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Factors Prior to Dry Period Associated with High and Low Levels of Cow Milk Somatic Cell Counts in Next Lactation

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Østerås O, and Edge VL: Factors prior to dry period associated with high and low levels of cow milk somatic cell counts in next lactation. Acta vet. scand. 2000, 41, 63-77. – Data from a randomized controlled field study of selective dry cow therapy were used in which 686 cows had been allocated to 2 control groups (sampling only or placebo) or 2 therapy groups. Possible factors from previous lactation were assessed in determining their association with the probability of 'failure', designated as a cow milk somatic cell count (CMSCC) of greater than 399 000 per ml in geometric mean of several measurements during subsequent lactation. Success cows were those with a CMSCC of less than 200 000 per ml. For our analyses, this targeted 187 success cows and 186 failure cows. Therapy was given as a total dose of 400 000 IU penicillin and 100 mg neomycin per infected quarter as dry cow preparation once, or as a lactation formula with a total dose of 1.2 million IU penicillin and 1 200 mg dihydrostreptomycin per infected quarter during a 1-week period. Significant factors in the predictive model for success included therapy, low level of CMSCC (geometric mean of the 3 last tests) in previous lactation, low level of CMSCC (weighted by daily milk yield mean) in the herd, young cows, and not having had a case of treatment for chronic clinical mastitis. Additional information on the probability of failure in treated and untreated cows can be predicted by number of quarters infected with *Staphylococcus aureus* approximately 1.5 months before drying off. The models derived are considered for use as tools in selective treatment and culling decisions.

Mastitis; SCC; Staphylococcus aureus; culling decision; selective dry cow therapy.

Introduction

Dry cow therapy can be evaluated in a number of ways with much depending upon the perspective of interest and subsequently the objectives involved. For veterinarians and researchers an important aspect would be evaluating the efficacy of antimicrobial drugs used in dry cow therapy. This type of work has been done using the data from this study and is presented in several papers (*Østerås et al.* 1991, *Østerås et al.* 1994, *Østerås & Sandvik* 1996, *Østerås et al.* 1999a, *Østerås et al.* 1999b).

Farmers who wish to meet the dairy industry's goal for high quality milk, however, would likely be more interested in how dry cow therapy affects the CMSCC expected in the next lactation. In many European countries the limit for shipping milk is 400 000 cells per ml. (De Europæiske Fællesskabers Tidende, 1992). Therefore, many dairies will not allow farmers to deliver milk to their processing plants, unless the farmers can limit their bulk milk somatic cell count (BMSCC) to 400 000 cells per ml for

a period of several months. In Norway, this limit is set to 400 000 per ml (geometric mean) over the last 3 months. Additionally, there are penalty and premium limits which are set yearly. Presently, the penalty is set at between 300 000 and 400 000 per ml, and the premium limit between 200 000 and 250 000 per ml (Landbruksdepartmentet, 1996). Thus, with respect to these penalties and premiums, being able to predict the performance of a cow in the next lactation is vital to the farmer's management strategy. To avoid being withdrawn from the market, it would be wise for a farmer to consider slaughtering those cows that tend to push the BMSCC above the limits imposed by the dairy. Conversely, it would be important to know if certain cows are expected to have CMSCC below 200 000 during the next lactation, as they would help to maintain a standard of premium quality milk. Such expected values could then potentially be used as guidelines for decision-making regarding culling and treatment strategies.

The results of a study on selective dry cow therapy by *Østerås & Sandvik* (1996) showed that despite dry cow therapy, about 20% of the cows remained above 399 000 per ml in mean CMSCC. Twenty-five percent of the cows in the (untreated) control group continued into their next lactation with a mean CMSCC below 200 000 per ml. Using these data, this study will attempt to distinguish between failure (non-responders) cows in the therapy group (those with an expected CMSCC of more than 399 000 in the next complete lactation), and success (responders) cows in the control group (less than 200 000), based on various recorded factors. In the paper of *Østerås & Sandvik* (1996), which was based on these same data, a model using all the cows and CMSCC as a continuous variable was presented. In this paper we wanted to explore in more detail what could predict the extremes of being a clear success or failure cow, using logistic regression models. Cows in the therapy group which are deemed 'failures' would be potential candidates for slaughter, whereas the success cows in the control group would be candidates for no treatment. Under practical mastitis control using selective dry cow therapy, cows not fitting either of these 2 extremes would be candidates for dry cow therapy.

Materials and methods

A total of 686 cows from 288 different herds representing 3 Norwegian regions fulfilled the initial inclusion criteria of the study design, which were to have above 100 000 per ml in CMSCC for the last 2 composite samples and a positive diagnosis for subclinical mastitis at any quarter 45 ± 32 days before drying off. These animals were systematically randomly allocated to 4 groups A, B, C and D; B and C were double blind. There were 104 cows in the control group, which were sampled without treatment of any kind (group A), and 116 cows in a second control group given a placebo with base ointment of Benestermycin® vet. `Leo' without antibiotics (group B). As descriptive statistics were unable to reveal a significant difference between the 2, groups A and B were considered as one control group for this study. Group C animals were given one injector of long-acting Benestermycin® vet. `Leo', (Ballerup, Denmark), at drying off. Group D was treated with 4 injectors (one every second day before drying off) of short-acting Leocillin® with Dihydrostreptomycin vet. `Leo' . Groups C and D consist of 222 and 244 cows respectively. A more detailed description of the data can be found in *Østerås et al.* (1991), *Østerås et al.* (1994) and *Østerås & Sandvik* (1996).

To qualify for inclusion in the modelling procedure, cows had to have at least a bacteriological diagnosis with a major pathogen (*Staph. aureus* (20% of all quarters), *Strep. dysgalactiae* (5%

Table 1. Proportion of samples[1] (p) testing positive before dry period, and odds ratio[2] (OR) of that class variable at the quarter level, when tested for the probability of being a failure[3] cow during the next lactation.

Variable code	Diagnosis	Quarter	p and OR (P-value)			
			First sample		Second sample	
V1/V5	Quarter	Left front	0.17	2.0 *	0.21	1.0 NS
V2/V6	diagnosis	Right front	0.21	2.5 ***	0.25	1.7 *
V3/V7	with major	Left hind	0.33	1.9 **	0.32	1.3 NS
V4/V8	pathogen at	Right hind	0.28	1.9 *	0.30	1.8 *
V9/V13	Isolation of	Left front	0.14	2.0 *	0.18	1.0 NS
V10/V14	*Staph. aureus*	Right front	0.20	2.4 **	0.21	1.5 NS
V11/V15	at	Left hind	0.26	1.7 *	0.27	1.3 NS
V12/V16		Right hind	0.25	1.5 (0.11)	0.27	1.7 *
V17/V21	Isolation of	Left front	0.01	0.51 NS	0.02	0.15 (0.10)
V18/V22	penicillin	Right front	0.03	0.88 NS	0.02	4.2 (0.12)
V19/V23	resistant	Left hind	0.03	1.2 NS	0.03	1.3 NS
V20/V24	strain of *Staph. aureus* at	Right hind	0.03	11.7 *	0.02	2.5 NS
V25/V29	Isolation with	Left front	0.06	0.73 NS	0.05	1.6 NS
V26/V30	coagulase	Right front	0.09	0.53 (0.10)	0.05	0.35 *
V27/V31	negative	Left hind	0.09	0.58 (0.16)	0.06	1.5 NS
V28/V32	staphylococci (CNS) at	Right hind	0.10	0.63 NS	0.09	0.87 NS

[1] First sample = 45 ± 32 days before drying off; Second sample = at drying off.
[2] Odds ratios adjusted for the effect of therapy.
[3] Failure = Cow having geometric mean CMSCC > 399 000 during the follow-up lactation compared to < 200 000 ml^{-1}.
NS; not significant; * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.

of all quarters) and one quarter with *Strep. agalactiae*), or a minor pathogen (mainly coagulase negative staphylococci) combined with a California Mastitis Test (CMT) score higher than 0 according to *Schalm et al.* (1971) in any quarter in first sampling 45 ± 32 days before drying off. Sampling was also done at drying off, at calving, and at 30 ± 17 days after calving. Bacteriological diagnoses were based on Nordic recommendations (*Klastrup & Madsen* 1974); for further description and results, consult *Østerås et al.* (1991 and 1994). The cow diagnosis at a specific sampling was defined as the highest diagnosis score in any quarter. Scores are defined as: 0 = healthy, low CMT score and no bacteriological findings; 1 = high CMT score and no bacteriological finding; 2 = high CMT score and isolation of minor pathogens; 3= normal CMT score, but with major pathogens; 4 = high CMT score and finding of major pathogens.

Bacterial resistance to penicillin was tested by using Neosensitabs®, (A/S Rosco, Taastrup, Denmark), according to *Cascals* (1983). All relevant production data and events such as calving, culling and disease, were extracted from the animal recording database run by the Norwegian Dairy Association (*Solbu* 1983).

Cows were classified as either success or failure according to the geometric mean of the CMSCC during the complete lactation after the

Table 2. Proportion of samples[1] (p) with a positive value[2], minimum and maximum values (Range) before dry period and odds ratio[3] (OR) of the variables of bacteriology diagnosis at the cow level when tested for probability of being a failure[4] cow during the next lactation.

Variable code	Variable (figure in brackets refer to cow diagnosis)	Sampling time	Range (min-max)	*Mean*	*p*	OR (P-value)
V33	Cow diagnosis with major pathogen	First	0-1		0.73	2.7 ***
V34	(<2)	Second	0-1		0.65	2.6 ***
V35	Cow diagnosis with major pathogen	First	0-1		0.39	1.7 *
V36	and positive CMT (>3)	Second	0-1		0.50	1.9 **
V37	Number of quarters with positive	First	0-4	1.36		1.0 NS
V38	CMT	Second	0-4	2.51		1.18 *
V39	Number of quarters with major	First	0-4	0.45		1.54 *
V40	pathogen and positive CMT (>3)	Second	0-4	0.72		1.55 ***
V41	Number of quarters with	First	0-4	0.85		1.84 ***
V42	*Staph. aureus* isolates	Second	0-4	0.92		1.36 **
V43	Having at least one quarter isolate of	First	0-1		0.61	2.37 ***
V44	*Staph. aureus*	Second	0-1		0.57	2.38 ***
V45	Isolation of penicillin resistant strain	First	0-1		0.08	1.84 (0.13)
V46	of *Staph. aureus* at any quarter	Second	0-1		0.08	1.36 NS
V47	Proportion of quarters with CNS	First	0-4	0.34		0.61 **
V48	isolates	Second	0-4	0.25		0.96 NS

[1] First sample = 45 ± 32 days before drying off; Second sample = at drying off.
[2] p = proportion with a value of 1 (positive);
[3] Odds ratios adjusted for the effect of therapy.
[4] Failure = Cow having geometric mean CMSCC > 399 000 during the follow-up lactation compared to < 200 000 ml^{-1}.
NS; not significant; * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.

dry period. All cows included in the model building part of the study had values either exceeding 399 000 per ml during that lactation (failure), or below 200 000 per ml (success), thus cows with values between 199 000 per ml and 400 000 per ml were excluded. This resulted in data from 187 success cows and 186 failure cows being used in the model building. The number of tests contributing to these mean values ranged from 3 to 7. The 123 excluded cows with CMSCC between 199 000 and 400 000 were used subsequently to test how the model would identify them as success or failure cows. One hundred cows were excluded due to less than 3 CMSCC samples in next lactation. Additionally, 90 cows had missing data from the lactation before therapy and thus could not be used in the model building.

Independent variables

The bacteriological results which were assessed as potential independent variables from first sample (45 ± 32 days) and at second sample (at drying off) are presented in Table 1 (at quarter level) and Table 2 (at cow level). Table 3 shows the independent variables generated from individual records of the animal recording scheme. These include different combinations of

Table 3. Mean values, minimum and maximum values (Range) for dairy recording variables during lactation before dry period, and odds ratio[1] (OR) when tested for probability of being a failure[2] cow during in the next lactation.

Variable code	Variable	Mean	Range	OR (P-value)
LAC2	Lactation number over one (class)	0.76	0 – 1	2.9 ***
LAC5	Lactation number over four (class)	0.18	0 – 1	2.3 **
V57	Mean natural log (ln) of all cow somatic cell count (CMSCC) [4] during lactation before therapy	5.811	3.33- 7.86	3.18 ***
V58	Weighted[3] CMSCC[4] during lactation	460	24 – 2 710	1.201 ***
V59	Ln of CMSCC[4] in last sampling before drying off	5.959	2.197-9.081	2.113 ***
V60	Mean ln of the two last CMSCC[4] before drying off	5.867	2.86- 7.74	3.11 ***
V61	Weighted[3] mean of the two last CMSCC[4] before drying off	500	17 – 4 390	1.161 ***
V62	Mean ln of the three last CMSCC[4] before drying off	5.784	2.68- 7.55	3.20 ***
V63	Weighted[3] mean of the three last CMSCC[4] before drying off	473	14 – 3 156	1.174 ***
V64	Treated for (t.) any mastitis in previous lactation (prev.lact.).	0.21	0-1	1.63 (0.06)
V65	T. chronic clinical mastitis prev. lact.	0.07	0-1	2.64 *
V66	T. acute clinical mastitis prev. lact.	0.13	0-1	1.10 NS
V67	T. teat tramp prev. lact.	0.02	0-1	1.39 NS
V71	Milk yield lactation before therapy (kg)	5.971	3 130-11 849	1.10 NS
V72	Number of dry days after therapy	77.0	29-242	1.00 NS

[1] Odds ratios adjusted for the effect of therapy.
[2] Failure = Cow having geometric mean CMSCC > 399 000 during the follow-up lactation compared to < 200 000 ml^{-1}.
[3] Weighted by milk yield on test day. [4] in 1 000 per ml
NS; not significant; * $P \leq 0.05$; ** $P \leq 0.01$; *** $P \leq 0.001$.

CMSCC, lactation number, milk yield, and clinical disease during the lactation before therapy. Lactation number was introduced by creating hierarchical dummy variables (*Walter* 1987); in all models, only 2 levels were found to be significant, namely lactation number greater than one and greater than four. At the herd level, variables included: mean milk production, weighted (by daily milk yield) arithmetic mean of all CMSCC, as well as geometric mean of all CMSCC for all cows in the herd during the study period, true incidence of cases treated for acute clinical mastitis, clinical mastitis, all types of mastitis, ketosis and milk fever. These are presented in Table 4. The variable codes used in the study are presented in Tables 1 through 4. The mean CMSCC and true incidence rates for cases were calculated according to the recommendations from the International Dairy Federation (IDF), (1997).

To evaluate the dynamics of CMSCC at the herd level, a cut-off value of 200 000 per ml, as proposed by *Dohoo & Leslie* (1991) was used to create 2 descriptive variables. Variable V83

Table 4. Mean values, minimum and maximum values (Range) for the herd level variables generated from the dairy recordings during the study period, and odds ratio[1] (OR) when tested for probability of being a failure[2] cow during in the next lactation.

Variable code	Variable	Mean	Range	OR (P-value)
V73	Mean number of cow-years	13.8	4 – 67	0.98 NS
V74	True incidence rate[3] of all mastitis treatments	0.39	0.00 - 1.22	0.97 NS
V75	True incidence rate[3] of all clinical mastitis treatments	0.38	0.00 - 1.22	0.94 NS
V76	True incidence rate[3] of acute clinical mastitis treatments	0.26	0.00 - 0.78	0.65 NS
V77	True incidence rate[3] of teat tramps treatments	0.04	0.00 - 0.25	0.05 NS
V78	True incidence rate[3] of ketosis treatments	0.22	0.00 - 1.26	0.57 NS
V79	True incidence rate[3] of milk fever treatments	0.06	0.00 - 0.29	3.50 NS
V80	True incidence rate[3] of culled cows	0.42	0.16 - 0.79	0.15 *
V81	Weighted CMSCC for all sampling in a herd in 1 000 per ml	279	103 – 737	1.007***
V82	Geometric mean of all CMSCC samples in the herd during the study period in 1 000 per ml	124	51 – 466	1.015***
V83	Incidence of new cow somatic cell counts >200 000 during study period divided by number of cows	0.60	0.26 - 1.14	38.6***
V84	Incidence of new cow somatic cell counts <200 000 during study period divided by number of cows	0.25	0.08 - 0.70	2.33 NS

[1] Odds ratios adjusted for the effect of therapy.
[2] Failure = Cow having geometric mean CMSCC > 399 000 during the follow-up lactation compared to < 200 000 ml^{-1}.
[3] True incidence rate = Number of events of interest divided by number of cow-years in the study period
NS; not significant; * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.

was calculated by dividing the total number of new events of CMSCC values exceeding the 200 000 per ml value, by the total number of cows within the herd. V84 was derived by dividing the number of new events less than the cut-off by the total number of cows in the herd (Table 4).

Statistics

Tables 1 to 4 outline the independent variables considered in simple logistic regression models, (*SAS Institute Inc.* 1987) with the probability of failure (CMSCC greater than 399 000 in the next lactation) as the outcome, and adjusting for the effect of therapy group. Quarter level variables (V1 to V32 in Table 1) were always included as sets of 4 quarters.

All variables having a p-value ≤0.15 were collected for assessment in a multi-variable model using logistic regression. Where correlation between independent variables at levels higher than 0.1 and significant at p≤0.05 was detected, only one of these was selected for inclusion in the multivariable analysis if other reasons for inclusion were not recognised.

Models included variables that used information from the first, second, and combinations of first and second bacteriological sampling. The backward elimination process was used to create the final multivariable models, retaining

those variables with a p-value of 0.05 or less. Interactions and second degree terms were tested with the final model variables seperately one by one. The effect of therapy was forced into all models. Since results within any given herd would likely be more similar than between, we tried to correct for this by treating this variable as random effects in PROC GENMOD (*SAS Institute Inc.* 1991). This serves to correct for the lower variation within, as opposed to between observations, for a given variable, in assessing the true effect of that variable in the overall model. The best fitting models were found when using an exchangeable working correlation structure.

Finally, cows having CMSCC above 399 000 per ml were contrasted with those having less than 200 000 per ml by using the model to estimate failure probabilities based on different sets of values for certain explanatory variables. The specificity and sensitivity for the models were also calculated within the restrictions of the selected material for the study population, excluding cows with CMSCC values between 199 000 and 400 000.

Results

The 187 success and 186 failure cows that qualified for inclusion were from the 2 therapy groups, C (n = 121) and D (n = 139), and control groups A (n = 58) and B (n = 55).

Groups C and D were not significantly different. With the probability of failure as the outcome under consideration, the comparison between the common control group and Group C, resulted in a crude odds ratio of 0.45 (with 95% confidence interval: 0.27-0.76; $p<0.01$). The OR resulting from the comparison of the control group and Group D was 0.55 (0.33-0.90; $p<0.05$).

Only 2 sets of quarter level variables were significantly associated with success or failure in CMSCC, when adjusted for therapy. These were the diagnosis of a major pathogen (V1 to V4) and an isolation of *Staph. aureus* (V9 to V12), both at first sampling. None of the quarter level diagnoses at drying off were significantly associated with success or failure in CMSCC. Though both sets, V9 to V12 and V1 to V4, were significant, the latter set was chosen for the multivariable model found in Table 1. This was because the grouping of V9 to V12 (*Staph. aureus*) is, in essence, a subset of the variable set V1 to V4 (major pathogen).

For data generated from bacteriological diagnoses at cow level (Table 2), most of the variables were highly significant. They also showed a strong correlation with variable V41 (number of quarters with *Staph. aureus* isolates at first sampling and at second sampling (drying off). In fact, V41 was also correlated with the quarter level set of variables V1-V4 (Table 1). Since it was the only variable that contributed significantly to the model when combining Tables 1 and 2, only V41 was used in the multivariable model, thus representing both the quarter and cow level diagnostics at first and second bacteriological tests.

Assessing the effect of lactation included as hierarchic variables (*Walter* 1987) and adjusting for therapy group revealed that with respect to the probability of being a failure cow, both lactation groups greater than one (OR = 2.9; $p<0.001$) and greater than four (OR = 2.3; $p<0.01$), were significant risk factors (Table 3). Other significant variables were the different combinations of the CMSCC for previous lactation, and the mean of the last 3 tests before drying off (V62). Due to the correlation between variables V57 through V63, which are based on different numbers of samples of CMSCC, only the best predictor (the mean of the last 3 tests) was selected for the final model. Of the clinical disease variables, V64 (the cow being treated for any mastitis the previous lactation) and V65 (treated for chronic clinical

Table 5. Odds ratio with 95% confidence interval (in parentheses)) from the multivariable models for predicting a failure[1] cow in next lactation after dry period. Two different models[2] are described.

Independent variable and model sensitivity and specificity	Odds ratio with confidence interval	
	Model 1a	Model 1b
Group C (long acting) versus controls (A+B)	0.35 (0.20-0.62)**	0.35 (0.19-0.63)***
Group D (short acting) versus controls (A+B)	0.45(0.25-0.81)**	0.47 (0.26-0.87)*
Above 1 lactation (DUMLAC2)	2.33 (1.38-3.93)**	2.4 (1.41-4.11)**
Above 4 lactations (DUMLAC5)	2.14 (1.07-4.29)*	2.12 (1.06-4.25)*
Number of quarters with *S. aureus* isolate (V41) OR increase per quarter infected		1.59 (1.21-2.1)***
Mean of 3 last CMSCC (623,000 versus 167,000) (V62)	2.41 (1.66-3.51)***	2.17 (1.48-3.20)***
At least 1 case of chronic clinical mastitis in previous lactation (V65)	2.78(1.12-6.91)*	2.82 (1.11-7.15)*
Weighted mean of CMSCC in the herd (V81) (364,000 versus 184,000)	2.60 (1.53-4.41)***	2.69 (1.53-4.73)***
"Best" sensitivity and specificity	0.70 and 0.70	0.70 and 0.70
Sensitivity at specificity=.90	0.38	0.40

[1] Failure = Cow having geometric mean CMSCC > 399000 during the follow-up lactation compared to < 200,000 ml^{-1}.

[2] Model 1a: Bacteriology not included; Model 1b: Bacteriology at 45 ± 32 days prior to drying off included. NS; not significant; * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.

mastitis the previous lactation) were found to be significant. Since V65 completely involved the effect of V64, as supported by their correlation, it was chosen as the best predictor to be used in further modelling.

Four significant variables which were found to be eligible for the multivariable model (Table 4) were: V80 (the true culling rate), V81 (the weighted mean CMSCC for all samples within a herd during the study period), V82 (the corresponding geometric mean) and V83 (the incidence of new CMSCC above 200,000 per ml during the study period). Variables V81, V82 and V83 were found to be significantly correlated, thus V81 was chosen to be representative of the effects of V82 and V83.

In summary, variables V41, V62, V65, V80, V81 and lactations greater than 1 and 4 were assessed in the final multivariable model. The effect of therapy groups C and D was forced into the model. All of these variables, except for V80, were significant in the multivariable situation.

Testing for interactions and second powers separately, the following significant terms were found: interaction between Group C and V62 ($p<0.05$); between V65 and lactation numbers greater than 4 ($p<0.05$), and V65 and V81 ($p<0.05$). The second power of V62 was significant at $p<0.01$; the second power of V81 was very close to significant ($p = 0.06$). Due to problems associated with overfitting, only simple effects were included in the final model. Additional knowledge of bacteriology (number of quarters with *Staph. aureus* isolate) improved the model, however, the sensitivity increased only slightly at very high specificity. The highly significant correlation between V41 and V62 ($p=0.24$; $p<0.001$) indicates that they are expressing similar information. However, inclusion of bacteriology information added significantly to the model, so both were retained.

Evaluation of Models

To evaluate the models that resulted from fitting the data, different scenarios can be described and estimates of the probabilities of failure can be determined by solving for p(y) = exp (ß) / [1 + exp (ß)]. The model equations described by Models 1a and 1b (Table 5) are as follows:

Model 1a:

ß = -6.774–1.052•C – 0.795•D + 0.844•Lac2 + 0.76•Lac5 + 0.88•V62
+ 1.02•v65 + 0.0053•v81

Model 1b:

ß = -6.617–1.062•C–0.75•D + 0.88•Lac2 + 0.751•Lac5 + 0.465•v41 + 0.776•v62
+ 1.037•v65 + 0.0054•v81

The sensitivity (proportion of cows with CMSCC above 399 000 correctly predicted as failure cows) and specificity (proportion of cows with CMSCC below 200 000 correctly predicted as success cows) for the selected material in the study for Models 1a and 1b are presented in Fig. 1.

Figs. 2 a - 2 d, which show probability curves for a cow in second or third lactation, not treated for chronic clinical mastitis during previous lactation and from a herd with weigthed CMSCC of 150 000 per ml and different situation of *Staph. aureus* infections, illustrate the use of these equations in calculating the probabilities of being a failure cow.

Table 6 presents the estimated mean probabilities of failure for each of the therapy groups (control, groups C and D) for cows used in this analysis, when fitting the model for that specific therapy group. Also given in this table are the outcomes for the cows that were excluded from the model process, namely those with a mean CMSCC in the next lactation which fell between 199,000 and 400,000 per ml, or those without a CMSCC tests result (possibly culled). The estimated probabilities for cows excluded from this study had a mean CMSCC that was closer to the failure cows than to the success cows.

Using the information for all the cows, Figs. 3 a through 3 c present the observed relative percentage of success, failure and "between" cows

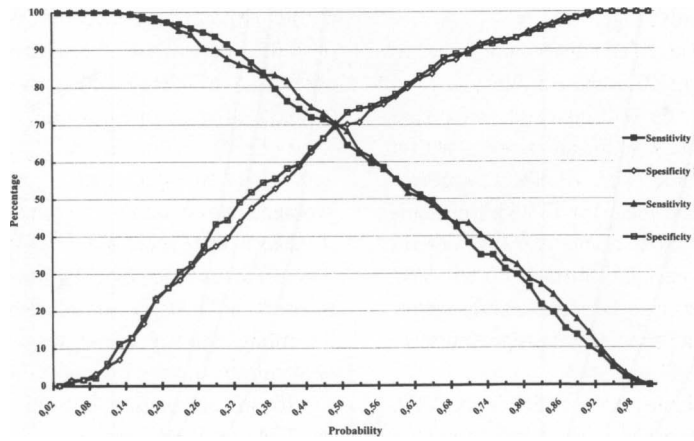


Figure 1. Sensitivity (percent failure cows classified correctly as failures) and specificity (percent success cows classified correctly as successes) according to estimated probability of a failure cows using Model 1a and 1b (Table 5).

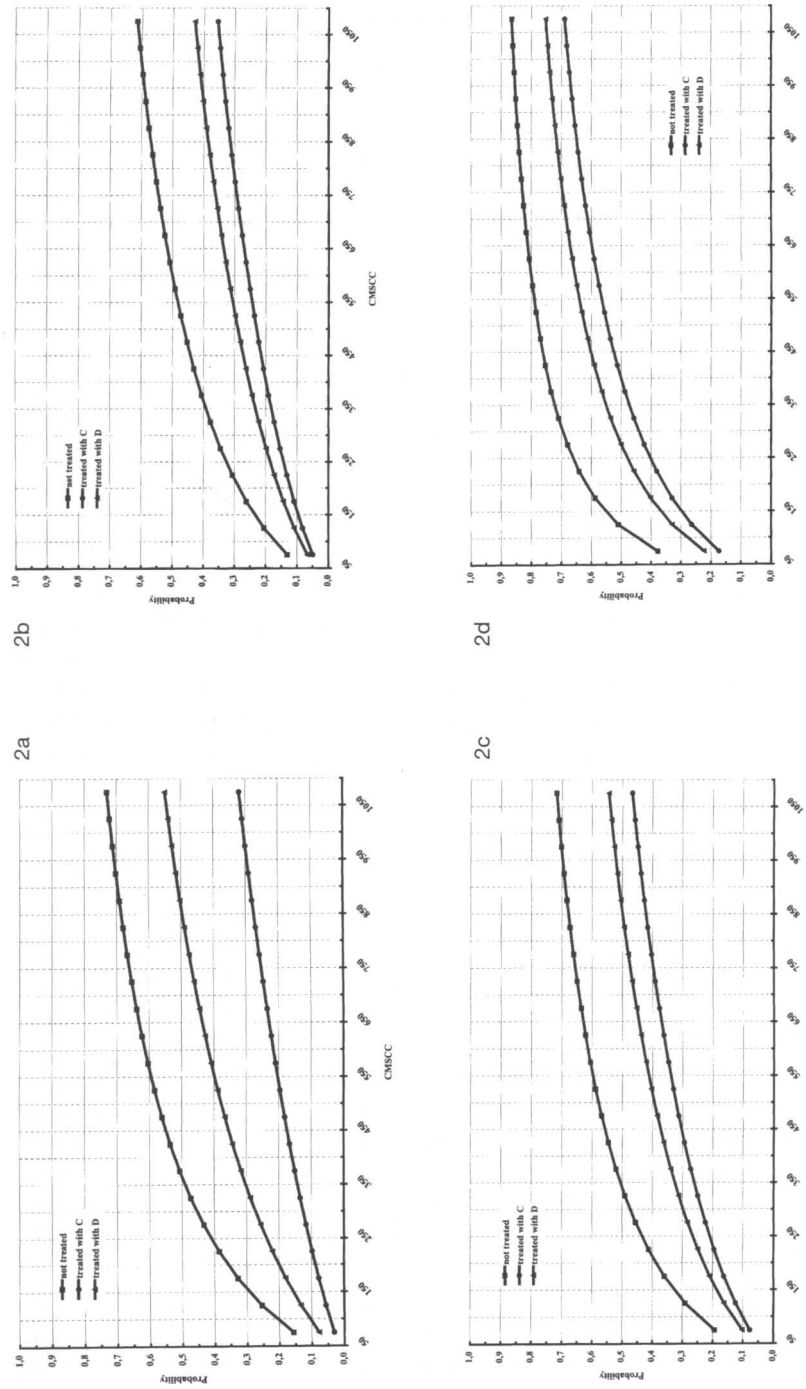


Figure 2 a to d. The probability of a cow having above 399 000 (failure) versus below 200 000 (success) per ml in geometric mean composite milk somatic cell count (CMSCC) for the next lactation after the dry period, plotted against the CMSCC in 1000 per ml as geometric mean of the 3 last tests before drying off on x-axis. The three curves represent a cow without therapy, with therapy C (long-acting) and with therapy D (short-acting), where that cow is in second or third lactation, not treated for chronic clinical mastitis during the previous lactation, and a herd mean of CMSCC weighted by daily milk yield during study period was 150 000 per ml. Figure 2a: Using model 1 a with no bacteriological knowledge; Figure 2b: Using model 1 b: Knowledge of no *Staph. aureus*, Figure 2c: Using model 1 b: Knowledge of one quarter with *Staph. aureus;* Figure 2d: Using model 1 b: Knowledge of three quarters with *Staph. aureus*.

Table 6. Mean estimated probabilities (p), according to Model 1b (Table 5) of being a failure cow[1] grouped according to the actual therapy group for all cows in the study.

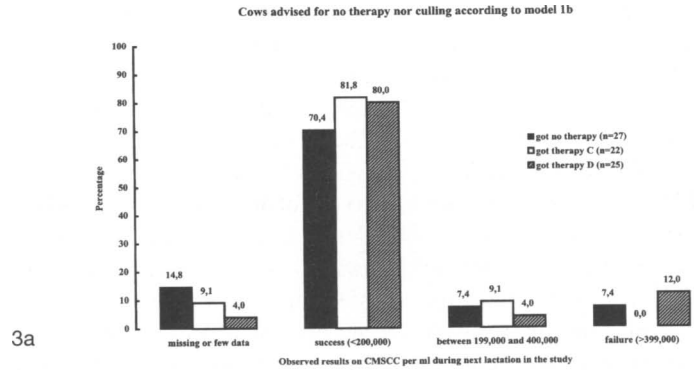
Observed geometric mean somatic cell count during lactation after the dry period.	Group D		Group C		Controls	
	n	p ± STD	n	p ± STD	n	P ± STD
a) <200,000 per ml	74	.36 ± .22	70	.33 ± .21	43	.44 ± .21
199,000 to 400,000 per ml	39	.56 ± .24	44	.43 ± .24	40	.59 ± .21
a) > 399,000 per ml	65	.58 ± .23	51	.55 ± .23	70	.73 ± .19
Missing or few data on geometric CMSCC in next lactation (possibly culled)	33	.61 ± .23	26	.46 ± .27	41	.61 ± .21
Unable to estimate model due to missing data in previous lactation	33		31		26	
Total number and mean estimates from model	244	.51 ± .25	222	.43 ± .25	220	.61 ± .23

[1] Failure = Cow having geometric mean CMSCC > 399 000 during the follow-up lactation compared to < 200,000 ml^{-1}.
a) These cows were used to build the models.

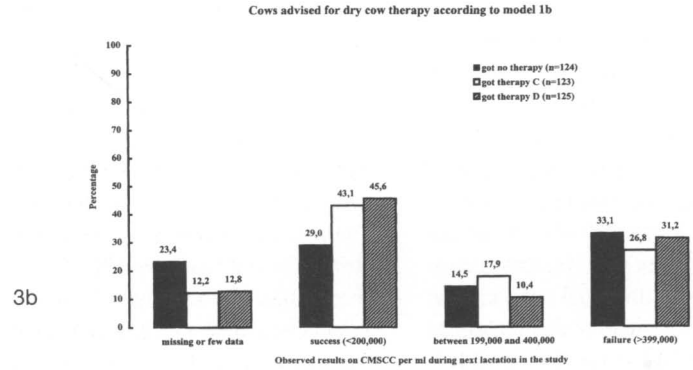
within groups of recommended advice for each cow, using Model 1 b, and what treatment was actually given in the study. These were calculated at a model specificity of 0.90. A probability of 0.70 for failure (from Fig. 1) was chosen as the cut-off value at which the farmer would be advised to cull. To advise no therapy, a sensitivity of 0.90 and thus a probability of 0.30 for failure (Fig. 1) were chosen as the cut-off points. For instance, Fig. 3 c describes those cows for which culling would have been recommended based on Model 1 b. Of all the cows which actually went untreated, 18.6% had less than 3 sampling results, 7.0% had a mean CMSCC less than 200 000 per ml (thus self cures), 11.6% had a mean CMSCC between 199 000 and 400 000 per ml, and 62.8% had a mean CMSCC of greater than 399 000 per ml (thus, failures). The largest differences between treated and untreated cows were seen in the group where culling would have been advised (Fig. 3c). Only 21.3% to 23.9% of these cows had success with therapy, and 7.0% without therapy. For cows where no dry cow therapy was recommended (Fig. 3a), 80% to 81.8% were successes in the treated groups (Groups D and C respectively), and 70.4% in the untreated group (a gain of 10% to 12%). In the group of cows where therapy would have been advised (Fig. 3 b) this corresponding gain was 14% to 17% (compared to Groups C and D respectively).

Discussion

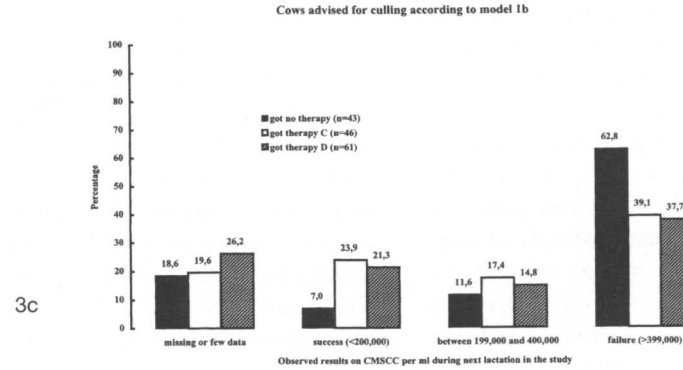
The results of this study are comparable to those in *Østerås & Sandvik* (1996), in which similar regression analyses were done, with the mean CMSCC after the dry period as a continuous dependent variable. They found that therapy, lactation number, geometric mean of all composite cow milk samples in previous lactation, and microbial findings were significant factors. No significant differences were determined between therapy Groups A and B, or between Groups C and D. Rather than using CMSCC as a continuous variable, this study defined success and failure categories that reflect important cut points in the Norwegian dairy quality production. This study can thus be characterised as a case / control (or contrast) study.



3a



3b



3c

Figure 3 a to c. Proportional rate (Percentage) of cows with the observed result according to the data in the study classified as missing or few data on cow milk somatic cell counts (CMSCC) in next laxtation, success (less than 200 000 per ml), "between" (199 000 and 400 000 per ml) or failure (>399 000 per ml) due to geometric mean of CMSCC during the next lactation; grouped according to the therapy the cows were actually given. Figure 3a consist only of cows that according to Model 1 b should be given the advice of not to be given dry cow therapy nor culled, figure 3b cows advised for dry cow therapy and figure 3c cows advised for culling.

This provides more of a pedagogical approach for general use in farming and veterinary practice with regards to utilizing the models derived here.

The factors identified as associated with failure are also relatively consistent with those associated with cure rate (defined by presence or absence of major pathogens) as found in *Østerås et al.* (1999a). Common predictive factors are the geometric mean of the 3 last tests for CMSCC before drying off, and mean of all CMSCC test results in the herd during the study period (V81) weighted by the yield on the sampling day.

The final model only contained simple effects, since fitting interactions made the model very unstable due to overfitting. The effect of this can be seen in the large variation in the OR values. For instance, including the interaction of therapy Group C and V62 resulted in a huge confidence interval on the OR (30.9) for the variable representing Group C versus the control group (0.44 to 2174) in Model 1 a. This was also found in Model 1 b, where the confidence interval on the OR of 47.8 was 0.67 to 3402. Without the interaction term, these values became much smaller, with reasonable confidence bands (Table 5). This resulted in the decision to model only the simple effects. Since the relatively small sample sizes available in this study could be the cause of the instability, these interaction effects might be tested more successfully in a larger scale study of this sort. Of particular interest is the interaction between therapy groups and cell counts.

The effect of clinical mastitis was different in this study as compared to the study of major pathogens (*Østerås et al.* 1999a), wherein the variable most significantly associated with failure was acute clinical mastitis. In this study, previous treatment of chronic clinical mastitis was the most significant variable. This could be due to acute cases potentially being caused by both *Escherichia coli* and major pathogens like *Staph. aureus,* whereas chronic cases are perhaps more related to major pathogens with low cure rate and thus high CMSCC.

The associations of both age and high CMSCC with failure in therapy are consistent with the results of *Sol et al.* (1994). It was found both in this study and in the study of major pathogens (*Østerås et al.* 1999a) that the geometric mean of the last 3 test values for CMSCC before drying off was a better predictor than the mean from fewer tests or from the complete lactation.

Due to the records available in Norway from the health card system and the animal recording system, it was also possible to test herd level variables. From this, it was discovered that when advisors and veterinarians are making recommendations to farmers in setting up a selective dry cow therapy program, it is important to take into account both the general level of CMSCC in the herd and previous treatments of clinical mastitis (individual cow).

Additionally, bacteriology at quarter level (number of quarters infected) can provide information in predicting the expected cure rate after therapy. It was surprising that the bacteriological test results at drying off had no significant association with the CMSCC outcome, however, the identification of number of quarters with *Staph. aureus* 1 month before drying off, as a predictor, is very consistent with the study of *Sol et al.* (1994). Due to the resulting sensitivity and specificity of the different models, there is an indication that the inclusion of bacteriological information does not add significantly to the model (Fig. 1). However, in considering cows that are borderline, with regards to the culling or treatment decision, the bacteriology could play an important role. An example of this would be cows with a status as presented in Figs. 2a-2c, having a mean CMSCC between 100 and 250 000. Treatment advice for cows in this CMSCC range would be improved depend-

ing on their bacteriological status. Since values within this particular CMSCC range are quite common in Norwegian dairy herds (approximately 20% to 25% of the cows, unpublished data), this information would be of great use to a large segment of the population.

Also of importance in the decision making process is the general herd level of the CMSCC. At levels of 300 000 and up, the probability curves change considerably in that they are much closer together, start at a higher probability level, and consequently indicate that blanket dry cow therapy would be appropriate. However, since the probability of failure is so high, the advice regarding culling would be directed at mean CMSCC levels of around 300 000 to 400 000 per ml. This is caused by estimated expected poor results from the dry cow therapy. The implications here are that improvements in general herd management would enhance the results of dry cow therapy.

The authors are aware that one should not test models based on the material upon which they were built. However, we did wish to use Table 6 and Figure 3 to illustrate how estimated probabilities in the excluded cows (due to missing data and CMSCC between 199 000 and 400 000 per ml in the next lactation) would compare to the cows used in the model. A true evaluation of the models have to be done in a new material before generalizing.

The models as described in this paper are useful as a tool in indicating cure rate, as well as self-cure rate, according to expected CMSCC level in next lactation. The presented predicted probabilities in fig. 2 indicates only means for simplicity reasons. However, one should be aware that the estimates have a certain variation indicated by the confidence intervals in Table 5. One should also be aware that the economic optimal time for culling decision for a pregnant cows is not at the time of drying off, but rather partly into the next lactation. Thus, care should be taken in how these results are used. However, in herds with mastitis problems, information on the level of expected CMSCC values in the next lactation could be used as a guide in helping farmers, veterinarians and other advisors to meet their goal of high quality milk production management through selective dry cow therapy and culling recommendations.

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Sammendrag

Faktorer før tørrperioden assosiert med høyt eller lavt nivå av kucelletall i påfølgende laktasjon.

Et behandlingsforsøk ved avsluttende laktasjon (sining) av kyr ble benyttet for å identifisere faktorer assosiert med sannsynligheten for suksess (n = 187) eller fiasko (n = 186) bedømt ut fra kucelletall i neste laktasjon. Suksesskyr var kyr med lavere enn 200 000 pr. ml i geometrisk middel kucelletall hele neste laktasjon, mens fiaskokyr hadde høyere enn 399 000 pr ml i hele neste laktasjon. Forsøket hadde 4 forsøksgrupper; en gruppe kyr med bare prøvetaking, en med placebo med basegrunnlaget av Benestermycin® vet. "LEO"; en gruppe med Benestermycin® vet. "LEO" og en gruppe med Leocillin® med dihydrostreptomycin vet. "LEO". Det ble benyttet logistisk regresjonsanalyse korrigert for effekt av kluster på gårdsnivå for å identifisere mulige risikofaktorer. Faktorer av betydning for å forutsi suksess ut fra modellen var lavt kucelletall (geometrisk middel av de 3 siste tester i kukontrollen) i forregående laktasjon, lavt beregnet buskapscelletall ut fra alle kucelletall (veid på melkemengde på kontrolldato) i hele forsøksperioden, yngre kyr (alder), og fravær av behandling for kronisk klinisk mastitt i foregående laktasjon. Tilleggsinformasjon om sannsynligheten for at ku ble en suksess eller fiasko etter en tørrperiode i både behandlede og ubehandlede kyr var antall kjertler infisert med *Staph. aureus* 45 ± 32 dager før avsining. Kyrne som ble klassifisert som fiaskokyr hadde 2,1 til 2,9 ganger så stor sjanse til å tilhøre den gruppen som ikke var behandlet med antibiotika ved avsining i forhold til de som var behandlet med antibiotika. Det var ingen betydelig forskjell mellom de to typer behandlingsregimer med antibiotika. På det materiale som var selektert til forsøket hadde denne modellen en sensitivitet og spesifisitet på 70% for å klassifisere suksess og fiaskokyrne i korrekt gruppe. Modellene som ble utledet blir vurdert som hjelpemidler til beslutningstagen om selektiv behandling i tørrperioden eller som støtteverktøy i utrangeringsbeslutninger.

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