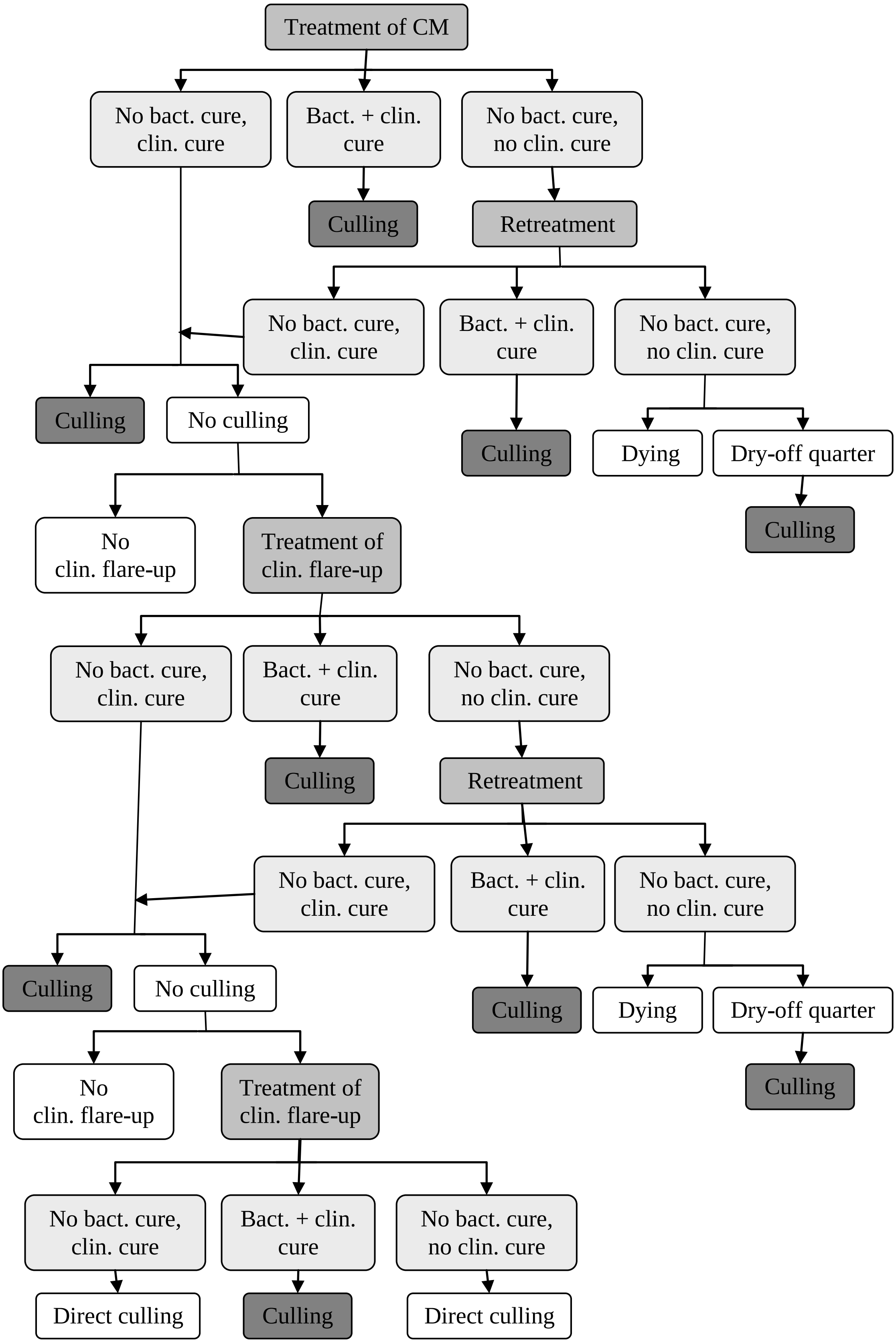
The costs for each culled cow were expressed using the retention pay-off (RPO) value of a cow. The RPO is defined as the maximum amount of money that should be spent to keep a cow in case of health problems. The RPO was calculated with a stochastic model developed by Houben et al. (1994).

The effect of CM on the degree of milk losses varies, depending on the causal pathogen (Schukken et al., 2009), the parity, time after CM case (Bar et al., 2007) and whether the cow was cured bacteriologically or not. For bacteriologically cured streptococci in heifers milk production losses varied between 6% (month 1) and 1% (month ≥8). For bacteriologically cured *S. aureus* and *E. coli* in heifers, 2% and 4% more production losses were assumed for each month after treatment of CM, respectively. For older cows, 5% more production losses were added. For non-bacteriologically cured CM cases 5% more production losses were added. Cows with dried-off quarters had in total 15% milk production losses in the remaining of lactation. By using the percentages, the total milk production losses for the remaining lactation were calculated based on Wood's lactation curve.

Table 2. Values and source of value of parameters used in the simulation model for antibiotic treatment of a clinical mastitis (CM) case.

Parameter	Value	Source
Probability of clinical cure for non-bacteriological cured CM cases	80%	Expertise
Probability of clinical flare-up for non-bacteriological cured CM cases		
Streptococci	10%	Swinkels et al., 2005b
S. aureus	12%	Swinkels et al., 2005a
E. coli	5%	Döpfer et al., 1999
Probability of being culled for non-bacteriological cured CM cases		
1 previous CM case	16%	Bar et al., 2008a + Expertise
2 previous CM cases	20%	
Probability of being culled for completely cured CM cases	5-25%[1]	Bar et al., 2008a + Expertise
Probability of dying for non-clinical cured retreated CM cases	5%	Bar et al., 2008a + Expertise
Probability of drying-off quarter for non-clinical cured retreated CM cases	95%	Expertise

[1]Dependent on the number of previous CM cases.



135 **Figure. 1.** Schematic representation of the simulation model for antibiotic treatment of a clinical mastitis (CM) case. (bact. = bacteriological, clin.= clinical). Culling represents a probability to be culled.

Results

The mean total costs of the four treatment regimes varied between €170 and €209, the mean costs for immediate culling was €599. The costs for milk production losses and culling decreased with the more intensive treatments (Table 3). The mean bacteriological cure rates of the four treatments were 51%, 59%, 64% and 73%, respectively.

Table 3. Mean total costs (€) for the four antibiotic treatment regimes and for immediately culling. Also costs for the different cost factors (5% and 95% percentiles given between brackets).

	Treatment regimes				
	INT1	INT2	INT_PAR1	INT_PAR2	Culling
Antibiotics	17	28	50	60	-
	(15; 30)	(25; 50)	(45; 90)	(55; 110)	
Milk withdrawal	27	37	27	37	-
	(9; 55)	(12; 73)	(9; 52)	(12; 61)	
Labour	15	21	15	21	-
	(13; 25)	(19; 37)	(14; 27)	(20; 39)	
Milk production losses	71	68	66	63	-
	(19; 147)	(19; 143)	(19; 136)	(18; 126)	
Culling	40	35	32	28	-
	(0; 383)	(0; 381)	(0; 365)	(0; 350)	
Total costs	170	189	190	209	599
	(61; 535)	(80; 543)	(90; 532)	(110; 530)	(176; 1020)

The input variables on costs of culling, probability of culling and amount of milk production losses had an effect on the total mean costs of the four defined antibiotic treatment regimes for CM (Table 4).

Table 4. The effect of different input variables on the mean total costs (€) for the four antibiotic treatment regimes.

	Antibiotic treatment regime			
	INT1	INT2	INT_PAR1	INT_PAR2
Default	170	189	190	209
Costs culling				
+ €100	182	197	199	220
- €100	158	184	182	203
Probability culling				
+ 5%	188	207	211	231
- 5%	153	171	172	193
Milk production losses				
+ 5%	197	221	221	238
- 5%	142	165	160	180

In total, for 65% of all 5,000 simulated CM cases the 3-day intramammary antibiotic treatment had the lowest costs and was defined optimal. For 23% of the cases an extended intramammary treatment was optimal, while for 10% and 1% of the cases the combination intramammary + parenterally and the combination extended intramammary + parenterally were optimal, respectively. For 1% of the cases immediate culling was optimal (Table 5). By looking to specific cow characteristics, the more intensive antibiotic treatments became more advantageous, for instance, for cows producing more than 35 kg, for cows with a repeated CM case and for cows in the first three months of lactation (Table 5).

Discussion

The costs of CM and, therefore, the choice of optimal treatment regime are highly influenced by the costs for milk production losses and costs of culling (Table 3). In the current study, probabilities of culling were included in the model. Culling, however, is a complex phenomenon, and the probability of cows being culled is farm dependent. To include culling in a more realistic way, farm-specific culling rules can be included or culling decisions can be optimized (Bar et al., 2008b).

Table 5. Effect of cow factors on the optimal treatment option for clinical mastitis.

	Optimal option (%)				
	INT1	INT2	INT_PAR1	INT_PAR2	Culling
Default	65	23	10	1	1
Causal pathogen					
Streptococci	72	20	6	1	1
S. aureus	52	26	16	4	2
E. coli	75	20	5	0	0
Daily milk production (kg)					
<20	74	19	4	1	2
20-25	77	13	7	0	3
25-30	75	17	6	0	2
30-35	70	17	8	1	4
35-40	63	26	10	1	0
>40	56	27	14	3	0
Clinical mastitis history					
No	66	22	9	2	1
Yes	58	26	12	3	1
Month in lactation					
1	55	26	14	3	2
2	57	28	12	2	1
3	58	28	12	2	0
4	74	19	5	1	1
5	79	14	5	0	2
6	77	13	7	1	2
7	79	12	7	1	1
≥8	74	21	3	1	1

For the current study, information on cure rates for four different antibiotic treatments was needed for cows with different parity, SCC history and CM history. Results of several clinical trials on effectiveness of antibiotic treatments were reported (e.g., Sol et al., 2000; McDougall et al., 2007; Bradley and Green, 2009), but such detailed information on cure rates was not available. Therefore, in the current study expertise of the authors was used to estimate the cure rates. The cure rates had a large influence on the optimal treatment. Because such detailed information on cure rates is not available, for further study it will be good to use more expert knowledge on cure rates.

In conclusion, the results of the current study show the potential for cow-specific treatment of CM. On average, for 35% of the CM cases the standard 3-day intramammary antibiotic treatment did not have the lowest costs. By taking into account specific cow information, it was possible to determine for which cows with CM the more intensive antibiotic treatment regimes were advantageous.

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