Selective dry cow treatment in dairy cows

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Aan Marle & Hugo

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Chapter 1

General introduction

Mastitis is an inflammation of the udder that is generally caused by bacteria that invade through the teat canal. Due to its quantitative and qualitative properties, mastitis is the most costly disease on a dairy farm which directly affects the production of milk, the primary source of income of the dairy farmer. Mastitis goes along with visible symptoms in milk or udder (clinical mastitis) or has no clinical signs (subclinical mastitis). For the cow, mastitis can be a painful disease, which affects the animals' welfare and the quality of the produced milk. In the perception of the dairy farmer, mastitis is also an annoying disease, which disturbs the milking routine and requires extra labor and expenditures. Although over the years much effort has been put in prevention programs (Neave et al., 1969; Bradley and Green, 2004; Lam et al., 2013), mastitis is a disease that cannot be eradicated. In most farms mastitis cases that need treatment will occur.

Mastitis is generally caused by intramammary infections (**IMI**) and occurs both in the dry and the lactating period of dairy cows (Barkema et al., 1998). Intramammary infections may lead to clinical mastitis (**CM**) either direct after infection or at a later stage as a clinical flare-up of subclinical mastitis (Bradley and Green, 2000). In some studies the incidence of new IMI was found to be highest during the dry period (Smith et al., 1985; Bradley and Green, 2004). It was described that approximately 50% of quarters with CM caused by environmental pathogens during the first 100 days in milk (**DIM**) were associated with IMI that occurred during the dry period. Consequently, prevention of IMI during the dry period is important for udder health during both, the dry and the lactating period. An effective approach to prevent IMI during the dry period is antimicrobial treatment at drying off, generally known as dry cow treatment (**DCT**).

DRY COW TREATMENT

To prevent the udder from new IMI during the dry period, the use of blanket DCT (**BDCT**) has been advocated for more than 50 years as part of the five-point mastitis prevention program (Neave et al., 1969). The goal of DCT is to reduce the prevalence of IMI, by eliminating IMI already present at drying off and by preventing new IMI from occurring during the dry period (Bradley and Green, 2001). Pearson (1950) published some of the first papers on DCT in response to great concerns about summer mastitis in heifers and dry cows. Oliver et al. (1962) described an experimental DCT trial and concluded that IMI with *Staphylococcus aureus* during the dry period were primarily due to pathogens that contaminated the teats after the last milking before drying off. They concluded that infusion of antimicrobials at the beginning of the dry period could provide nearly full protection against infection with *Staphylococcus* spp. and *Streptococcus* spp. (Oliver et al., 1962). Since the '60s of the previous century DCT was advocated in most countries, where generally a blanket approach, treating all cows with antimicrobials at drying off, was promoted.

In the first decade of the current millennium BDCT was widely adopted, with i.e. a 80% and a 88% uptake at the herd level in the United States and Canada, respectively (Dufour et al., 2012; USDA, 2016). In the Netherlands, approximately 90% of all dairy cows were treated with dry cow antimicrobials in the period 2005-2010 (Lam et al., 2013). In the United Kingdom, antimicrobial DCT is estimated to be even higher, with 99% of dairy farms treating all their cows at drying off with dry cow antimicrobials (Berry and Hillerton, 2002).

RESTRICTED ANTIMICROBIAL USE AT DRYING OFF

Antimicrobial use creates a selective pressure on bacterial populations and contributes to development of antimicrobial resistance (Tacconelli, 2009; Landers et al., 2012). In the dairy industry in the Netherlands, intramammary treatments counted for approximately 60% of antimicrobial use (**AMU**) for many years, of which roughly two third was related to DCT (Kuipers et al., 2016). Although the relationship between AMU and the development of antimicrobial resistance in mastitis bacteria is complex and unclear, there is a potential effect, and from a precautionary perspective, prudent use of antimicrobials is therefore warranted. Prudent use of antimicrobials in the dairy industry requires evaluating BDCT, which includes preventive use of antibiotics in non-infected quarters.

Not applying DCT, however, may have a detrimental effect on udder health by eliminating an important part of the prevention of new and of the cure of existing IMI. In the Netherlands for instance, a study from the early 90's showed that not applying DCT leads to an unacceptable high incidence rate of CM (Schukken et al., 1993), which was confirmed in a meta-analysis of Halasa et al. (2009). In some countries, specifically in Scandinavia, however, selective DCT (**SDCT**) has been applied as part of their national mastitis control program for a long time (Osteras and Solverod, 2009). Nevertheless, in for instance Norway a 60% reduction in treatments of CM was realized between 1994 and 2007, as well as a reduction in bulk milk somatic cell count from 250,000 cells/ml to 114,000 cells/ml, and a total reduction in the costs of mastitis from 9.2% to 1.7% of the milk price. This reduction was mainly attributed to changes in attitude and a better implementation of mastitis prevention programs.

Apparently DCT has a big influence on udder health, although there is evidence that other factors play an important role too, and possibly can compensate for not practicing BDCT. In the Netherlands this is the more of interest, because since 2012 preventive use of antimicrobials is no longer allowed. Selective use of antimicrobials at drying off, treating only infected cows, however, is an acceptable solution and was introduced in 2013 as an alternative for BDCT. How to select cows for DCT, and what the effect of SDCT on udder health would be under Dutch circumstances, is unknown.

POSSIBLE CONSEQUENCES OF CHANGING BLANKET TO SELECTIVE DRY COW TREATMENT

The effect of the transition from BDCT to SDCT likely depends on parameters and their thresholds used to select cows for DCT. Selective DCT and therefore the chosen criteria potentially has an effect on the incidence of CM and subclinical mastitis (**SCM**), milk quality, public health, AMU, welfare and practical feasibility. These effects can be contradictory; SDCT as compared to BDCT may decrease initial AMU while it leads to more CM and a higher somatic cell count (**SCC**). Udder health, welfare, production losses, AMU and economic consequences are all important parameters, but are measured in different units, that cannot be mutually compared. Therefore effects that move in different directions cannot be summed. A potential solution to solve this problem partly is by expressing effects on different parameters in economic units. This can be helpful for parameters such as CM, SCM and AMU. Although for parameters such as animal welfare and public health this may not be helpful, the economic comparison may help in taking decisions on DCT approaches.

Based on this approach, earlier model studies showed a beneficial economic effect of SDCT as compared to BDCT (Huijps and Hogeveen, 2007). In the real life situation in the field, results likely are different, but the same economic approach may be of value. Therefore an economic evaluation, along with an evaluation of animal welfare, legislation and public health effects, may be helpful in making decisions on DCT strategies on the national level.

ATTITUDE OF FARMERS AND VETERINARIANS

There is a great effect of the attitude of farmers and veterinarians on the implementation and execution of different mastitis management measures (Jansen et al., 2010; Speksnijder et al., 2015; Swinkels et al., 2015). Therefore a favorable attitude of both, farmer and veterinarian towards SDCT seems crucial for a successful transition from BDCT to SDCT. Given the fact that BDCT is a proven effective management measure that has been promoted for half a century (Lam et al., 2013), transforming this management measure to SDCT seems quite a challenge.

It is likely that the attitude towards SDCT is related to the attitude towards AMU in general. Several European studies describe the influence of veterinarians on farmers' AMU (De Briyne et al., 2013; Postma et al., 2016; Higgins et al., 2017). Other studies describe the influence of the mindset of farmers on udder health and AMU (Lam et al., 2011; Jones et al., 2015). Understanding the attitude of farmers and veterinarians towards AMU in general and towards SDCT specifically, therefore seems crucial in order to maintain and improve responsible AMU in dairy farms, while this attitude is unknown in the Netherlands.

ECONOMICS

One of the factors influencing whether or not management measures are implemented is the economic effect of the measure (Halasa et al., 2007; Lam et al., 2017). It has been described that farmers' decision-making on DCT is not only based on udder health effects such as CM and SCM, but also on monetary terms, e.g. economic losses due to treatment decisions related to mastitis (Hogeveen et al., 2011). As such, economic consequences along with legislation, udder health effects, animal welfare, and public health concerns, may be helpful in decision-making on SDCT at the herd level and need specific attention.

There are a few studies that describe the economic consequences of DCT. Most economic analyses have concluded that BDCT is financially beneficial, because of increased milk yield, lower SCC or reduced CM cases, when compared with SDCT or no DCT (McNab and Meek, 1991; Berry et al., 1997; Yalcin and Stott, 2000). Most of these calculations were, however, based on uncertain assumptions and there was much variation in the results. In a stochastic model described by Huijps and Hogeveen (2007), SDCT was economically most attractive. In that study differences between BDCT and SDCT were small and with regard to selection of the appropriate animals, the assumptions on probabilities for selecting the right cows for DCT and the assumptions for AMU were unclear. None of the above studies described the level of reduction of AMU related to DCT while practicing SDCT which therefore needs further attention.

The economic impact of SDCT likely varies for different types of herds and for different levels of AMU related to DCT. Studies describing and evaluating economic consequences of SDCT on herd-level can be used by dairy farmers and their advisors to help them to optimize decisions on DCT, thereby minimizing costs. Thus, the economic consequences of SDCT need further attention.

SELECTION CRITERIA FOR DRY COW TREATMENT

The effect of SDCT compared to BDCT is influenced by the criteria used to select cows for DCT (Torres et al., 2008; Cameron et al., 2014). Worldwide, cow level SCC is used to identify cows that are subclinically infected with mastitis pathogens. Although it is not perfect, the use of SCC to measure the inflammatory response to an IMI is a cheap and practical tool to evaluate the udder health status (Schukken et al., 2003). Different countries use different SCC-thresholds for a cow or a quarter to be defined as infected. In the Netherlands, SCC selection thresholds for IMI are 150,000 cells/mL for heifers and 250,000 cells/mL for multiparous cows (**150/250**) (de Haas et al., 2008; Windig et al., 2010). Although different studies use different criteria to select cows for SDCT, selecting cows based on SCC with 150/250 cutoff seems a practical and executable alternative for bacteriological culturing of individual cow or quarter samples, which theoretically would be the ideal approach.

The most feasible selection method seems to be based on monthly SCC, data that is readily available in many herds. SCC has a reported sensitivity of 70% and specificity of 63% to identify quarters with IMI at drying off (Torres et al., 2008). In that study cows were selected for DCT based on an SCC cutoff level of 200,000 cells/mL and the history of CM. In many studies that compared SDCT with BDCT, combinations of selection criteria were used to select cows for DCT. Combining information on the dairy farm, however, requires high quality data, i.e. on CM cases, and frequent SCC measurement, and therefore complicates selection of cows for DCT. Using a single SCC measurement may be a very practical and cheap alternative to select cows for DCT on all farms, and thus may help in an easy transition from BDCT to SDCT at the national level.

AIM AND SCOPE OF THE THESIS

Udder health is associated with mastitis management, of which BDCT has been an important part for decades (Lam et al., 2009). However, based on legislation, preventive use of antimicrobials in veterinary medicine is prohibited since 2012 in the Netherlands and therefore SDCT is a given. Selection of cows for DCT is an important part of SDCT and probably has a great effect on the consequences of SDCT. However, not much research has been done in this field. At the same time the approach to select cows for DCT has to be supported and picked up by all approximately 18,000 dairy farmers in the Netherlands. Therefore, practical applicability is an important issue. In order to smoothen the transition from BDCT to SDCT, it is valuable to evaluate the effect of various approaches to select cows for DCT on udder health, AMU, and economics. Understanding and balancing these issues contributes to an optimization of DCT approaches.

The aims of this thesis therefore are to quantify the effects of SDCT on clinical and subclinical mastitis, AMU and economics. Additionally the effect of different SCC threshold-scenarios for selecting cows for DCT on these parameters will be evaluated. The economic consequences of using different levels of AMU in DCT will be evaluated as will be the attitude of the dairy farmer and the veterinarian with respect to reduction of AMU and of SDCT. During the execution of this study BDCT changed to SDCT in the Netherlands and all of the aforementioned aspects will be evaluated in the perspective of this transition.

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Chapter 2

Evaluation of the use of dry cow antibiotics in low somatic cell count cows

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SUMMARY

The goal of dry cow therapy (DCT) is to reduce the prevalence of intramammary infections (IMI) by eliminating existing IMI at drying off and preventing new IMI from occurring during the dry period. Due to public health concerns, however, preventive use of antibiotics has become questionable. This study evaluated selective DCT in 1,657 cows with low somatic cell count (SCC) at the last milk recording before drying off in 97 Dutch dairy herds. Low SCC was defined as <150,000 cells/mL for primiparous and <250,000 cells/mL for multiparous cows. A split-udder design was used in which 2 quarters of each cow were treated with dry cow antibiotics and the other 2 quarters remained as untreated controls. The effect of DCT on clinical mastitis (CM), bacteriological status, SCC, and antibiotic use were determined at the quarter level using logistic regression and chi-squared tests. The incidence rate of CM was found to be 1.7 times (95% confidence interval = 1.4–2.1) higher in quarters dried off without antibiotics as compared with quarters dried off with antibiotics. *Streptococcus uberis* was the predominant organism causing CM in both groups. Somatic cell count at calving and 14 d in milk was significantly higher in quarters dried off without antibiotics (772,000 and 46,000 cells/mL, respectively) as compared with the quarters dried off with antibiotics (578,000 and 30,000 cells/mL, respectively). Quarters with an elevated SCC at drying off and quarters with a positive culture for major pathogens at drying off had a higher risk for an SCC above 200,000 cells/mL at 14 d in milk as compared with quarters with a low SCC at drying off and quarters with a negative culture for major pathogens at drying off. For quarters that were culture-positive for major pathogens at drying off, a trend for a higher risk on CM was also found. Selective DCT, not using DCT in cows that had a low SCC at the last milk recording before drying off, significantly increased the incidence rate of CM and SCC. The decrease in antibiotic use by drying off quarters without DCT was not compensated by an increase in antibiotic use for treating CM. Total antibiotic use related to mastitis was reduced by 85% in these quarters.

INTRODUCTION

Mastitis is the consequence of IMI and occurs both in the dry and the lactating period of dairy cows (Barkema et al., 1998). New IMI may arise in the dry and the lactating period, possibly leading to clinical mastitis (**CM**) either directly after infection or later (Bradley and Green, 2000). The incidence of new IMI is highest during the dry period (Smith et al., 1985; Bradley and Green, 2004). To prevent the udder from acquiring new IMI during the dry period, the use of blanket dry cow therapy (**DCT**) has been advocated for almost 50 years as part of the 5-point mastitis management program (Neave et al., 1969). Intramammary infusion of long-acting antibiotics at the end of lactation is an integral part of this program and was widely adopted in the Netherlands, with 87% of herds using blanket DCT and 11% using selective DCT in 2007 (Sampimon et al., 2008).

The goal of DCT is to reduce the prevalence of IMI, both by eliminating IMI already present at drying off and by preventing new IMI from occurring during the dry period (Bradley and Green, 2001). Antibiotic use, however, creates a selective pressure on bacterial populations and contributes to development of antimicrobial resistance (Tacconelli, 2009; Landers et al.,

2012). Organizations, such as the World Health Organization, recommend reducing the use of antibiotics. In the dairy industry, prudent use of antibiotics comprises looking carefully at the use of blanket DCT, which includes preventive use of antibiotics in noninfected quarters.
In some countries, DCT is only applied for curative reasons, leading to a very low antibiotic use. Specifically, Nordic countries have used selective DCT as part of their national mastitis control program (Osterås and Sølverød, 2009). In the Netherlands, a study in the early 1990s showed that a decrease in DCT led to dramatic consequences, such as a 10 times higher incidence rate of clinical mastitis (**IRCM**) in quarters dried off without antibiotics (Schukken et al., 1993). In that study, however, a within-cow comparison on the effect of DCT was performed without separating uninfected and subclinically infected cows (Schukken et al., 1993).
Worldwide, cow-level SCC is used to identify cows that are likely subclinically infected with mastitis pathogens. Although this parameter is not perfect, the use of SCC to measure the inflammatory response to an IMI is a practical tool to evaluate udder health (Schukken et al., 2003). In the Netherlands, over the years, SCC selection thresholds for IMI were 150,000 cells/mL for primiparous and 250,000 cells/mL for multiparous cows (de Haas et al., 2008; Windig et al., 2010).
The current study aimed to evaluate DCT in cows with low SCC (primiparous cows <150,000 cells/mL and multiparous cows <250,000 cells/mL) at the last milk recording before drying off. The effect on CM, bacteriological status, SCC, and antibiotic use was evaluated when no DCT was administered in low-SCC cows. Additionally, the effect of bacteriological status and SCC at drying off on CM and SCC at 14 DIM was assessed.

MATERIALS AND METHODS

Trial Design

The effect of selective DCT was evaluated by no longer using antibiotics at drying off in low-SCC cows. Cows were classified as low-SCC cows when SCC at the last milk recording before drying off was <150,000 cells/mL for primiparous and <250,000 cells/mL for multiparous cows (de Haas et al., 2008), the thresholds used in the Dutch national milk recording. A split-udder design was used in which 2 lateral quarters of each cow were treated with antibiotics and the other 2 quarters remained as untreated controls, without antibiotics. The antibiotic treatment was randomly assigned to either the 2 right quarters or the 2 left quarters of each cow.

Treatment

Immediately after collection of the drying-off samples, the technician administered the treatment as outlined herein. The dry cow product contained 314 mg of potassium benzylpenicillin, 1,000 mg of procaine benzylpenicillin, and 500 mg of neomycin sulfate (Supermastidol, Virbac, Barneveld, the Netherlands). Technicians wore disposable gloves throughout the sanitization, sampling, and treatment process. After treatment, all 4 teats were disinfected with the disinfectant that was routinely used by the herdsman and the cow was marked as a dry cow. Herdsmen were blinded as to which quarters were treated with dry cow antibiotics.

Sampling

Milk samples were taken from each quarter at drying off (**DRY**) by the technician, within 12 h after calving (**D0**) by the herdsmen, and again at 14 (± 7) DIM (**D14**) by the technician. Quarters with CM were identified and sampled by the herdsmen, all of whom had been trained in identification and sample collection. Milk samples collected by the technicians were stored at 3 to 8°C during shipment to the laboratory. All milk samples were collected aseptically by technicians and herdsmen after scrubbing teats using cotton-wool pledgets in 70% ethanol solution. Foremilk samples were collected according to IDF recommendations (IDF, 1981). Samples collected by the herdsmen were frozen at -20°C at the farm and were taken to the laboratory for bacteriological analysis at the next visit by one of the technicians.

Herds

Herds were recruited throughout the Netherlands by advertisements in dairy magazines and agricultural websites. Farms participated on a voluntary base. Only conventional (nonorganic) farms with a minimum of 40 dairy cows who participated in the 4-, 5-, or 6-wk milk recording, including SCC measurement, were included. Ninety-nine herds were recruited, of which 2 dropped out, leaving 97 herds for analysis. One herd had a clinical outbreak of *Klebsiella* mastitis in an early stage of the study that was unrelated to the study. The herdsman of the other farm had underestimated the amount of labor associated with the study. The 97 herds were between 44 and 465 cows in size, with a median herd size of 94 cows.

Animals

Cows were eligible for recruitment to the study if they had no significant teat lesions, were in good health at the time of drying off (no clinical disease symptoms), and had 4 functional quarters. Herds were enrolled between June 2011 and March 2012. Cows were followed until October 2012. Herdspersons were not allowed to preselect animals. Every eligible cow within the study period was enrolled in the trial, with a maximum of 30 animals per herd, ensuring no bias was introduced from cow selection. A total of 1,680 animals were recruited from the 97 participating herds, of which 1,657 were available for analysis. Data of 657 primiparous cows (40%) and 1,000 multiparous cows (60%) were analyzed. Twenty-three animals did not finish the study due to early culling, death (not mastitis related), or missing data. The proportion of primiparous cows included in the study was relatively high compared with the age distribution of the herds (32% primiparous cows in the herds). The total number of cows included per herd varied from 3 to 30 animals, with a median of 19. The percentage of cows included per herd varied from 4 to 37%, with a median of 17%. All animals were followed from drying off to 100 d in lactation.

Antibiotic Use

Data on all individual antibiotic treatments were collected during the trial, comprising active compound, application route, dosage, frequency, and duration of treatment. Standardization of quantification of antibiotic use to compare animals presents difficulties due to differences in treatment regimens, dosages, metabolic differences within species, and a wide range in animal bodyweight. Antibiotic use in this study was expressed as the number of animal daily dosages (**ADD**). One ADD is defined as a standardized 1-d treatment, being the average dose for a 1-d treatment of a registered veterinary drug for its main indication (Jensen et al., 2004). In this approach 1 ADD is calculated as the dosage multiplied by the application frequency per day. Both, parenteral and intramammary treatment of an adult cow over 2 yr of age is expressed per 600 kg, which is the defined standard bodyweight. Antibiotic use for DCT was calculated as 1 ADD per quarter treated with antibiotics at drying off, as defined by the standard operating procedure of the expert panel of the Netherlands Veterinary Medicines Authority. In our study, intramammary antibiotic treatments as well as parenteral antibiotic treatments related to mastitis were summed and allocated to the affected quarters. Total antibiotic use was calculated at the quarter level as antibiotics for DCT augmented with antibiotics used for intramammary and parenteral treatment of CM.

Laboratory Analysis

Somatic cell count was determined using SomaScope LFC 300 HP (Delta Instruments, Drachten, the Netherlands) according to the method of the International Dairy Federation (IDF, 1981). Bacteriological culturing was performed according to National Mastitis Council (NMC, 1999) recommendations. For routine samples 0.01 mL of milk was inoculated on 6% sheep blood agar and *Streptococcus*-selective Edward's agar (Biotrading, Mijdrecht, the Netherlands). A quarter was considered infected based on colony counts of the initial culture (≥100 cfu/mL). Plates were incubated for 48 h at 37°C and examined after 24 and 48 h of incubation. Bacterial colonies were put on a template with a matrix. A matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (Bruker Daltonics, Bremen, Germany) was used for species identification allowing bacterial identification with high confidence and speed (Barreiro et al., 2010).

Statistical Analysis

Analysis was performed at the quarter level. In case a quarter was affected by CM, this quarter was considered to be no longer at risk for CM; therefore, repeat cases of CM were not included in the analysis. To compare quarters dried off with or without antibiotics, IRCM was calculated for each group taking into account the number of quarter-days at risk in each group. Clinical mastitis, bacteriological status, and the percentage of quarters with a SCC above 200,000 cells/mL (**QSCC200**) were compared between the groups using a chi-squared test. Mean SCC was compared using Kruskal-Wallis analysis.

The effect of SCC and bacteriological status for major pathogens at drying off on IRCM, as well as on the percentage of QSCC200 at D14, was analyzed using a multilevel logistic regression with 2 levels, adjusting for inclusion of multiple cows per herd and multiple quarters per cow. Data were analyzed using Stata12SE (Statacorp, College Station, TX). Results with $P < 0.05$ were considered significant.

Definitions

A primiparous cow was defined as a first-lactation cow until the time she calved for the second time. A multiparous cow was defined as a cow that has calved at least twice. When a primiparous cow was dried off, this referred to drying off at the end of the first lactation. The CM that occurred during the dry period of primiparous cows was related to the dry period of animals before their second calving. Therefore, CM during the subsequent lactation of primiparous cows occurred in their second lactation.

A new IMI was defined as an IMI with a mastitis pathogen in a quarter at D0 or D14 if the quarter was culture-negative or culture-positive with another pathogen at drying off. Clinical mastitis occurred when visible changes in the milk or the quarter were observed, such as watery milk, clots or flakes, and changes and swelling or redness of the affected quarter. Clinical mastitis diagnosis was made by the herdsmen. Quarters were considered at risk from the date of drying off until 100 DIM in the following lactation, unless the quarter was censored earlier because of CM or if the animal left the farm. An elevated SCC at the cow level was defined as an SCC >150,000 cells/mL for primiparous and >250,000 cells/mL for multiparous cows. An elevated SCC at the quarter level was defined as an SCC >200,000 cells/mL (QSCC200).

RESULTS

CM

In 86 out of 97 herds (89%), 1 or more cases of CM were detected in the period from drying off to 100 DIM. A total of 319 quarter cases in 243 cows were observed, with 69 primiparous cows (28%) and 174 multiparous cows (72%). Of 243 cows, 182 had 1 affected quarter, 50 had 2 affected quarters, 7 had 3 affected quarters, and in 4 cows all 4 quarters were affected at some point during the study. The distribution of CM cases during different stages of lactation in quarters dried off with or without antibiotics is presented in Table 1. In the quarters dried off without antibiotics, 200 quarter cases of CM were observed, with 119 quarter cases of CM in quarters dried off with antibiotics ($P < 0.001$). Across the whole study period, the IRCM in quarters dried off without antibiotics was 1.7 times (95% CI = 1.4–2.1) higher than in quarters dried off with antibiotics. The highest IRCM occurred during the first 21 d of lactation. The largest difference in IRCM, however, was found in the dry period, where quarters dried off without antibiotics had 3.7 times (95% CI = 1.8–8.3) higher odds to acquire CM than quarters dried off with antibiotics. The distribution of pathogens for CM cases did not significantly differ between the quarters dried off with or without antibiotics. The predominant organism causing CM in both groups was *Streptococcus uberis* (Table 2).

An elevated quarter SCC at drying off was not associated with the occurrence of CM. Being culture-positive at the quarter level for major pathogens at drying off showed a trend for a higher risk of CM (Table 3).

Table 1. Clinical mastitis (n = 319) in quarters that did not (NOAB) or did (AB) receive dry cow antibiotics in low-SCC cows from 97 Dutch dairy herds[1]

Item	NOAB (n = 200)	AB (n = 119)	Ratio	*P*-value
Dry period	37 (19)	10 (8)	3.70	<0.001
Calving	33 (17)	22 (19)	1.50	0.14
First 100 DIM	130 (65)	87 (73)	1.49	<0.05
IRCM[2]	0.41×10^{-3} (0.35×10^{-3} – 0.47×10^{-3})	0.24×10^{-3} (0.20×10^{-3} - 0.30×10^{-3})	1.71	<0.001

[1] Values are no. (%) or median (25th–75th percentile).
[2] Incidence rate of clinical mastitis per quarter-day at risk.

Table 2. Bacteriological results (no., with percentage in parentheses) from clinical mastitis (n = 319) in quarters that did not (NOAB) or did (AB) receive dry cow antibiotics in low-SCC cows from 97 Dutch dairy herds

Item	NOAB (n = 200)[1]	AB (n = 119)[1]	*P*-value
Culture negative	50 (25)	32 (27)	0.30
Other bacteria[2]	7 (4)	7 (6)	0.13
Contaminated	6 (3)	3 (3)	0.94
No sample	37 (19)	34 (29)	
Major pathogen	83 (42)	36 (30)	0.17
Minor pathogen	18 (9)	8 (7)	0.67
Major pathogen (n = 83 and 36 for NOAB and AB, respectively)			
Staphylococcus aureus	24 (12)	7 (6)	0.13
Escherichia coli	14 (7)	6 (5)	0.66
Klebsiella spp.	0	1 (1)	0.17
Streptococcus uberis	31 (16)	12 (10)	0.31
Streptococcus dysgalactiae	7 (4)	7 (6)	0.21
Trueperella pyogenes	10 (5)	6 (5)	0.80
Minor pathogen (n = 18 and 8 for NOAB and AB, respectively)			
CNS	12 (6)	8 (7)	0.59
Corynebacterium spp.	6 (3)	0	0.07

[1] Samples could be culture positive for more than one pathogen.
[2] Other bacteria, such as *Proteus* spp., *Bacillus* spp., *Enterococcus* spp.

Table 3. Results of the multilevel, multivariable model for the association between SCC and culture positive for major mastitis pathogens at drying off (DRY) and the occurrence of clinical mastitis (CM) and the percentage of quarters with SCC >200,000 cells/mL (QSCC200) at d 14[1]

Item	CM, OR[2] (95% CI)	QSCC200 (d 14), OR[2] (95% CI)
QSCC200 (DRY)	1.3 (0.96; 1.8)	1.5 (1.2; 1.8)
Culture positive for major mastitis pathogen (DRY)	1.8 (0.89; 3.7)	1.6 (0.95; 2.6)
Untreated	2.0 (1.5; 2.5)	2.0 (1.7; 2.3)

[1] Model adjusted for multiple cows per herd and multiple quarters per cow.
[2] OR = odds ratio.

Bacteriological Status

Data on the bacteriological status of all quarters in the study at DRY, D0, and D14 are presented in Table 4. No significant difference was found between the groups of treated and untreated quarters in bacteriological status at DRY. Of all quarters, 65% were culture negative, approximately 24% of samples were positive for minor pathogens (CNS and *Corynebacterium* spp.), and approximately 2.4% for major pathogens.

At D0, significantly more samples were culture-negative in quarters dried off with antibiotics (62%) as compared with quarters dried off without antibiotics (51%). Significantly fewer samples were culture-positive for major pathogens (4.3 vs. 9.3%) and minor pathogens (12.2 vs. 18.2%) in quarters dried off with antibiotics as compared with quarters dried off without antibiotics (Table 4). Although prevalence of culture positive samples had slightly decreased at D14, comparable differences were found for major pathogens (3.4 vs. 6.2%) as well as minor pathogens (12.2 and 22.1%) in quarters dried off with antibiotics as compared with quarters dried off without antibiotics. The largest differences were found for *Escherichia coli*, *Strep. uberis*, and *Corynebacterium* spp. (Table 4).

Table 4. Prevalence of pathogens in all quarters that did not (NOAB) or did (AB) receive dry cow antibiotics at drying off (DRY), at calving (D0), and at 14 DIM (D14) in low-SCC cows from 97 Dutch dairy herds

	DRY				D0				D14			
	NOAB (n = 3,314)[1]		AB (n = 3,314)[1]		NOAB (n = 3,314)[1]		AB (n = 3,314)[1]		NOAB (n = 3,314)[1]		AB (n = 3,314)[1]	
Item	no.	%	no.	%	no.	%	no.	%	no.	%	no.	%
Culture negative	2,171	66.0	2,155	65.0	1,693**	51.0	2,039**	62.0	1,958**	59	2,380**	72.0
Other bacteria[2]	157	4.7	142	4.3	186	5.6	189	5.7	135	4.1	146	4.4
Contaminated	132	4.0	137	4.1	278	8.4	275	8.3	149	4.5	126	3.8
No sample	0		0		286	8.6	281	8.5	170	5.1	156	4.7
Major pathogen	71	2.1	86	2.6	307	9.3	141	4.3	206	6.2	113	3.4
Minor pathogen	793	24.0	807	24.0	603	18.0	405	12.0	732	22	405	12
Major pathogen[3]												
Staphylococcus aureus	18	0.5	12	0.4	62**	1.9	36**	1.1	56**	1.7	32**	1.0
Escherichia coli	4	0.1	2	0.1	33**	1.0	14**	0.4	21**	0.6	4**	0.1
Klebsiella spp.	0		0		3	0.1	1	0.0	2	0.1	2	0.1
Streptococcus agalactiae	0		0		0		1	0.0	0		0	
Streptococcus uberis	13	0.4	21	0.6	94**	2.8	32**	1.0	53**	1.6	20**	0.6
Streptococcus dysgalactiae	7	0.2	11	0.3	44*	1.3	23*	0.7	14	0.4	8	0.2
Serratia marcescens	0		0		3	0.1	0		4	0.1	0	
Trueperella pyogenes	1	0.0	0		16	0.5	10	0.3	6	0.2	11	0.3
Alpha-hemolytic streptococci	28	0.8	40	1.2	52*	1.6	24*	0.7	50	1.5	36	1.1
Minor pathogen[4]												
CNS	283	8.5	277	8.4	416	13.0	357	11	295	8.9	286	8.6
Corynebacterium spp.	510	15.0	530	16.0	187**	5.6	48**	1.4	437**	13	119**	3.6

[1] Samples could be positive for more than one pathogen.
[2] Other bacteria such as *Proteus* spp., *Bacillus* spp., *Enterococcus* spp.
[3] Major pathogens were found in 71, 86, 307, 141, 206, and 113 quarters of NOAB (DRY), AB (DRY), NOAB (d 0), AB (d 0), NOAB (d 14), and AB (d 14), respectively.
[4] Minor pathogens were found in 793, 807, 603, 405, 732, and 405 quarters of NOAB (DRY), AB (DRY), NOAB (d 0), AB (d 0), NOAB (d 14), and AB (d 14), respectively.
* Quarters dried off without antibiotics differed significantly ($P < 0.05$) from quarters dried off with antibiotics.
** Quarters dried off without antibiotics differed significantly ($P < 0.01$) from quarters dried off with antibiotics.

SCC

The percentage of quarters with a QSCC200 at DRY, despite a low cow SCC, was 36%. The mean SCC at drying off did not significantly differ between quarters dried off with or without antibiotics. Similarly, the groups did not significantly differ in the percentage of QSCC200 at drying off. At D0 and D14, SCC was significantly higher in quarters that were not dried off with antibiotics (Table 5).

Table 5. Quarter SCC and number of quarters with SCC >200,000 cells/mL (QSCC200) in quarters (n = 6,628) that did not (NOAB) or did (AB) receive dry cow antibiotics in low-SCC cows from 97 Dutch dairy herds

	NOAB			AB			
Item	no.	Median (p25–p75)[1]	No. affected (%)	no.	Median (p25–p75)[1]	No. affected (%)	P-value
Quarter SCC (x 1,000 cells/mL)							
At drying off	3,314	121 (46–310)		3,314	120 (47–315)		0.77
At calving	1,450	772 (225–2,035)		1,472	578 (180–1,380)		<0.01
14 DIM	3,100	46 (18–143)		3,103	30 (13–76)		<0.01
Number of quarters with high QSCC200							
At drying off	3,314		1,182 (36)	3,314		1,177 (36)	0.88
14 DIM	3,100		610 (20)	3,103		388 (13)	<0.01

[1] p25–p75 = 25th–75th percentile.

Quarters with an elevated SCC at DRY had a higher risk for an SCC above 200,000 cells/mL at D14. Similarly, quarters with a positive culture for major pathogens at DRY had a higher risk for an SCC above 200,000 cells/mL at D14. The last effect was confounded by the risk of an elevated SCC in the multivariable model (Table 3).

Antibiotic Use

In quarters dried off with antibiotics 3,314 ADD were used for DCT. For treatment of first cases of CM during the dry period and the first 100 d after calving in these quarters, 265 intramammary treatments with 12-h treatment intervals and 107 intramammary treatments with 24-h treatment intervals were used, resulting in 239.5 intramammary ADD. Additionally, for parenteral treatment of CM in quarters dried off with antibiotics, 138.5 ADD were used. This resulted in a total of 3,692 ADD (Table 6).

Table 6. Antibiotic use at quarter level related to dry cow and clinical mastitis treatment expressed as animal daily dosages (ADD) in low-SCC cows from 97 Dutch dairy herds

Item	ADD quarters dried off with antibiotics (n = 3,314)	ADD quarters dried off without antibiotics (n = 3,314)
Dry cow therapy	3,314.0	0.0
Intramammary mastitis treatment	239.5	293.0
Parenteral mastitis treatment[1]	138.5	248.5
Total ADD	3,692.0	541.5

[1] Parenteral mastitis treatment was calculated based on clinical mastitis cases occurring in the specific quarters.

In quarters dried off without antibiotics, obviously no ADD were used for DCT. For treatment of first cases of CM during the dry period and the first 100 d after calving in these quarters, 366 intramammary treatments with 12-h treatment intervals and 110 intramammary treatments with 24-h treatment intervals were used, resulting in 293 intramammary ADD. Additionally, for parenteral treatment of CM in quarters dried off without antibiotics, 248.5 ADD were used. This resulted in a total of 541.5 ADD (Table 6). In quarters dried off without antibiotics, total antibiotic use is 85% [100% x (541.5/3,692) x 100%] lower than in quarters dried off with antibiotics.

DISCUSSION

The IRCM during the dry period and the first 100 d of lactation of quarters dried off without antibiotics was significantly higher than in quarters treated with dry cow antibiotics. The high IRCM found during the dry period may have been influenced by herdsmen paying specific attention to the udders of participating cows during the dry period. Because herdsmen were not aware of which quarters received dry cow antibiotics, this potential bias was similar for quarters dried off with or without antibiotics.

In the current study, the IRCM in quarters dried off without antibiotics was 1.7 times higher than in quarters dried off with antibiotics. Previous work found similar results. Hassan et al. (1999) found 1.4 times more CM in quarters dried off without antibiotics and Schukken et al. (1993) reported 2 times more new IMI with major and minor pathogens in quarters dried off without antibiotics in a herd with a low bulk tank SCC. Given that in these studies, cows were not selected based on SCC as they were in our study, the relative risk of no dry cow treatment in our study was fairly large.

The highest IRCM in our study was found during the dry period and the first 21 d of lactation, with *Strep. uberis* as the predominant organism causing CM. This is similar to previous reports on the incidence of new IMI and prevalence of *Strep. uberis* in the dry period (Woolford et al., 1998; Berry and Hillerton, 2002). Up to 50% of enterobacterial CM cases that occur within the first 100 DIM arise in quarters that were already infected during the dry period (Bradley and Green, 2000). This suggests that antimicrobial DCT did not actually work as effectively as depicted. It also shows a relationship between IMI present during the dry period and CM cases occurring after calving seems to exist. Although dry cow antibiotics are no longer active during lactation, a significant effect on IRCM still occurs during the first 100 DIM.

When comparing the effect of severity of CM cases in both groups, quarters dried off with and without antibiotics show equal percentages of mild and severe cases (data not shown). This judgment of severity was based on whether or not parenteral treatment was administered to treat the CM case. Additionally, ADD per CM cases were similar in both groups of quarters. Thus, severity of CM did not seem to be influenced by the use of dry cow antibiotics.

When evaluating the preventive effect of DCT, Halasa et al. (2009) found that quarter-level selection for drying off with antibiotics protected significantly better against new IMI during the dry period up to 21 d postcalving compared with quarters dried off without antibiotics. In a meta-analysis of 5 studies, blanket DCT was compared with selective DCT and showed no significant difference in protection against new IMI in 3 studies when cow-level selection was practiced for drying off with antibiotics. This indicates no preventive effect of DCT in this approach (Rindsig et al., 1978; Browning et al., 1994; Williamson et al., 1995). However, these studies are hard to compare with our study because they were carried out over 20 years ago in herds with different housing systems and with different production levels. In spite of the differences in results between these studies, the overall conclusion is that blanket DCT has a protective effect against new IMI as compared with selective DCT, which is in line with our findings.

In the current study, variation in the treatment groups due to herd or cow factors was minimal because of the split-udder design. The benefit of a split-udder design is that cow- and herd-level factors are the same for both groups of quarters and cannot influence the results. Both groups of quarters have the same genetic background, eat the same ration, are milked by the same milking machine, experience the same infection pressure, and so on. A disadvantage of the split-udder design is that quarters dried off with or without antibiotics may influence each other, possibly leading to an underestimation of effect (Lam et al., 1996). Due to the advantages mentioned, however, a within-cow comparison is often used as an approach in these types of studies (Schukken et al., 1993; Bradley et al., 2010). For differences between herds we used multilevel models adjusted for random herd effects. Herds may differ in their pathogen prevalence and environmental management, thus dry cow treatment effects can be very different between herds (Halasa et al., 2009; Rajala-Schultz et al., 2011). For that reason the number of cows per herd was maximized, forcing us to include a high number of herds in the study. Nevertheless optimal dry cow antibiotic application may vary from herd to herd.

Somatic cell count and QSCC200 at D0 and D14 were significantly higher in quarters dried off without antibiotics. An elevated SCC or being culture-positive for major pathogens at DRY were associated with a higher QSCC200 at D14. Being culture-positive for major pathogens at DRY was neither significantly associated with CM during the period of study nor with QSCC200 at D14. This is possibly due to the low numbers of samples positive for major pathogens at DRY (2.4%). The limited statistical power may also explain why an SCC above 200,000 cells/

mL at quarter level at DRY was neither associated with CM during the dry period, nor with QSCC200 at D14 in the multivariable model.

In daily practice, different criteria can be used to select cows for DCT or no DCT. Decision-making can be done on the herd level (e.g., bulk tank milk SCC), cow level (e.g., SCC, CM history, parity), or quarter level (e.g., SCC, teat end condition). In our study, we chose to select primiparous cows with an SCC <150,000 cells/mL and multiparous cows with an SCC <250,000 cells/mL on the last milk recording before drying off because of the practical implementation in daily practice when using milk recording data. We chose SCC at the quarter level as a dependent variable for obvious reasons, with 200,000 cells/mL as a threshold. This was chosen to minimize diagnostic error, as described by Schukken et al. (2003).

Despite more antibiotic use for treatment of CM, total antibiotic use related to mastitis was substantially reduced, 85% based on calculated ADD at the quarter level, in quarters dried off without antibiotics. Calculating a DCT injector as 1 ADD underestimates the possible effect of antibiotic use, because the real activity of the antimicrobial compound in DCT lasts longer than 1 d. Using another unit for antibiotic use due to DCT would have increased the difference in antibiotic use between quarters dried off with or without antibiotics even further.

Although selective DCT leads to more cases of CM and higher SCC in low-SCC cows, the reduction in antibiotic use is substantial. The effects on mastitis and antibiotic use, which are parameters of different magnitude, have to be weighted when deciding on applying blanket or selective DCT. To judge the importance of reduction of antibiotic use, the effect on antibiotic resistance has to be estimated, which was not part of the current study. Future studies should focus on whether a reduction of the use of dry cow antibiotics has an effect on selective pressure and thus on the risk on development of antimicrobial resistance. In conclusion, selection of animals for therapy with dry cow antibiotics based on their SCC at the last milk recording before drying off gives a substantial reduction in antibiotic use, but leads to an increase in CM, subclinical mastitis, and culture-positive quarters.

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Chapter 3

Effect of different scenarios for selective dry-cow therapy on udder health, antimicrobial usage, and economics

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SUMMARY

The goal of dry-cow therapy (**DCT**) is to reduce the prevalence of intramammary infections (**IMI**) by eliminating existing IMI at drying off and preventing new IMI from occurring during the dry period. Due to public health concerns, however, preventive use of antimicrobials has become questionable. In this study the effects of eight scenarios for selecting animals for DCT were evaluated, taking into account variation in parity and cow-level somatic cell count (**SCC**) at drying off. The aim of this study was to evaluate udder health, antimicrobial usage, and economics at the herd level when using different scenarios for selecting cows for DCT.

To enable calculation and comparison of the effect of different scenarios to select cows for DCT in an 'average' herd, an example herd was created, with a virtual herd size of 100 dairy cows to be calving during a year. Udder health, antimicrobial usage and economics were evaluated during the dry period and the first 100 days in lactation, the period during which the greatest effect of DCT is expected. This leads to an estimated 13,551 cow-days at risk during a year in a 100-cow dairy herd. In addition to a blanket DCT (**BDCT**) scenario, 7 scenarios to select cows for DCT based on SCC were developed. The scenarios covered a range of possible approaches to select low-SCC cows for DCT, all based on cow-level SCC thresholds on the last milk recording before drying off. The incidence rate of clinical mastitis in the example herd varied from 11.6 to 14.5 cases of CM per 10,000 cow-days at risk in the different scenarios, and the prevalence of subclinical mastitis varied from 38.8% in scenario 1 (BDCT) to 48.3% in scenario 8. Total antimicrobial usage for DCT and CM treatment varied over the scenarios from 1.27 (scenario 8) to 3.15 animal daily dosages (BDCT), leading to a maximum reduction in antimicrobial usage of 60% for scenario 8 compared with BDCT. The total costs for each of the scenarios showed little variation, varying from € 4,893 for scenario 5 to € 5,383 for scenario 8.

The effect of selective DCT as compared to BDCT on udder health, antimicrobial usage and economics is influenced by the SCC criteria to select cows for DCT. Scenario 2 resulted in the lowest increases in clinical and subclinical mastitis compared with BDCT. The greatest reduction in antimicrobial usage was achieved under scenario 8. From an economic perspective, lowest costs were achieved with scenario 5. Drying off dairy cows with antimicrobials has an effect on udder health, antimicrobial usage and economics.

INTRODUCTION

Since the 1970s, the 5 Points Mastitis Control Plan has been used successfully to manage and control contagious mastitis (Dodd et al., 1969). One of the points recommended is the use of dry cow therapy (**DCT**) to reduce the level of intramammary infections (**IMI**), both by eliminating IMI present at drying off and new IMI from developing during the dry period (Neave et al., 1969). A study in the 1990s showed that the use of dry-cow antimicrobials reduced clinical mastitis (**CM**) compared with untreated controls (Schukken et al., 1993). In that study, however, a within-cow comparison on the effect of DCT was performed without separating uninfected and infected cows (Schukken et al., 1993). Bradley and Green (2000) showed that approximately 50% of quarters with CM due to environmental pathogens in the first 100 days in milk (**DIM**) were infected with the causative pathogen during the dry period, even though they were treated with dry cow antimicrobials. Thus, DCT has consequences for udder health during both, the dry and lactation. In the United States and Canada, uptake of blanket dry cow therapy (**BDCT**) by dairy herds is estimated at 72 and 88% respectively (USDA, 2008; Dufour et al., 2012). In the Netherlands, approximately 90% of all dairy cows were treated with dry-cow antimicrobials in the period period from 2005 to 2010 (Lam et al., 2013). In the United Kingdom, DCT use is estimated to be even higher, with 99% of dairy cows treated at drying off (Berry and Hillerton, 2002). In 2013, antimicrobial use for DCT counted for 49% of the total antimicrobial use in the Dutch dairy industry (SDa, 2014).

Although the relationship between antimicrobial use and the development of antimicrobial resistance in bacteria is complex and unclear (Oliver et al., 2011), correlation between veterinary antimicrobial use and antimicrobial resistance in animal pathogens is likely (Chantziaras et al., 2014). Global concern about antimicrobial resistance propagates prudent and restricted use of antimicrobials, including DCT, in the dairy industry (Oliver et al., 2011). Therefore, in the Netherlands preventive use of antimicrobials in DCT is no longer allowed and selective dry cow therapy (**SDCT**) was introduced in 2013, as an alternative for BDCT. To correctly select cows for curative use of antimicrobials in DCT, IMI at drying off need to be identified. This identification can be based on different criteria, such as SCC, bacteriological culture and CM history (Torres et al., 2008; Rajala-Schultz et al., 2011). Herd level parameters, such as bulk milk SCC (**BMSCC**) can also be taken into account. Application of a SDCT regime, based on withholding DCT from multiparous cows with SCC < 250,000 cells/mL and primiparous cows with SCC < 150,000 cells/mL at the last milk recording before drying off has been evaluated (Scherpenzeel et al., 2014). This approach significantly increased the incidence rate of CM **(IRCM) as well as** subclinical mastitis **(SCM)** and had potential consequences for animal welfare and economics, but resulted in a substantial decrease in antimicrobial usage.

Farmers' decision-making on DCT is not only based on the description of the udder health situation in terms of disease (e.g., incidence of CM or SCM) but also in monetary terms (e.g., economic losses; Hogeveen et al., 2011). Earlier work showed that SDCT is attractive from an economic point of view (Huijps and Hogeveen, 2007). In that study, however, the probability of treatment for SDCT depended on the sensitivity and specificity of the selection procedure: with a high sensitivity of selection, infected cows are more likely to be treated; with a high specificity, uninfected cows are less likely to be treated. It was assumed that the right animals, those who have not developed IMI, were selected and not treated with antimicrobials at drying off, but he authors did not describe how to select these animals. Given the variety in possible approaches for selecting cows for DCT when implementing SDCT in practice, and the consequences of that for udder health and economics, selection criteria need further attention. Therefore, in this study the effects of 8 scenarios for selecting animals for DCT were evaluated, taking into account variation in parity and cow-level SCC at drying off. The aim of this study was to evaluate udder health, antimicrobial usage and economics at the herd level when using different scenarios for selecting cows for DCT.

MATERIALS AND METHODS

Field data

A field trial was carried out between June 2011 and March 2012 in the Netherlands. A total of 1,657 lactating cows, 657 primiparous cows (40%) and 1,000 multiparous cows (60%), from 97 herds were dried off in the study and were followed from drying off until 100 DIM. Bulk milk SCC of the participating herds varied from 41,000 to 387,000 cells/mL, with an average of 184,000 cells/mL. The effect of SDCT was evaluated using a split-udder design in which 2 lateral quarters of each cow were treated with antimicrobials and the 2 contralateral quarters remained as untreated controls. All cows enrolled had a low SCC at the last milk recording before drying off. Low SCC was defined as < 150,000 cells/mL for cows at the end of their first lactation and < 250,000 cells/mL for older cows, thresholds used in the Dutch national milk recording for indicating an elevated SCC (de Haas et al., 2008). A more detailed description of this field trial can be found in Scherpenzeel et al. (2014).

Age groups

Because different age groups have different characteristics with regard to the dry period and udder health, cows in first and later lactation were judged separately. The youngest group is the group of animals after their first calving. In this study, this group was referred to as heifers (group **H**). At the end of the first lactation these animals are dried off. Mastitis in the first dry period, and 100 DIM after (the second) calving is related to the dry-cow treatment at the end of the first lactation. This group of animals, until they were 100 DIM, was referred to as first dry period (**FDP**) animals. Multiparous cows are animals that had calved at least twice. Cows that were dried off for the second or later time, were referred to as multi dry period (**MDP**) animals during their dry period and the first 100 DIM of the subsequent lactation. As such, terminology related to parity was considered as parity at drying off.

Example herd

To enable calculation and comparison of the effect of different scenarios to select cows for DCT in an 'average' herd, an example herd was created. This herd had a virtual herd size of 100 dairy cows calving during a year, with an average age-distribution of Dutch dairy herds following the Royal Dutch Cattle Syndicate, in which 33% of animals had calved once (heifers), 26% had calved twice (FDP animals), and 41% had calved more frequently (MDP animals) (CRV, 2014). The number of cows calving in an age group was used as the number of cows for dry-cow treatment decisions. Therefore, of the 100 cows, 33 had no dry period, 26 were FDP animals and 41 were MDP animals. The distribution of high-SCC and low-SCC animals was based on cow-level SCC data from the last milk recording before drying off of all animals of the 97 herds included in the field trial (Table 1). The proportion of FDP animals below the trial threshold of 150,000 cells/mL was 80,5%. The proportion of MDP animals below the trial threshold of 250,000 cells/mL was 71,6%. Thus, the example herd had 19,5% of FDP (n=5) and 28,4% of MDP (n=12) animals being above the trial SCC threshold. The cows below the trial threshold were subdivided into cows above and below the scenario threshold as described below, which was based on the distributions found in the study of Scherpenzeel et al. (2014).

Table 1. Cow-level somatic cell count (SCC) distribution at the end of first and later lactations, of all cows of the 97 herds in the field trial

SCC category (*10^3 cells/mL)	First lactation (%)	Later lactation (%)
0-49	40.7	14.0
50-99	27.5	19.9
100-149	12.3	17.5
150-199	5.9	11.9
200-249	3.9	8.3
≥250	9.7	28.4

Scenarios

Besides a BDCT scenario, 7 scenarios to select cows for DCT based on SCC were developed (Table 2). In all SDCT scenarios, cows exceeding the trial threshold at the last milk recording before drying off (FDP ≥ 150,000 cells/mL and MDP ≥ 250,000 cells/mL) were dried off with antimicrobials. The scenarios cover a range of possible approaches to select low-SCC cows for DCT, all based on cow-level SCC scenario thresholds on the last milk recording before drying off.

Table 2. Eight scenarios with SCC thresholds to select cows for treatment with antimicrobials at drying off, based on cow-level SCC at the last milk recording before drying off, for first and later dry periods

Scenario	SCC end of first lactation	SCC end of later lactations
	(x 10^3 cells/mL)	(x 10^3 cells/mL)
1	> 0	> 0
2	> 50	> 50
3	> 100	> 100
4	> 150	> 150
5	> 150	> 50
6	> 150	> 100
7	> 150	> 200
8	> 150	> 250

Three scenarios used the same scenario threshold for all cows, not differentiating between FDP and MDP animals, being 50,000 (scenario 2), 100,000 (scenario 3) and 150,000 cells/mL (scenario 4). Four scenarios differentiated scenario thresholds for FDP and MDP animals (FDP/MDP) and were 150,000/50,000 (scenario 5), 150,000/100,000 (scenario 6), 150,000/200,000 (scenario 7) and 150,000/250,000 cells/mL (scenario 8).

Table 3. Distribution of cows in an example dairy herd of 100 calving cows for the 7 groups in the 8 different scenarios (1-8) with their cow level SCC-thresholds (x 103 cells/mL), for heifers, first dry period and multi dry period animals

	Heifers	First dry period animals				Multi dry period animals			
Scenario	Group H	Scenario threshold	Group FDPLNA[1]	Group FDPLWA[2]	Group FDPHWA[3]	Scenario threshold	Group MDPLNA[4]	Group MDPLWA[5]	Group MDPHWA[6]
1	33	0	-	21	5	0	-	29	12
2	33	50	11	10	5	50	6	23	12
3	33	100	18	3	5	100	14	15	12
4	33	150	21	-	5	150	21	8	12
5	33	150	21	-	5	50	6	23	12
6	33	150	21	-	5	100	14	15	12
7	33	150	21	-	5	200	26	3	12
8	33	150	21	-	5	250	29	-	12

[1] First dry period animals with SCC at drying off < scenario threshold, dried off without antimicrobials (FDPLNA)
[2] First dry period animals with SCC at drying off ≥ scenario threshold and < trial threshold, dried off with antimicrobials (FDPLWA)
[3] First dry period animals with SCC at drying off ≥ trial threshold, dried off with antimicrobials (FDPHWA)
[4] Multi dry period animals with SCC at drying off < scenario threshold, dried off without antimicrobials (MDPLNA)
[5] Multi dry period animals with SCC at drying off ≥ scenario threshold and < trial threshold, dried off with antimicrobials (MDPLWA)
[6] Multi dry period animals with SCC at drying off ≥ trial threshold, dried off with antimicrobials (MDPHWA)

Per scenario, the 100 cows in the example herd were divided into 7 groups according to parity and cow-SCC at drying off as presented in Table 3. Distribution of cows over the different SCC groups was in accordance with the average SCC distribution in the 97 herds in the field trial. Based on these groups, cows were selected to be eligible for DCT when meeting the threshold values in the different scenarios, except the group of heifers (group H, n=33) that, obviously, had not been dried off. Subsequently, data from the selected cows in each scenario were used based on the data as available from the 97 herds and were analyzed with respect to CM, number of quarters with SCC > 200,000 cells/mL (**QSCC>200**) at 14 DIM, antimicrobial usage and economics. Data of these 4 parameters were used for the related groups of animals in each of the scenarios. FDP animals with SCC less than the scenario threshold at drying off were dried off without antimicrobials (group **FDPLNA**). FDP animals with SCC greater than the scenario-threshold but less than 150,000 were dried off with antimicrobials (group **FDPLWA**), MDP animals with SCC less than the scenario-threshold were dried off without antimicrobials (**MDPLNA**), and MDP animals with SCC greater than the scenario-threshold but less than 250,000 were dried off with antimicrobials (**MDPLWA**). In all scenarios in the example herd, FDP animals with SCC ≥ 150,000 at drying off (group **FDPHWA**, n=5), and MDP animals with SCC ≥ 250,000 at drying off (group **MDPHWA**, n=12) were dried off with antimicrobials. For groups H, FDPHWA and MDPHWA no data were collected in the above described field trial, and, therefore, values values were based on literature before analysis, all data were checked for unlikely values, but no data were excluded for that reason.

Clinical mastitis

Clinical mastitis analysis were based on IRCM in the different groups as described above. Clinical mastitis data of cows below the trial threshold were based on CM cases as recorded by the farmers in the specific groups in the field trial (Scherpenzeel et al., 2014). The IRCM at quarter level **(QIRCM)** was calculated as the number of quarter cases per quarter-day at risk. Quarters were at risk during the time the cow was enrolled in the study; that is, from from the day of drying off until 100 DIM, unless a quarter was censored due to CM or other reasons. Repeat cases of CM were not recorded and therefore not included in the analysis. To recalculate the QIRCM gathered from the within-cow comparison to an IRCM at cow-level (**CIRCM)** in groups FDPLNA, FDPLWA, MDPLNA and MDPLWA, the QIRCM was adjusted for the average number of affected quarters per cow (= total number of quarter cases of CM in the field trial, divided by the total number of cows with CM). The average number of quarters per cow with CM was also determined separately for the quarters that were dried off with and without antimicrobials (results not shown). Very little difference was observed between those groups and thus the overall average number of quarters with CM was used. The outcome was multiplied by four quarters per cow:

$$\text{CIRCM} = \left(\text{QIRCM} \Big/ \left(\frac{\text{total number of quarter cases of CM}}{\text{total number of cows with CM}} \right) \right) \times 4 \text{ quarters/cow} \qquad [1]$$

For groups FDPLNA, FDPLWA, MDPLNA and MDPLWA the IRCM was calculated based on the results from the study, and multiplied by the number of cows in that specific group. For group H a CIRCM of 1.4×10^{-3} CM cases per cow-day at risk was assumed, and for groups FDPHWA and MDPHWA a CIRCM of 2.2×10^{-3} CM cases per cow-day at risk, based on Barkema et al. (1998). The CIRCM was multiplied by the number of cows in the specific group. Heifers were included from the day of calving until 100 DIM. The example herd consisted of 33 heifers during the first 100 DIM and 67 multiparous cows during the dry period with an average length of 53 days and the first 100 DIM, leading to 13,551 cow-days at risk in a 100-cow dairy herd. The IRCM for the dry period and 100 DIM for the example herd (**HIRCM**) in CM cases per 10,000 cow-days at risk was calculated for scenarios 1 to 8:

$$\begin{aligned} HIRCM_{1\ldots8} = & \left[(1.4 \times 10^{-3} \times 33) \times 100 \text{ days} \right] \\ & + \Big[\Big(\sum (CIRCM_{FDPLNA} \times n_{FDPLNA})_{1\ldots8} + (CIRCM_{FDPLWA} \times n_{FDPLWA})_{1\ldots8} \\ & + (2.2 \times 10^{-3} \times 5) + (CIRCM_{MDPLNA} \times n_{MDPLNA})_{1\ldots8} \\ & + (CIRCM_{MDPLWA} \times n_{MDPLWA})_{1\ldots8} + (2.2 \times 10^{-3} \times 12) \Big) \times 153 \text{ days} \Big] / 1.3551 \end{aligned} \qquad [2]$$

where $HIRCM_{1\ldots8}$ = IRCM in the example herd for scenarios 1 to 8; $CIRCM_{FDPLNA,\ FDPLWA,\ MDPLNA,\ MDPLWA}$ = CIRCM in groups FDPLNA, FDPLWA, MDPLNA and MDPLWA; and $n_{FDPLNA,\ FDPLWA,\ MDPLNA,\ MDPLWA}$ = number of cows in groups FDPLNA, FDPLWA, MDPLNA and MDPLWA. The number of cows and the CIRCM for groups FDPLNA, FDPLWA, MDPLNA and MDPLWA per scenario are shown in tables 3 and 4.

Subclinical mastitis

Quarters with SCC > 200,000 cells/mL and no signs of CM at 14 DIM were considered as subclinically infected, and therefore QSCC>200 was used to determine the prevalence of subclinical mastitis at 14 DIM. To calculate the number of cows with one or more quarters with QSCC>200 (**CSCC200)** based on the data gathered from the within-cow comparison in the field trail, QSCC>200 was adjusted for the average number of high-SCC quarters per cow (total number of QSCC>200 in the field trail, divided by the total number of cows with one or more QSCC>200). The average number of high-SCC quarters per cow was also determined separately for the quarters that were dried off with and without antimicrobials (results not shown). Very little difference was observed between those groups and thus the overall average number of high-SCC quarters was used. The outcome was multiplied by 4 quarters per cow:

$$CSCC200 = \left(QSCC{>}200 \Big/ \left(\frac{\text{total number of QSCC>200}}{\text{total number of cows with QSCC>200}} \right) \right) \times 4 \text{ quarters/cow} \qquad [3]$$

For groups FDPLNA, FDPLWA, MDPLNA and MDPLWA the prevalence of CSCC200 cases was calculated based on the results from the field trial, and multiplied with the number of cows in that specific group. For group H a CSCC200 at 14 DIM of 40%, and for groups FDPHWA and MDPHWA a CSCC200 at 14 DIM of 53% was assumed, based on Sampimon et al. (2010). The CSCC200 was multiplied by the number of cows in that specific group. The CSCC200 for the example herd (**HSCC200**) was calculated for the different scenarios by summing the results of the different groups.

$$HSCC200_{1...8} = (0.40 \times 33) + (CSCC200_{FDPLNA} \times n_{FDPLNA})_{1...8} + (CSCC200_{FDPLWA} \times n_{FDPLWA})_{1...8} + (0.53 \times 5) + (CSCC200_{MDPLNA} \times n_{MDPLNA})_{1...8} + (CSCC200_{MDPLWA} \times n_{MDPLWA})_{1...8} + (0.53 \times 12) \quad [4]$$

where $HSCC200_{1...8}$ = prevalence of CSCC200 cases in the example herd for scenarios 1 to 8; $CSCC200_{FDPLNA,\ FDPLWA,\ MDPLNA,\ MDPLWA}$ = CSCC200 in groups FDPLNA, FDPLWA, MDPLNA and FDPLWA; $n_{FDPLNA,\ FDPLWA,\ MDPLNA,\ MDPLWA}$ = number of cows in groups FDPLNA, FDPLWA, MDPLNA and FDPLWA.

Antimicrobial usage

Data on all individual antimicrobial treatments regarding udder health were collected during the field trial, comprising active compound, application route, dosage, frequency, and duration of treatment.

Antimicrobial usage for DCT and CM treatments was expressed as the number of animal daily dosages (**ADD**) for each of the scenarios in the example herd. One ADD is defined as a standardized one day treatment, being the average dose for a one day treatment of a registered veterinary drug for its main indication as described in detail previously (Scherpenzeel et al., 2014). In this calculation, DCT of one quarter was calculated as 1 ADD according to the definitions provided by the Dutch Veterinary Medicines Authority (SDa, 2014). Intramammary antimicrobial treatments as well as parenteral antimicrobial treatments related to CM were allocated to the affected quarters and summed per CM case. The average ADD per CM case was calculated and used to estimate antimicrobial usage for CM in the different scenarios in the example herd by multiplying the number of CM cases by this average ADD per CM case. Antimicrobial usage for DCT was calculated based on the number of cows in the different groups in the different scenarios. Subsequently, antimicrobial usage due to DCT and CM in the dry period and first 100 DIM was summed for each of the scenarios in the example herd.

Economic analysis

To calculate the economic consequences for each of the scenarios in the example herd, the total costs related to DCT, CM in the dry period and the first 100 DIM, and SCM were calculated. All calculations were done in euros.

The default economic losses for a CM case were set at € 221, an average taken from Huijps et al. (2008), who calculated € 235 for month 1, € 225 for month 2 and € 204 for month 3 after calving. For each scenario, the costs of CM were calculated as the total number of CM cases in the example herd times € 221.

The economic losses for SCM were calculated as milk production losses due to SCM multiplied by the related costs per kilogam milk loss. Halasa et al. (2009) estimated milk production losses for different levels of increased SCC without differentiating parities. The average milk production loss of all cows with cow-level SCC > 200,000 cells/mL was 0.81 kg/d (Halasa et al., 2009). Average duration of a SCM case, irrespective of the causative pathogen was set at 80 days, based on Lam et al. (1997). The costs of production losses due to SCM in a non-quota system were set at €0.25/kg, adapted from Huijps et al. (2008). The prevalence of SCM at 14 DIM was used to calculate differences in economic losses due to SCM in the different scenarios. Thus, the economic losses for a case of SCM were €16.20 for the cows in all groups in the example herd. For each scenario, the costs of SCM of the cows in all groups were summed.

The costs of DCT consisted of antimicrobials and labor of the farmer. It was estimated that it took on average 15 minutes to dry off a cow correctly, at an hourly rate of €18, leading to €4.50 per cow (Halasa et al., 2009). The costs for dry-cow antimicrobials were set at €10/cow (Halasa et al., 2009). For each scenario, DCT costs were calculated by multiplying the total number of cows dried off with antimicrobials by €14.50. Finally, costs of CM, SCM, and DCT were summed for each of the scenarios.

Sensitivity analysis

As described above, the model used was based on data from the large field trial (Scherpenzeel et al., 2014). Clinical and subclinical mastitis data of cows below the trial threshold were based on CM cases as recorded by the farmers and on QSCC>200 data measured in the specific groups in the field trial. For group H, FDPHWA and MDPHWA, CIRCM and SCC200 were based on literature from Barkema et al. (1998) and Sampimon et al. (2010).

A sensitivity analysis was performed to evaluate the effect of variation in the most important input variable, HIRCM, on the most important output variables, antimicrobials, and estimated costs. Herd-level IRCM was varied, by halving and doubling the effect of SDCT, multiplying QIRCM by 0.5 as the lower limit and by 2.0 as the upper limit for all age groups in the scenarios. The sensitivity analysis was carried out for all scenarios to determine the effect on antimicrobial usage and estimated costs.

RESULTS

Clinical mastitis

In the 1,657 cows in the 97 study herds in the field trial, 319 quarter cases of CM in 243 cows were recorded during the dry period and 100 DIM, with a QIRCM of 0.32×10^{-3} cases per quarter-day at risk with, on average, 1.3 CM quarters per cow. The CIRCM for groups FDPLNA, FDPLWA, MDPLNA and MDPLWA in the example herd are presented in Table 4. Over all scenarios and all SCC-thresholds, CIRCM was higher in quarters of MDP compared with FDP animals, especially when no DCT was applied.

For FDP animals there was no substantial difference in CIRCM using different thresholds. The CIRCM varied from 0.59 to 0.74×10^{-3} cases per cow-day at risk. For MDP animals, however, differences in CIRCM between scenarios were greater (Table 4).

The HIRCM for different scenarios in the example herd are presented in Figure 1 and Table 5. The HIRCM in the example herd varied from 11.6 to 14.5 cases of CM per 10,000 cow-days at risk in the different scenarios.

Scenario 1 (BDCT) had the lowest HIRCM with 11.6 CM cases per 10,000 cow-days at risk. The SCDT scenarios with the lowest HIRCM, were scenario 2 (50/50) and scenario 5 (150/50) with, respectively, 11.8 and 12.1 CM cases per 10,000 cow-days at risk. The highest HIRCM occurred in scenario 8 (150/250) with an HIRCM of 14.5 CM cases per 10,000 cow-days at risk.

Table 4. Incidence rate of clinical mastitis at cow level (values are x 10^{-3} cases per cow-day at risk) per dry off group for different scenarios for selective dry cow therapy (1-8) with their SCC thresholds (x 10^3 cells/mL), for first dry period and multi dry period animals

	First dry period animals			Multi dry period animals		
Scenario	Scenario threshold	Group FDPLNA[1]	Group FDPLWA[2]	Scenario threshold	Group MDPLNA[3]	Group MDPLWA[4]
1	0	-	0.62	0	-	0.83
2	50	0.62	0.59	50	1.26	0.80
3	100	0.65	0.74	100	1.88	0.80
4	150	0.74	-	150	1.60	0.99
5	150	0.74	-	50	1.26	0.80
6	150	0.74	-	100	1.88	0.80
7	150	0.74	-	200	1.63	0.46
8	150	0.74	-	250	1.63	-

[1] First dry period animals with SCC at drying off $<$ scenario threshold, dried off without antimicrobials (FDPLNA)
[2] First dry period animals with SCC at drying off $\geq$ scenario threshold and $<$ trial threshold, dried off with antimicrobials (FDPLWA)
[3] Multi dry period animals with SCC at drying off $<$ scenario threshold, dried off without antimicrobials (MDPLNA)
[4] Multi dry period animals with SCC at drying off $\geq$ scenario threshold and $<$ trial threshold, dried off with antimicrobials (MDPLWA)

Subclinical mastitis

In the field trial 1,003 cases of QSCC>200 at 14 DIM occurred in 652 cows, with a QSCC>200 prevalence of 38.5%, and on average 1.5 quarters with a high SCC per cow. The HSCC200 for the different scenarios in the example herd are presented in Figure 2 and in Table 5. The HSCC200 for the different scenarios in the example herd varied from 38.8% in scenario 1 (BDCT) to 48.3% in scenario 8 (150/250).

The number of CSCC200 at 14 DIM for groups FDPLNA, FDPLWA, MDPLNA and MDPLWA in the example herd are presented in Table 6. The prevalence of SCM was found to be higher in MDP than in FDP animals, both when cows were dried off with, and without antimicrobials.

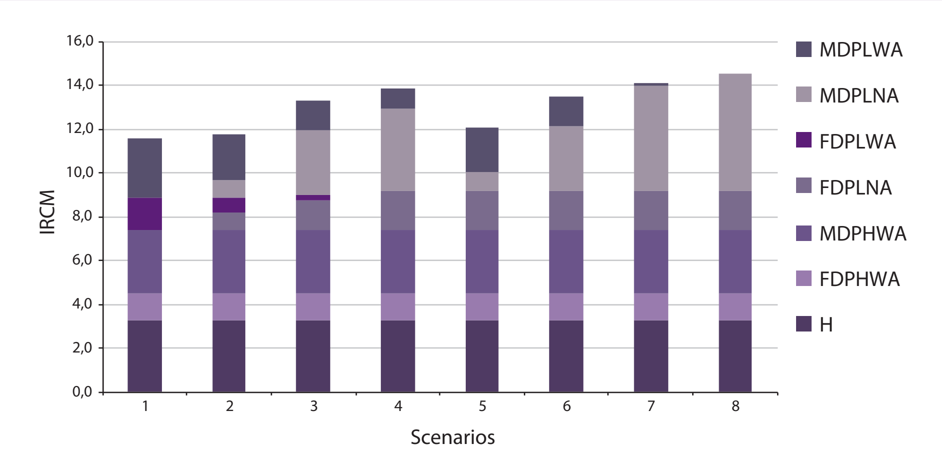

Figure 1. Estimated herd-level incidence rate of clinical mastitis (IRCM) per 10,000 cow-days at risk in an example dairy herd of 100 calving cows with different scenarios for selective dry cow therapy (1-8) based on specific treatment groups[1]

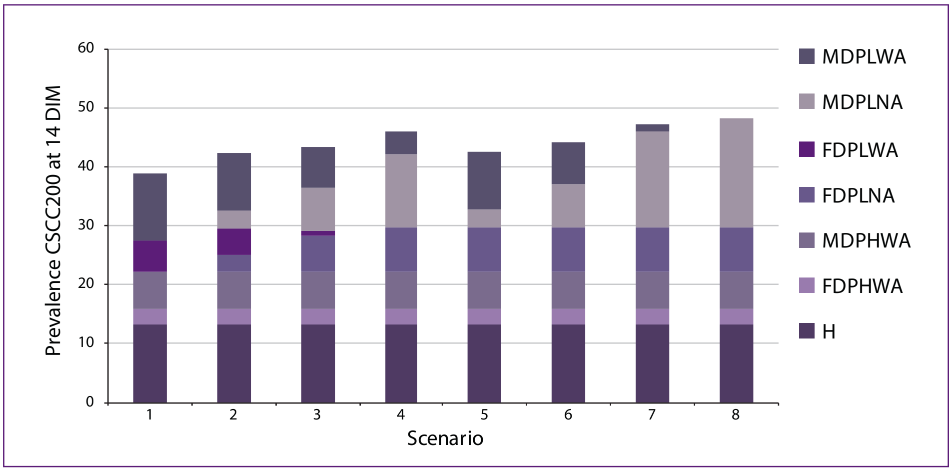

Figure 2. Estimated herd-level prevalence (%) of cows with subclinical mastitis at cow level (CSCC200; one or more quarters with SCC > 200,000 cells/mL) at 14 days in milk in an example dairy herd of 100 calving cows with different scenarios for selective dry cow therapy (1-8) based on specific treatment groups[1]

[1] MDPLWA = multi dry period animals with SCC at drying off ≥ scenario threshold and < trial threshold: dried off with antimicrobials; MDPLNA = multi dry period animals with SCC at drying off < scenario threshold: dried off without antimicrobials; FDPLWA = first dry period animals with SCC at drying off ≥ scenario threshold and < trial threshold: dried off with antimicrobials; FDPLNA = first dry period animals with SCC at drying off < scenario threshold: dried off without antimicrobials; MDPHWA = multi dry period animals with SCC at drying off ≥ trial threshold: dried off with antimicrobials; FDPHWA = first dry period animals with SCC at drying off ≥ trial threshold: dried off with antimicrobials; H = first lactation heifers.

Table 5. Evaluation of different scenarios for selective dry cow therapy (1-8) with their SCC thresholds (x 103 cells/mL) for an example dairy herd of 100 calving cows, with respect to the incidence rate of clinical mastitis on herd level (HIRCM), prevalence of subclinical mastitis on herd level (HSCC200), antimicrobial usage (AB) and estimated costs ( )

Scenario	Threshold FDP/ MDP[1]	HIRCM[2]	HSCC200	AB[3]	€
1	0/0	11.6	38.8	3.15	5,070
2	50/50	11.8	42.3	2.48	4,946
3	100/100	13.3	43.5	1.94	5,190
4	150/150	13.9	45.9	1.56	5,261
5	150/50	12.1	42.5	2.09	4,893
6	150/100	13.5	44.1	1.83	5,223
7	150/200	14.1	47.2	1.37	5,276
8	150/250	14.5	48.3	1.27	5,383

[1] Scenario thresholds for first dry period (FDP) animals and multi dry period (MDP) animals
[2] expressed as clinical mastitis cases per 10,000 cow-days at risk
[3] expressed as animal daily dosages

Antimicrobial usage

Results on antimicrobial usage related to udder health were divided in DCT and CM treatments, and are presented for the different scenarios in Figure 3 and Table 5. The average antimicrobial usage per CM case was calculated to be 3.0 ADD including both, intramammary and parenteral treatment. Treatment of CM during the dry period and the first 100 DIM, resulted in a maximum difference of 0.12 ADD between scenarios with the highest and the lowest IRCM, being scenario 1 (0.47 ADD) and scenario 8 (0.59 ADD) in the example herd, respectively (Figure 3). Given this small difference, potential effects due to different antimicrobial usage for CM in different groups were not analyzed further. For DCT, the differences in antimicrobial usage per group were much larger, with a maximum difference of 2.00 ADD between BDCT (scenario 1; 2.68 ADD) and scenario 8 (0.68 ADD) (Figure 3).

Total antimicrobial usage for DCT and CM treatment varied over the scenarios from 1.27 ADD (scenario 8) to 3.15 ADD (scenario 1) (Figure 3, Table 5), leading to a maximum reduction in antimicrobial usage of 60% for scenario 8 as compared with BDCT. In none of the SDCT scenarios did additional antimicrobial treatment of CM exceed the total amount of antimicrobials saved for DCT.

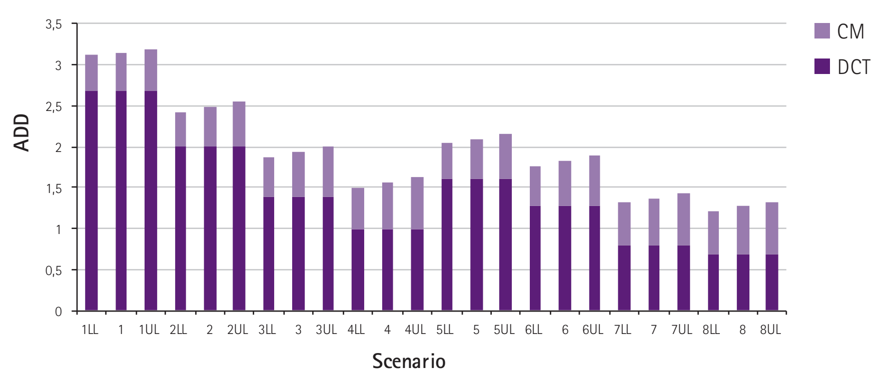

Figure 3. Estimated herd-level antimicrobial usage for dry cow therapy (DCT) and clinical mastitis (CM) expressed in animal daily dosages (ADD) in an example dairy herd of 100 calving cows with different scenarios for selective dry cow therapy (1-8). For each scenario, lower limits (LL) and upper limits (UL) are presented, indicating the herd-level antimicrobial usage if herd-level incidence rate of CM were halved or doubled.

Table 6. Number of cases of subclinical mastitis at cow level (CSCC200; one or more quarters with SCC > 200,000 cells/mL) at 14 DIM, per dry off group, for different scenarios for selective dry cow therapy (1-8) with their SCC thresholds (x 10^3 cells/mL), for first dry period and multi dry period animals

	First dry period animals			Multi dry period animals		
Scenario	Scenario threshold	Group FDPLNA[1]	Group FDPLWA[2]	Scenario threshold	Group MDPLNA[3]	Group MDPLWA[4]
1	0	-	6.7	0	-	18.0
2	50	3.6	5.9	50	4.5	15.6
3	100	7.7	1.0	100	11.6	11.1
4	150	9.6	-	150	19.4	6.1
5	150	9.6	-	50	4.5	15.6
6	150	9.6	-	100	11.6	11.1
7	150	9.6	-	200	25.6	2.1
8	150	9.6	-	250	29.3	-

[1] First dry period animals with SCC at drying off < scenario threshold, dried off without antimicrobials (FDPLNA)
[2] First dry period animals with SCC at drying off ≥ scenario threshold and < trial threshold, dried off with antimicrobials (FDPLWA)
[3] Multi dry period animals with SCC at drying off < scenario threshold, dried off without antimicrobials (MDPLNA)
[4] Multi dry period animals with SCC at drying off ≥ scenario threshold and < trial threshold, dried off with antimicrobials (MDPLWA)

Economic analysis

The costs of DCT varied from € 972 for BDCT (scenario 1) to € 247 for scenario 8. The costs of CM varied from € 3,470 for BDCT (scenario 1) to € 4,354 for scenario 8. The costs of SCM varied from € 629 for BDCT (scenario 1) to € 782 for scenario 8 (Figure 4).

The total costs for each of the scenarios was found to have limited variability, varying from € 4,893 for scenario 5 to € 5,383 for scenario 8 (Table 5).

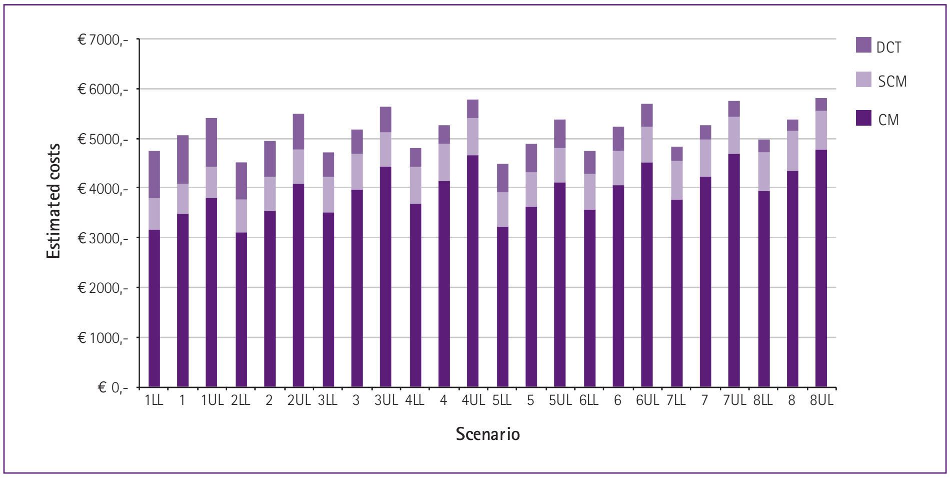

Figure 4. Estimated costs (€) due to clinical mastitis (CM), subclinical mastitis (SCM) and dry-cow therapy (DCT) in an example dairy herd of 100 calving cows with different scenarios for selective dry cow therapy (1-8). For each scenario, lower limits (LL) and upper limits (UL) are presented, indicating the herd-level estimated costs if the herd-level incidence rate of CM were halved or doubled.

Sensitivity analysis

The changes in herd-level antimicrobial usage and total costs related to DCT, CM, and SCM, due to potential variability in HIRCM, evaluated in the sensitivity analysis, are presented in Figures 3 and 4. The results of the model were influenced by a doubled or halved QIRCM, with estimated costs being more sensitive than antimicrobial usage to this change. The average increase over the scenarios for antimicrobial usage, comparing the lower limit with the upper limit was +7.0%, varying from +2.8% to +9.4%. The average increase of the estimated costs in the different scenarios, comparing the lower limit with the upper limit is +18,7%, varying from +13.5% to +22.1%.

DISCUSSION

In this study, we evaluated the impact of different scenarios for selecting animals for DCT on udder health, antimicrobial usage, and economics. To control mastitis, BDCT has been used successfully in many parts of the world for quite some time and has been prescribed by the National Mastitis Council as part of their Mastitis Control Program (NMC, 2006). Due to a changing view on antimicrobial usage in the animal industry preventive use of antimicrobials, including BDCT, is no longer allowed in several European countries, including the Netherlands. The consequences of SDCT depend on which cows are selected for DCT. Therefore, the effect of different scenarios for selecting cows for DCT was evaluated in this paper.

Some studies have used. quarter-, cow- and herd-level criteria as selection method to select cows for dry cow therapy. Decision-making can be based on bacteriological culture (Robinson et al., 1988; Browning et al., 1990), SCC and CM history (Rindsig et al., 1978; Torres et al., 2008; Rajala-Schultz et al., 2011), the California Mastitis Test (Rindsig et al., 1978; Bhutto et al., 2012) and N-acetyl-ß-D-glucosaminidase (Hassan et al., 1999) with different accuracies in identification of infected cows. When used in low-BMSCC herds (< 250,000 cells/mL) to diagnose IMI in cows with a low SCC (< 200,000 cells/mL) before drying off, a Petrifilm-based on-farm culture system for SDCT performed well, with a sensitivity of 85% and specificity of 73% (Cameron et al., 2013). Selecting cows for DCT with Petrifilm did not affect the risk of IMI at calving or the risk of a first case of CM in the first 120 d of lactation compared with BDCT (Cameron et al., 2014). The most feasible selection method, however, is based on monthly SCC, which has a reported sensitivity of 70% and specificity of 63% to identify quarters with IMI at drying off (Torres et al., 2008). In that study, SCC cutoff level used was < 200,000 cells/mL and no history of CM. Most of the studies described above compared SDCT with BDCT, where multiple (combinations of) selection criteria were used to administer SDCT. Our study compared 7 different SDCT scenarios based on monthly SCC with each other in addition to a BDCT scenario.

Dry-cow therapy affects udder health, which was quantified by the IRCM and the prevalence of SCM. Cows dried off without antimicrobials will have up to 1.7 times more CM and 1.6 times more SCM at 14 DIM than cows dried off with antimicrobials (Scherpenzeel et al., 2014). At the herd level, however, this effect is much smaller. The IRCM in the example herd varied from 11.6 to 14.5 cases of CM per 10,000 cow-days at risk for the different scenarios evaluated, in line with earlier reports on IRCM in Dutch dairy herds (Barkema et al., 1998; Sampimon et al., 2010; Lam et al., 2013). The prevalence of SCM at 14 DIM varied from 38.8 to 48.3% of cows with one or more quarters with SCC > 200,000 cells/mL which is somewhat higher than the findings of van den Borne et al. (2010). In the latter study, all cows were dried off with antimicrobials, leading to a subclinical mastitis prevalence of 12.8% for primiparous and 39.6% for multiparous cows (van den Borne et al., 2010).

Although the effect of DCT is of major importance (Scherpenzeel et al., 2014), it apparently is only one of the management factors influencing udder health. The prevalence of SCM at 14 DIM was lower in FDP than in MDP animals, which is in accordance with studies comparing SCM in heifers with multiparous cows (Fox, 2009; Santman-Berends et al., 2012). If more cows were left untreated with antimicrobials at drying off, higher IRCM and higher prevalence of SCM were seen. Thus, SCC-thresholds to select cows for DCT do influence udder health for both, FDP and MDP animals, although the effect was greater for MDP animals. Previous work in a BDCT situation also indicated that IRCM and SCM increased as parity increased (Barkema et al., 1998) demonstrating that the effect of SDCT is likely greater in MDP animals and that it may be wise to use different selection criteria for FDP and MDP animals.

Recalculating the effect of CM and SCM from the quarter level to the cow and herd levels of our data, that were based on a within cow comparison in a field trial, may lead to an underestimation of effect (Scherpenzeel et al., 2014). The data were collected in low-SCC cows and were to be evaluated in an example herd situation, completed with data from literature. By definition this leads to a proxy of the real-life situation, due to effects such as differences in composition of herds, and herd dynamics. Because these biases likely are equal for the different scenarios evaluated, comparison of different scenarios is possible, and the relative ranking seems robust. We chose a deterministic approach for our model and therefore cannot claim statistical differences between scenarios. Using a stochastic simulation model leads to an estimation of variance in results. To be able to use that approach, however, clear information on the actual variation in outcomes occurring, using different thresholds for selecting cows for DCT, would be needed. This information was not available. To collect that type of data, a herd level intervention study would be needed, which would be very difficult, if not impossible to perform, given the many factors apart from DCT that influence HIRCM.

Our goal was to evaluate herd-level effects of using different thresholds to select cows for drying off with antimicrobials. To our knowledge, no data on this topic have been published to date. We chose to use a deterministic model because that was accomplishable. The limitation of such a model is that some parameters and associations need to be assumed (e.g., the relationship between mastitis and production losses and risk of culling). We used the best available estimates for the Dutch situation to prevent potential bias as much as possible. The sensitivity analysis showed that the effect of variability in HIRCM has a limited effect on the herd-level antimicrobial usage, which is logical because most antimicrobials are used in DCT, which is given in the scenarios used. The effect on economic results at the herd level are also limited, showing that the relative ranking of the scenarios is robust using our deterministic approach.

To calculate total antimicrobial usage on herd level for different scenarios, antimicrobial usage for DCT and CM was summed. The average ADD per CM case was used in all calculations, because differences in antimicrobial usage due to CM between scenarios were very small compared with DCT (Figure 3). This may ignore possible differences in effect of parenteral versus intramammary use of antimicrobials on development of antimicrobial resistance. The same is true for differences between the effect on development of antimicrobial resistance of long-acting intramammary antimicrobials as used for DCT or an intramammary tube used for treatment of CM, both calculated as 1 ADD (Jensen et al., 2004). These effects were, however, outside the scope of this study.

Given the relatively low costs of dry-cow antimicrobials, economic consequences of SDCT are mainly influenced by CM and SCM, which are known to be expensive diseases (Hogeveen et al., 2011). Despite of the simplification of the economic calculations presented in this paper, it is clear from an economic point of view that BDCT does not seem to be more attractive than

SDCT. This is in line with the findings of Huijps and Hogeveen (2007). Our findings indicate that selecting cows on low SCC for SDCT does not predict if cows will or will not get infected with mastitis pathogens during the dry period.

When searching for optimal selection criteria for DCT, udder health and antimicrobial usage can be compared in an economic evaluation. This oversimplifies the potential effect of DCT on development of antimicrobial resistance, the public opinion on preventive antimicrobial usage, political issues and animal welfare. Although the perspective of animal welfare differs between citizens and farmers (Vanhonacker, 2008), mastitis, specifically CM, does affect animal welfare (Fogsgaard et al., 2015). Finally, for a system such as a selection protocol for DCT to be succesfully implemented in practice, its applicability is important.

CONCLUSIONS

The effect of SDCT compared with BDCT on udder health, antimicrobial usage, and economics was influenced by the SCC criteria used to select cows for DCT. The SCC criteria chosen affect not only quantifiable parameters, such as udder health, antimicrobial usage, and economics, but also non-quantifiable parameters, such as welfare and practical achievability. Depending on the weight given to these parameters, optimal selection criteria should be chosen when implementing SDCT.

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Chapter 4

Economic optimization of selective dry cow treatment

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SUMMARY

The objective of this study was to develop a mathematical model to identify a scenario with the lowest costs for mastitis associated with the dry period while restricting the percentage of cows to be dried off with dry cow antimicrobials. Costs of clinical and subclinical mastitis as well as antimicrobial use were quantified. Based on data from a large field trial, a linear programming model was built with the goal to minimize the costs associated with antimicrobial use at drying off. To enable calculations on minimizing costs of dry cow treatment on herd-level by drying-off decisions in an 'average' herd, we created an example herd. Cows were projected on 3 different types of herds, based on bulk tank somatic cell count, and were categorized in groups based on parity and somatic cell count from the last test recording before drying-off. Economically optimal use of antimicrobials was determined while restricting the maximum percentage of cows dried of with antimicrobials from 100% to 0%. This restriction reveals the relationship between the maximum percentage of cows dried off with antibiotics and the economic consequences. A sensitivity analysis was performed to evaluate the effect of variation in the most important input variables, with the effect of dry cow antimicrobials resulting in a lower or higher percentage of clinical and subclinical mastitis depending on being dried off with or without dry cow antimicrobials, respectively, and the milk price.

From an economic perspective, blanket dry cow treatment seems not to be the optimal approach of dry cow therapy, although differences between approaches were small. With lower bulk tank somatic cell counts, more dry cow antimicrobials can be omitted without economic consequences. The economic impact of reducing the percentage of clinical mastitis was found to be much larger than reducing the bulk tank somatic cell count. The optimal percentage of cows to be dried off with antimicrobials depends on the udder health situation, expressed as the bulk tank somatic cell count and the incidence of clinical mastitis. For all evaluated types of herds, selective dry cow treatment was economically more beneficial than blanket dry cow treatment. Economic profits of selective dry cow treatment are greater if bulk tank somatic cell count and clinical mastitis incidence are lower. Economics is not an argument against reduction of dry cow antimicrobials by applying selective dry cow treatment.

INTRODUCTION

Control of mastitis is of major importance for the dairy sector. Apart from other consequences, mastitis leads to high monetary costs because of treatment, discarded milk and major production losses (Hogeveen et al., 2011). In the dairy industry, antimicrobials are mainly used for treatment of clinical mastitis (**CM**) and dry cow treatment (**DCT**). For many years, approximately 60% of the antimicrobial use (**AMU**) in dairy cows in the Netherlands was related to mastitis, of which roughly two third related to DCT (Kuipers et al., 2016).

One of the points recommended since the 1970s in the 5 Points Mastitis Control Plan (Neave et al., 1969) was blanket dry cow treatment (**BDCT**) to control the risk of new intramammary infections (**IMI**) during the dry period (Dodd et al., 1969). The main goal of DCT was to reduce the prevalence of IMI, both by eliminating IMI present at drying off and preventing new IMI from occurring during the dry period (Bradley and Green, 2001). In many countries, more than

90% of all dairy cows were treated with antibiotics during the dry period, e.g., 94% in the Netherlands (Lam et al., 2013) and 99% in the United Kingdom (Berry and Hillerton, 2002).

Due to public health concerns and risk for antimicrobial resistance (**AMR**), prudent and restricted use of antimicrobials is promoted and preventive use of antimicrobials for all food animals has been prohibited since 2012 in the Netherlands (Santman-Berends et al., 2016). Selective dry cow treatment (**SDCT**), not using DCT in cows that had a low-SCC at the last milk recording before drying off, significantly increased the incidence rate of CM as well as SCC post-partum in a study in the Netherlands (Scherpenzeel et al., 2014).

A meta-analysis done by Halasa et al. (2009a) showed that BDCT seemed to protect better against new IMI than SDCT, which seemed to protect better than no DCT at all. It was also shown in AMU due to SDCT was substantial and by no means compensated by an increase in AMU due to an increased incidence rate of CM (Scherpenzeel et al., 2016).

The effect of SDCT compared with BDCT on udder health, AMU, and economics is influenced by the criteria used to select cows for DCT (Cameron et al., 2014; Scherpenzeel et al., 2016). The chosen criteria have an effect on quantifiable parameters, such as CM incidence, AMU, and economics, but also non-quantifiable parameters, such as welfare and practical feasability. These effects can be contradictory; SDCT as compared with BDCT leads to more CM cases and a higher SCC, whereas it decreases AMU substantially (Scherpenzeel et al., 2014). Udder health, welfare, production losses, AMU and economic consequences are all parameters that are influenced by decisions on DCT, but that potentially move in different directions. Additionally, although the relationship between AMU and development of AMR in mastitis pathogens is complex and unclear (Oliver et al., 2011), there is a potential effect of AMU on the development of AMR (Chantziaras et al., 2014). In decision making of farmers this can, however, be considered as an externality, because these consequences are experienced by the environment or society while they are not necessarily directly experienced by the farmer. A common way to quantify different parameters, with the exception of animal welfare and public health, is in economic units. As such, economic consequences along with animal welfare, legislation and public health concerns, may be helpful in making decisions on animal health strategies.

A few studies describe the economic consequences of DCT. Most economic analyses have concluded that BDCT is financially beneficial, because of increased milk yield, lower SCC or reduced CM cases, when compared with SDCT or no DCT (McNab and Meek, 1991; Berry et al., 1997; Yalcin and Stott, 2000). Most of these calculations were, however, based on uncertain assumptions and there was much variation in the results. In a study done by Huijps and Hogeveen (2007), SDCT was economically most attractive. In that study, however, differences between BDCT and SDCT were small and with regard to selection of the appropriate animals, the assumptions for DCT were rough. None of the above studies described the level of reduction of AMU while practicing SDCT.

The economic impact of SDCT likely varies for different types of herds and for different levels of DCT use. Studies describing and evaluating economic consequences of SDCT on herd-level can be used by dairy farmers and their advisors to help them to optimize decisions on DCT, thereby minimizing costs. Thus, the economic consequences of decisions on DCT need further attention. Therefore the objective of this study was to develop a mathematical model to minimize economic costs while restricting the percentage of cows to be dried off with DCT, accounting for effects of CM, subclinical mastitis (**SCM**) and AMU.

MATERIALS AND METHODS

A randomized controlled field trial was carried out between June 2011 and March 2012 in the Netherlands in which the effect of DCT on CM, bacteriological status, SCC and antibiotic use was evaluated (Scherpenzeel et al., 2014). Based on these data, data from literature for high-SCC cows dried off with antimicrobials (Barkema et al., 1998) and smoothed data based on regression analysis for high-SCC cows dried off without antimicrobials (data not shown) a linear programming (**LP**) model was built with the goal to minimize the costs associated with AMU at drying off. In this model different approaches of selecting cows for DCT were compared based on the SCC at the last milk recording before drying off (Scherpenzeel et al., 2016). A timeframe of 1-year was used to take seasonal differences into account and to represent the financial planning horizon of dairy farmers. The general purpose of an LP approach is to maximize or minimize a goal variable (e.g., maximize profit or minimize costs) by finding the optimal combination of different parameters with respect to a set of fixed constraints. Microsoft Excel (Microsoft Corp., Redmond, WA) was used to develop and run the LP model, using the Simplex Algoritm for optimization.

Definition of the herd

To enable calculations on minimizing costs of DCT on herd-level by drying-off decisions in an 'average' herd, we created an example herd. Cows that were dried off at the end of their first lactation were referred to as first dry period (**FDP**) cows at drying off, during the dry period and the first 100 DIM of the subsequent lactation. Cows that were dried off for the second or later time were referred to as multiple dry period (**MDP**) cows at drying off, during their dry period and the first 100 DIM of the subsequent lactation.

Nine cow groups (i=1-9) were considered, consisting of 4 classes of FDP cows (0-50,000 cells/mL; 51,000-100,000 cells/mL; 101,000-150,000 cells/mL; and > 150,000 cells/mL) and 5 classes of MDP cows (0-50,000 cells/mL; 51,000-100,000 cells/mL; 101,000-150,000 cells/mL; 151,000-250,000 cells/mL; and > 250,000 cells/mL). For each of these cow groups there were 2 options regarding DCT (j = 1,2), either dried off with (1) or without (2) dry cow antimicrobials. Thus, in total 18 units of activity were included in the model.

Three different types of herds with respect to bulk tank SCC (**BTSCC**) were defined. One with a low BTSCC < 150,000 cells/mL (**BT_L**), one with an average BTSCC ≥ 150,000 cells/mL and < 250,000 cells/mL (**BT_A**), and one with a high BTSCC ≥ 250,000 cells/mL but < 400,000 cells/mL (**BT_H**), based on Barkema et al. (1998). The distribution of cows over the 9 cow groups (1-9) for a low-BTSCC, average-BTSCC and high-BTSCC herd (Table 1) was based on the approach of Huijps et al. (2008) and on Dutch averages.

Table 1. Distribution of cows at drying-off in groups (1-9) in a 75-cow example herd, based on their SCC (x10^3 cells/mL) and parity at the last milk recording before drying off for a low-BTSCC herd (BT_L), an average BTSCC herd (BT_A), and a high-BTSCC herd (BT_H), and cow-level incidence of clinical mastitis (I_{CM}), and subclinical mastitis (I_{SCM}) when dried off with (j=1) or without (j=2) dry cow antimicrobials

Group	Somatic Cell Count	Parity[1]	Number of cows included in the model			I_{CM} (%)		I_{SCM} (%)	
			BT_L	BT_A	BT_H	j=1	j=2	j=1	j=2
1	0-50	FDP	14	10	4	9.9	11.8	4.8	7.2
2	51-100	FDP	6	7	4	9.1	10.8	10.6	19.0
3	101-150	FDP	2	3	3	13.5	18.2	8.2	17.7
4	> 150	FDP	3	5	14	14.4	20.0	11.3	25.0
5	0-50	MDP	28	7	8	12.8	20.1	7.3	17.3
6	51-100	MDP	13	10	9	15.2	26.8	13.6	18.8
7	101-150	MDP	4	9	5	9.0	19.1	15.7	24.8
8	151-250	MDP	4	10	5	16.5	24.1	18.4	31.7
9	> 250	MDP	1	14	23	16.6	24.4	22.6	37.4

[1] FDP = First dry period cows; MDP = Multiple dry period cows

Model description

Total economic costs of mastitis are the sum of preventive costs and failure costs. The preventive costs were the costs for use of DCT, where other preventive costs were not evaluated in this paper because they were assumed to be the same for the different approaches. Failure costs are the economic values of the losses and the economic values of the expenditures related to the occurrence of mastitis. Losses are costs associated with a cow being affected by CM or SCM (e.g., production losses, culling, discarded milk). Expenditures are the payments made by the farmer to treat mastitis.

Calculation of the total economic costs of mastitis (**TC_M**) for the example herd was done by summing the total costs of mastitis per unit of activity (**TC_{Mij}**), multiplied by the number of cows in each unit of activity (**N_{ij}**):

$$TC_M = \sum_{i=1}^{9}\sum_{j=1}^{2} TC_{Mij} \times N_{ij} \qquad [1]$$

where TC_M = total economic costs of mastitis, i = cow group 1 to 9, j = treatment with (1) or without (2) dry cow antimicrobials, TC_{Mij} = total costs of mastitis per unit of activity, and N_{ij} = the number of cows in each unit of activity.

The total economic costs of mastitis per unit of activity (**TC_{Mij}**) are the sum of the total costs of CM, SCM and DCT per unit of activity:

$$TCCM_{ij} = TC_{CMij} + TC_{SCMij} + TC_{DCTij} \quad [2]$$

The total costs of CM in each unit of activity (**TC_{CMij}**) is the incidence of CM in this unit of activity (**I_{CMij}**) multiplied with the number of cows in this unit of activity (**N_{ij}**) and the costs of a case of CM (**C_{CM}**);

$$TC_{CMij} = I_{CMij} \times N_{ij} \times C_{CM} \quad [3]$$

The total costs of SCM in each unit of activity (**TC_{SCMij}**) is derived equally by multiplying the incidence of SCM in this unit of activity (**I_{SCMij}**) with the number of cows in this unit of activity (**N_{ij}**) and the costs of a case of SCM (**C_{SCM}**);

$$TC_{SCMij} = I_{SCMij} \times N_{ij} \times C_{SCM} \quad [4]$$

The total costs of DCT in each unit of activity (**TC_{DCTij}**) is the number of cows to be dried off in this unit of activity (**N_{DCTij}**) times the costs per cow for dry cow treatment (**C_{DCT}**);

$$TC_{DCTij} = N_{DCTij} \times C_{DCTj} \quad [5]$$

For cows dried off without antimicrobials (j=2) there are no costs of DCT ($TC_{DCTij} = 0$).
Data on all individual antimicrobial treatments regarding CM and DCT were collected during the field trial, consisting of active compound, application route, dosage, frequency, and duration of treatment. Antimicrobial usage for DCT and CM treatments was expressed as the calculated number of animal defined daily dosage (**ADDD**; i.e., the average number of days a cow receives antimicrobial treatment). One ADDD is defined as a standardized 1-d treatment, being the average dose for a 1-d treatment of a registered veterinary drug for its main indication. A cow dried off with antimicrobials was calculated as 4.0 ADDD (Santman-Berends et al., 2016), and a case of CM as 3.0 ADDD, including both intramammary and parenteral treatment (Scherpenzeel et al., 2016). Antimicrobial treatment of SCM during lactation was not taken into account.

Parameterization

The example herd had a herd size of 100 dairy cows with an average age distribution of Dutch dairy herds (CRV, 2015), in which 33% of animals had calved once, and 67% had calved twice or more. Given a calving interval of 412 days (CRV, 2015), an average culling rate of lactating cows in Dutch dairy herds of 30% (Mohd Nor et al., 2014), and 90% of cows to be culled that were not dried off, the total number of cows for drying-off during a year in the example herd was 75, of which 25 were FDP cows and 50 were MDP cows. The distribution of high-SCC and low-SCC animals was based on cow-level SCC data from the last milk recording before drying off of all animals of 97 herds included in a previously described field trial (Scherpenzeel et al., 2016). Cows that were dried off were grouped based on parity (FDP/MDP) and SCC at the last milk recording before drying off.

The failure costs for a case of CM were calculated based on the average costs for CM cases during the first 3 months of lactation and were adapted from Huijps et al. (2008). In that study, all cost categories, such as milk production losses, discarded milk, veterinary support, drugs, labor, and culling were included, but were based on a quotum situation. In our study, the average costs for a CM case were recalculated based on the calculation method of Huijps et al. (2008) and using an average milk price levels in the post-quotum era of € 0,35/kg and an average price level of concentrate feed-costs of € 0.13/kg milk, making the net costs of milk production losses € 0.22/kg milk. Based on that, the costs of a case of CM in the first 100 DIM were set at € 242.

The failure costs for a case of SCM were calculated as milk production losses due to SCM multiplied by the related costs per kilogram of milk loss. Halasa et al. (2009b) estimated milk production losses for different levels of increased SCC without differentiating parities and calculated that the average milk production loss of all cows with cow-level SCC >200,000 cells/mL was 0.87 kg/d. We set the average duration of an SCM case, irrespective of the causative pathogen at 85 d, based on Lam et al. (1997). The costs of production losses due to SCM were calculated as above, and were € 0.22/kg. Thus, the economic losses for a case of SCM were € 16.27 per case.

The preventive costs of DCT consisted of AMU and labor of the farmer. It was estimated that it took on average 15 minutes to correctly dry-off a cow, at an hourly rate of € 18, leading to € 4.50 per cow (Halasa et al., 2009b). The costs for dry-cow antimicrobials were assumed to be € 11.00/cow, which makes C_{DCT1} € 15.50. The milk price was calculated by taking the average prices over the last 5 years from the Agrimatie database (Agrimatie, 2016).

Cow-level incidences of CM and SCM (Table 1) were based on quarter-level incidences from the field study for low-SCC cows, assuming that on average 1.3 CM quarters were affected per cow. For high-SCC cows, assumptions were based on literature from Barkema et al. (1998), as is described in more detail in Scherpenzeel et al. (2016).

Optimization

The LP model in the optimization phase will select cows within the groups (i=1-9) for being dried-off with (j=1) or without (j=2) dry cow antibiotics. The optimal situation for the example herd is the situation in which TC_M is lowest. To calculate this, the LP model will give the minimal TC_M related to mastitis in the dry period and first 100 DIM, based on the number of cows affected by CM and SCM and the amount of antimicrobials used for each unit of activity for different herd situations based on BTSCC.

The restrictions for the groups in the model were:

$$\sum_{i=1}^{9} N_{i1} \leq P_{DCT} \times N \qquad [6]$$

where P_{DCT} = the maximum percentage of cows to be dried off with antimicrobials, and

$$N_{i1} + N_{i2} = N_{ij} \qquad [7]$$

where N_{ij} = the number of cows per unit of activity.

Simulation

In the optimization part of the study, the LP model was used while restricting the maximum percentage of cows dried off with antimicrobials in SDCT from 100% to 0%. This restriction reveals the relationship between the percentage of cows dried off with antimicrobials and the economic consequences. The number of cows to be dried off with antimicrobials was reduced by steps of 5%, leading to 21 restriction levels, and for every level the LP model was run. Based on the restriction level, the LP model selected the cows in each group for being treated (j=1) or not being treated (j=2) with dry cow antimicrobials at drying off, to find the situation with the lowest TC_M in the dry period and the first 100 DIM. Additionally, the average incidence of CM and SCM and the ADDD were calculated by the model for every restriction level.

In the baseline level, all cows were allowed to be dried off with dry cow antimicrobials (100%). Drying off none of the cows with antimicrobials (0%) was the other extreme. All other levels applied SDCT, and cows were selected by the model for being treated with (j=1) or without (j=2) dry cow antimicrobials, depending on their parity (FDP or MDP) and their SCC at the last milk recording before drying off.

Variation in herd level CM incidence

Clinical mastitis is an expensive disease (Hogeveen et al., 2011) and strongly influences TC_M. Because CM incidence can vary in herds with the same BTSCC (Barkema et al., 1998) we varied the initial incidence of CM per unit of activity as input parameter within the three types of herds. Thus, we modeled BT_L, BT_A and BT_H herds with low (BT_LC_L; BT_AC_L; BT_HC_L), with average (BT_LC_A; BT_AC_A; BT_HC_A), and with high (BT_LC_H; BT_AC_H; BT_HC_H) incidence of CM as the initial situation. These incidences per type of herd were calculated by summing the multiplifications of doubled (for high incidence) or halved (for low incidence) I_{CMij} per unit of activity multiplied with N_{ij}, and divided by 75 animals (formulas [8] and [9]).

$$C_H = \sum_{i=1}^{9} I_{CMij} \times 2.0 \times N_{ij} \,/\, 75 \text{ cows}, \tag{8}$$

$$C_L = \sum_{i=1}^{9} I_{CMij} \times 0.5 \times N_{ij} \,/\, 75 \text{ cows}, \tag{9}$$

where I_{CMij} = the incidence of clinical mastitis in this unit of activity.

Variation in the initial situation of the incidence of CM per unit of activity led to variance in the dependent output variable, being the mean herd-level incidence of CM.

Sensitivity analysis

A sensitivity analysis was performed to evaluate the effect of variation in the most important input variables, being the effect of dry cow antimicrobials (Δ_{DCT}) resulting in a lower or higher incidence of CM and SCM and the effect of milk price. Both these parameters directly affect the most important output variable in this study, TC_M. To evaluate the effect of the use of dry cow antimicrobials, Δ_{DCT} was varied per group by multiplying the difference between I_{CMi1} and I_{CMi2} per group with 0.5 as the lower limit and with 2.0 as the upper limit. The incidences of CM and SCM in the treated groups were the constant baseline and the incidences of CM and SCM in the untreated groups were varied, to analyze the sensitivity of the model. We expected that assumptions about milk price would have a substantial effect on TC_M. Therefore we multiplied the average milk price of € 35 / 100 kg by 0.775 as the lower limit and by 1.225 as the upper limit. This resulted in € 27 / 100 kg of milk for a low milk price and € 43 / 100 kg of milk for a high milk price. The sensitivity analysis was carried out for all 21 restriction levels in the BT_L-, BT_A-, and BT_H-herd to determine the effect on the minimal TC_M.

RESULTS

Simulation

All 21 DCT-restriction levels were evaluated to study the effect of reducing the maximum percentage of cows to be dried off with antimicrobials on mastitis, AMU and TC_M during the dry period and the first 100 DIM. Results for CM, SCM, ADDD, and economics for the 21 restriction levels for the 3 types of herds (BT_L; BT_A; BT_H) are presented in Table 2. Costs per cow to be dried off per year varied from € 45 on a BT_L herd were 100% of the cows were allowed to be dried off with antimicrobials to € 56 on a BT_H herd where no dry cow antimicrobials were allowed (Table 2). Clinical and subclinicial mastitis incidence in the different types of herds varied from 9.9% to 16.1% and from 8.2 to 19.6% respectively. Antimicrobial use varied from 0.6 ADDD when no dry cow antimicrobials were allowed (0%) in a BT_L, BT_A, and a BT_H herd to 3.9 ADDD when 100% of cows were allowed to be dried off with antimicrobials in a BT_H herd.

Table 2. Mean incidence of clinical mastitis (I_{CM}), mean incidence of subclinical mastitis (I_{SCM}), animal defined daily dosage per year (ADDD), and total economic costs of mastitis per cow per year (€). Calculations were done using the maximum percentage of dry cow antimicrobials (%AMU) as restriction level, which was reduced in steps of 5% from 100% to 0%, for a low BTSCC herd (BT_L), an average BTSCC herd (BT_A), and a high-BTSCC herd (BT_H)

%	BT_L				BT_A				BT_H			
AMU	I_{CM}	I_{SCM}	ADDD	€	I_{CM}	I_{SCM}	ADDD	€	I_{CM}	I_{SCM}	ADDD	€
100	9,9	8,2	3,2	44,52	10,4	11,4	3,3	47,42	11,0	11,9	3,9	51,17
95	9,9	8,2	3,2	44,52	10,4	11,4	3,3	47,42	11,0	11,9	3,9	51,17
90	9,9	8,2	3,2	44,52	10,4	11,4	3,3	47,42	11,0	11,9	3,9	51,17
85	9,9	8,2	3,2	44,52	10,4	11,4	3,3	47,42	11,0	11,9	3,9	51,17
80	9,9	8,2	3,2	44,52	10,4	11,4	3,3	47,42	11,2	12,4	3,6	51,18
75	9,9	8,2	3,2	44,52	10,4	11,4	3,3	47,42	11,4	13,0	3,4	51,19
70	9,9	8,2	3,2	44,52	10,5	11,7	3,2	47,43	11,6	13,4	3,3	51,20
65	10,1	8,7	3,0	44,57	10,8	12,2	3,0	47,49	11,8	13,9	3,1	51,26
60	10,4	9,1	2,8	44,77	11,1	12,6	2,8	47,68	12,1	14,3	2,9	51,45
55	10,7	9,5	2,6	44,97	11,3	13,1	2,6	47,91	12,4	14,7	2,7	51,66
50	10,9	9,8	2,5	45,11	11,6	13,5	2,5	48,11	12,6	15,1	2,5	51,86
45	11,2	10,2	2,3	45,31	11,9	14,0	2,3	48,37	12,9	15,7	2,3	52,16
40	11,5	10,6	2,1	45,51	12,2	14,6	2,1	48,67	13,3	16,3	2,1	52,47
35	11,8	11,1	1,9	45,70	12,5	15,2	1,9	48,98	13,6	16,9	1,9	52,78
30	12,0	11,4	1,7	45,85	12,7	15,6	1,7	49,21	13,8	17,3	1,8	53,01
25	12,3	11,9	1,5	46,10	13,0	16,2	1,5	49,52	14,1	17,9	1,6	53,32
20	12,6	12,3	1,3	46,52	13,5	16,6	1,3	50,08	14,4	18,5	1,4	53,63
15	13,1	12,6	1,1	47,16	13,9	16,9	1,1	50,64	14,8	18,9	1,2	54,13
10	13,4	12,8	1,0	47,69	14,2	17,1	1,0	51,13	15,1	19,2	1,0	54,59
5	13,9	13,0	0,8	48,41	14,7	17,3	0,8	51,85	15,6	19,4	0,8	55,31
0	14,3	13,2	0,6	49,13	15,1	17,6	0,6	52,57	16,1	19,6	0,6	56,02

Variation in herd level CM incidence

Results of variation in the initial herd level CM incidence on the effect of a SDCT approach on TC_M and the comparison with a BDCT approach for different types of herds are presented in Table 3 and Figure 1. If a BDCT approach was applied, 100% of the cows had to be dried off with dry cow antimicrobials and therefore the units of activity were forced in DCT-group j=1. If a SDCT approach was applied, a maximum of 100% of dry cow antimicrobials was allowed, which does not mean that 100% of the cows were placed in the dry cow treatment group (j=1).

Table 3 shows that the effect of CM is greater than the effect of BTSCC, with BDCT being always more expensive than SDCT and no dry cow antimicrobials (0%) being cheaper than BDCT if the incidence of CM is low.

When the maximum percentage of cows to be dried off with antimicrobials decreased from 100% to 0%, TC_M of an SDCT approach remained lower than the TC_M for a BDCT approach, until a certain point where the TC_M of SDCT becomes higher than the TC_M of BDCT (figure 1). For the BT_HC_H-herd this point was 80%, for the BT_AC_H-herd 65%, and for the BT_LC_H-herd 60%. For the BT_HC_A-herd this point was 40%, for the BT_AC_A-herd 20%, and for the BT_LC_A-herd 10%. When the incidence of CM was low (BT_LC_L; BT_AC_L; BT_HC_L), in all 21 situations a SDCT approach was more beneficial than a BDCT approach.

Table 3. Total economic costs € of mastitis in a blanket dry cow treatment (BDCT) approach and minimized total economic costs of mastitis when 100% and 0% dry cow antimicrobials are allowed for a 100-cow dairy herd with 75 cows to be dried off. Calculations were done for a high-BTSCC herd (BT_H), an average BTSCC herd (BT_A), and a low-BTSCC herd (BT_L), each with a low (C_L), an average (C_A), and a high (C_H) incidence of clinical mastitis and the difference between 100% and BDCT and between 0% and BDCT

Herd type	BDCT	100% dry cow antimicrobials allowed	Difference 100% – BDCT	0% dry cow antimicrobials allowed	Difference 0% – BDCT
BT_HC_H	6,512	6,464	-48	8,085	1,573
BT_AC_H	6,152	6,049	-103	7,601	1,449
BT_LC_H	5,828	5,705	-123	7,155	1,327
BT_HC_A	3,928	3,838	-90	4,202	274
BT_AC_A	3,741	3,557	-184	3,943	202
BT_LC_A	3,554	3,339	-215	3,685	131
BT_HC_L	2,636	2,260	-376	2,260	-376
BT_AC_L	2,538	2,114	-424	2,114	-424
BT_LC_L	2,417	1,949	- 468	1,949	-468

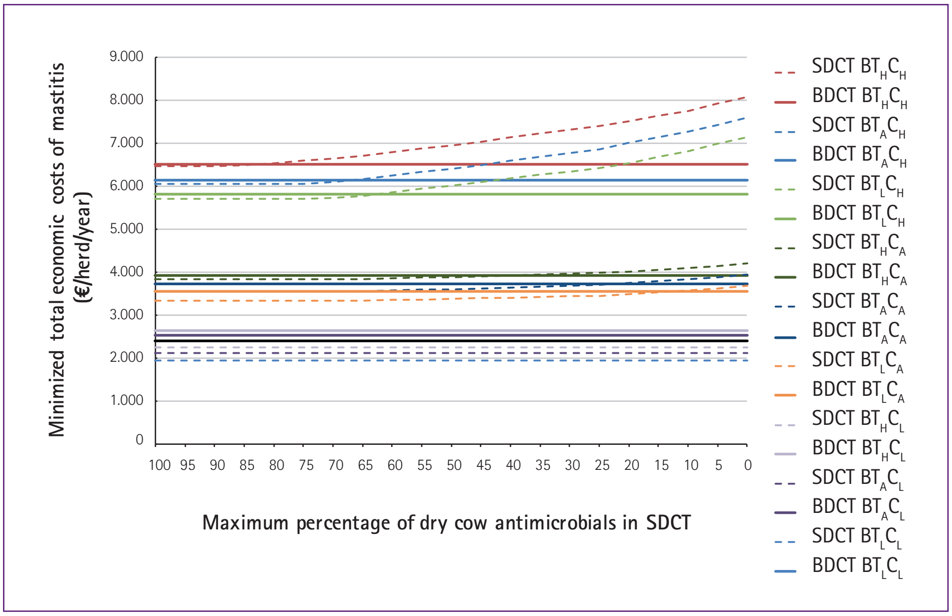

Figure 1. Minimized total economic costs of mastitis for a 100-cow dairy herd with 75 cows to be dried off applying selective dry cow treatment (dashed lines) and reducing the maximum percentage of dry cow antimicrobials from 100% to 0% for a low-BTSCC herd (BT_L), an average BTSCC herd (BT_A), and a high-BTSCC herd (BT_H), each with a low (BT_LC_L; BT_AC_L; BT_HC_L), an average (BT_LC_A; BT_AC_A; BT_HC_A), and a high (BT_LC_H; BT_AC_H; BT_HC_H) incidence of clinical mastitis (SDCT) and for blanket dry cow treatment (solid lines) in these 9 types of herds (BDCT).

Sensitivity analysis

Minimal TC_M, was influenced by changes in Δ_{DCT} and changes in milk price as is presented in Table 4. If the effect of DCT is smaller (Δ_{DCT} x 0.5), incidence of CM in dry cow treated cows will be lower than in the baseline situation, as will be the TC_M. The effect of a decreased Δ_{DCT} is substantial (up to 9%), while it is limited for an increased Δ_{DCT} (maximal 3%). The sensitivity analysis showed that the effect of variability in milk price has a substantial effect on the minimal TC_M for SDCT in both directions. If the milk price was € 27 / 100 kg, BDCT was not beneficial for any type of herd (data not presented). Changing milk prices had a greater effect on minimal TC_M than changing Δ_{DCT}, up to 16% in both directions. The lowest minimal TC_M was € 2,809 per year for a BT_LC_A-herd when the milk price was € 27 / 100 kg. The highest minimal TC_M was € 4,422 per year for a BT_HC_A-herd when the milk price was € 43 / 100 kg.

Table 4. Results of the sensitivity analysis by halving and doubling the effect of dry cow treatment (Δ_{DCT}) and variation in milk price on the calculated minimal total economic costs of mastitis (TC_M). Calculations were done for a low-BTSCC herd (BT_LC_A), an average BTSCC herd (BT_AC_A), and a high-BTSCC herd (BT_HC_A) with an average incidence of clinical mastitis when 100% of cows are allowed to be dried off with antimicrobials

	Minimal TC_M (€/year/herd)					
Sensitivity analysis	BT_LC_A		BT_AC_A		BT_HC_A	
Baseline, 100% SDCT	3,339		3,557		3,838	
Δ_{DCT} x 0.5	3,038	-9%	3,261	-8%	3,484	-9%
Δ_{DCT} x 2.0	3,445	+3%	3,665	+3%	3,887	+1%
Milk price € 27 / 100 kg	2,809	-16%	2,982	-16%	3,205	-16%
Milk price € 43 / 100 kg	3,850	+15%	4,113	+16%	4,422	+15%

DISCUSSION

To control mastitis, much research has been done to evaluate the effects of DCT, generally indicating a positive effect of DCT on udder health (Halasa et al., 2009a). Due to a changing view on AMU in the animal industry, preventive use of antimicrobials, including BDCT, is no longer allowed in several European countries, including the Netherlands (Santman-Berends et al., 2016). Economic consequences likely contribute to farmers' decision-making on the use of dry cow antimicrobials and therefore are of interest with regard to SDCT as compared with BDCT.

Our model compared different SDCT approaches based on monthly SCC. Some studies have used quarter-, cow-, and herd-level criteria to select cows for dry cow therapy. Decision-making to select cows for DCT can be based on bacteriological culture (Browning et al., 1990; Cameron et al., 2014), SCC and CM history (Rindsig et al., 1978; Torres et al., 2008; Rajala-Schultz et al., 2011), the California Mastitis Test (Rindsig et al., 1978; Bhutto et al., 2012) and N-acetyl-ß-D-glucosaminidase (Hassan et al., 1999) with different accuracies in identification of infected cows. The most feasible selection method, however, is based on monthly SCC, which has a reported sensitivity of 70% and specificity of 63% to identify quarters with IMI at drying off (Torres et al., 2008). These are not ideal test characteristics, which may lead to false positive or false negatives in cow selection for dry cow treatment. This, however, was found not to lead to big problems when implemented in field studies (Scherpenzeel et al., 2016).

Although epidemiological consequences and effects of reducing DCT were extensively evaluated in the last three years (Cameron et al., 2014; Santman-Berends et al., 2016; Scherpenzeel et al., 2016), attention for economic consequences of different approaches of DCT was limited to a few studies in the last 10 years (Halasa et al., 2007; Huijps and Hogeveen, 2007). In our study, our main finding was that from an economic perspective, although differences were small, BDCT seems not to be the optimal approach of DCT. The maximum percentage of cows to be dried off with dry cow antimicrobials in an SDCT approach could on herds with different BTSCC and CM incidence levels be decreased to a certain level, without seeing an increase in TC_M. We found that the maximum percentage of dry cow antimicrobials in SDCT, where the minimal TC_M for SDCT equals TC_M for BDCT, is influenced by the udder health situation of a herd, both by BTSCC as well as CM. The effect of the incidence of CM, as well as the BTSCC were evaluated, showing that the effect of the incidence of CM on minimal TC_M was much greater than the effect of BTSCC. This indicated that BDCT is not the economically optimal DCT approach as compared with 100% SDCT in all types of herds and as compared with 0% SDCT in all types of BTSCC-herds with a low incidence of CM (BT_LC_L; BT_AC_L; BT_HC_L) .

Comparison of the TC_M for a BDCT approach and the minimal TC_M for SDCT showed limited economic effects due to small differences between different approaches. This is in line with the findings of Huijps and Hogeveen (2007), who concluded that SDCT was economically the best approach to dry-off cows, although the differences with BDCT were small. They concluded that a small change in the probabilities of the rate of infection and costs associated with mastitits moved the economically optimal decision toward BDCT. Assumptions on failure and preventive costs to estimate TC_M, however, can differ per herd. We used the best available estimates for the Dutch situation to prevent potential bias as much as possible. The sensitivity analysis showed that the effect of variability in milk price and changes in Δ_{DCT} has substantial effect on the TC_M, although the conclusions do not change. This shows that our conclusions are robust using our deterministic approach.

Evaluating the effect of the incidence of CM in a BT_A-herd showed a great effect on the minimized TC_M (Figure 1). The minimized TC_M was 3 times higher for a BT_AC_H-herd than for a BT_AC_L-herd. In a BT_H-herd, effects of the incidence of CM were similar to a BT_L-herd (Figure 1) as they were in a BT_A-herd (results not shown). In all types of herds, the minimal TC_M for a low incidence of CM was always lower for SDCT than for BDCT (Figure 1). The largest difference in minimal TC_M when applying 100% SDCT was between a BT_H-herd with a high incidence of CM (BT_HC_H) and a BT_L-herd with a low incidence of CM (BT_LC_L), being € 4,515 per year per herd.

In our optimization model, the relation between DCT and the incidence of CM and SCM was modeled in a straightforward manner. The limitation of the optimization approach is that some parameters and associations need to be assumed. We were, however, able to base the probabilities of mastitis on a large prospective field trial. In this field trial, no internal teatsealants were used, although the use of internal teatsealant is an important preventive tool. Usage of internal teat sealants was previously found to have a protective effect on the incidence of new CM cases because teat sealants help prevent colonization of quarters with bacteria during the dry period (Rabiee and Lean, 2013). A model including the effect of the use of internal teatsealants would be worthwhile, but was beyond the scope of this study.

The economic effect of an improved udder health situation on the herd, e.g., having a lower BTSCC or a lower incidence of CM, is much greater than the economic effect of restricting the maximum percentage of dry cow antimicrobials used. For the minimal TC_M on some types of herds (e.g., a BT_HC_A-herd), economic benefits of SDCT were very small, as compared to a BDCT approach. From a risk avoidance approach one could therefore choose for a BDCT approach. For reasons of prudent antimicrobial use, however, it is not desirable to use more dry cow antimicrobials than needed and there also seems no economic reason to do so. Thus, for several reasons investments and efforts should be made to reduce BTSCC and the incidence of CM, rather than using more dry cow antimicrobials.

For all BTSCC levels it was economically beneficial to reduce the incidence of CM, in order to improve general udder health management. While searching for the economically optimal DCT approach, we compared udder health and AMU, because of opposite effects of limiting the use of dry cow antimicrobials on these parameters. When searching for optimal selection criteria for DCT, the incidence of mastitis, BTSCC and AMU can be compared in an economic evaluation. This oversimplifies the potential effect of DCT, given the potential effect of antimicrobial resistance, the public opinion on preventive antimicrobial use, political issues, and animal welfare. This study, however, shows that economics is not an argument against reduction of the use of dry cow antimicrobials by applying SDCT.

CONCLUSIONS

From an economic perspective, BDCT seems not to be the optimal approach of DCT, although differences between approaches were small. For all evaluated BTSCC levels, SDCT was economically more beneficial than BDCT with greater economic profits in herds with lower incidence of CM and lower BTSCC. In all types of herds, the use of dry cow antimicrobials can be reduced without economic consequences. In herds with low incidence of CM the use of no dry cow antimicrobials at all is cheaper than BDCT. The economic impact of improvement of the udder health situation, both the incidence of CM and BTSCC, however, is bigger than the effect of the DCT approach. Economics is not an argument against reduction of the use of dry cow antimicrobials by applying SDCT.

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Chapter 5

Farmers' attitude toward the introduction of selective dry cow therapy

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SUMMARY

The attitude of Dutch dairy farmers toward selective dry cow treatment (**SDCT**) is unknown, although a favorable mindset toward application of SDCT seems crucial for successful implementation. Given the fact that blanket dry cow treatment has been strongly promoted until recently, the implementation of SDCT was expected to be quite a challenge. This study aimed to provide insight into the level of implementation of SDCT in 2013 in the Netherlands, the methods used by farmers for selection of cows for dry cow treatment (**DCT**), the relation between SDCT and udder health and antimicrobial usage (**AMU**) in 2013, and the mindset of farmers toward SDCT.

In 2014, a questionnaire was conducted in a group of 177 herds included in a large scale udder health study in 2013 and recorded all clinical mastitis cases during this year. In addition, data on somatic cell count (**SCC**) parameters and AMU was available for these herds. The questionnaire included questions with regard to DCT with special emphasis on farmers attitude and mindset with regard to applying DCT in 2013. The data that were obtained from the questionnaire were combined with the data on clinical mastitis, SCC and AMU. Descriptive statistics were used to evaluate the data and to study the association between DCT, udder health and AMU. Univariable and multivariable logistic regression models with a logit link function were applied to evaluate potential associations between DCT and farmers' mindset.

Selective DCT was taken up progressively by the farmers in our study, with 75% of them implementing SDCT in 2013. The main criterium used to select cows for DCT was the SCC history during the complete previous lactation. The herds were divided in 3 groups, based on the percentage of cows dried off with antibiotics in 2013 as indicated by the farmers during interviews. The first group applied BDCT and the herds that applied SDCT were split in 2 equally sized groups based on the median percentage of cows dried off with antibiotics (67%). The incidence rate of subclinical and clinical mastitis were comparable between the groups. Results of the multivariabel model showed that 4 factors related to farmers' mindset were associated with the probability to apply SDCT, i.e. 'financial consequences of SDCT', 'uncertainty whether a cow will recover without antimicrobials', the statement 'I do not have a problem with the (potential) negative consequences of SDCT' and the usage of internal teat sealants. Application of SDCT appeared to be associated with farmers' attitude. The mindset of farmers with respect to reduction of AMU and the implementation of SDCT was generally positive.

INTRODUCTION

Use of antimicrobials for treatment of bacterial infections in both humans and food-producing animals can lead to decreased antimicrobial susceptibility (Chantziaras et al., 2014) and is a concern of the general public in many countries (Freimuth et al., 2000). Although the relationship between antimicrobial use (**AMU**) and the development of antimicrobial resistance (**AMR**) in bacteria is complex and unclear (Oliver et al., 2011), a relation between veterinary AMU and veterinary AMR is likely (Chantziaras et al., 2014).

Antimicrobials in dairy are mainly used for treatment of clinical mastitis (**CM**) and dry cow treatment (**DCT**). For many years, approximately 60% of the antimicrobial use in dairy cattle was related to mastitis, of which roughly two-thirds was related to DCT (Kuipers et al., 2016). Blanket dry cow therapy (**BDCT**), an approach to treat every quarter of every cow at drying off with antibiotics, is common practice in many countries in the world including, until recently, the Netherlands (Sampimon et al., 2008). In the Netherlands, however, preventive use of antimicrobials in animal husbandry has been prohibited since 2013 and BDCT is no longer allowed.

Since then, farmers have been using selective DCT (**SDCT**). No guidelines were available describing how to select animals for DCT. Nevertheless, most farmers implemented a form of SDCT according to their own criteria (Santman-Berends et al., 2016). In January 2014, the Royal Dutch Veterinary Association launched guidelines to be used when implementing SDCT (KNMvD, 2014).

The attitude of Dutch dairy farmers toward SDCT is unknown, while a favourable mindset toward application of SDCT seems crucial for successful implementation. Several studies describe the huge influence of the mindset of farmers on udder health (Lam et al., 2011; Jones et al., 2015). Given that BDCT has been fiercely promoted until recently (Lam et al., 2013), the implementation of SDCT was expected to be quite a challenge.

This study aimed to provide insight into the level of implementation of SDCT in 2013 in the Netherlands, the methods used by farmers for selection of cows for DCT, the relation between SDCT and udder health and AMU in 2013, and the mindset of farmers toward SDCT.

MATERIALS AND METHODS

Study population

In 2012, a random selection of 1,352 Dutch dairy farmers were contacted by mail to participate in a study on CM occurrence (Santman-Berends et al., 2015; Santman-Berends et al., 2016). Conventional farms with a traditional milking system (no automatic milking system) who participated in a milk recording program on a 4-6 week interval (Dutch Royal Cattle Syndicate CRV, Arnhem), including SCC measurement, were eligible for inclusion. Farmers representing a total of 233 dairy herds participated in this study and completed the requested registration. Farmers were asked to observe and register all CM cases in their herd and to communicate these data on a monthly basis from January 1 to December 31, 2013. The participating farmers were instructed on the definition of CM and the recording procedure. They also gave consent for the use of their routinely collected data, which included data on cow identification and registration (I&R, provided by the Dutch Enterprise Agency RVO, The Hague), data on AMU (ZuivelNL, The Hague), SCC data on bulk tank level (**BTSCC**) (Qlip laboratories, Zutphen) and on cow-level (CRV, Arnhem).

Survey Questionnaire

Data regarding implementation of SDCT and the mindset of the farmer toward AMU and SDCT were collected using a detailed questionnaire, that contained demographic items about the herds, items about implementation of DCT in 2013 and items on the attitude toward AMU and DCT. The questionnaire consisted of open questions, questions with pre-defined answer categories, and statements the farmers were asked to rate on a 5-point Likert scale (Likert, 1932). To find out the most important positive and negative aspects of reduction of AMU, farmers were asked to rank their top three of positive and negative aspects, without using pre-defined answer categories.

The questionnaire was pre-tested on completeness, wording and time needed to complete by 2 farmers, and their feedback was incorporated in the final version. Three interviewers were trained to ask the questions in a similar way. The interviewee was the person who was responsible for dry cow management in the herd. Careful attention was given to asking the questions in an open manner to prevent socially desirable answering instead of true opinions. Additionally at the start of each interview, it was stated clearly that the answers provided by the farmers would be analyzed summed over herds, would be presented anonymously and that it would not be possible to trace any answer back to an individual farmer. The questionnaires were conducted by telephone between April 17 and May 16, 2014.

Definitions of mastitis and antimicrobial usage

A description of the calculation of the udder health parameters that were evaluated can be found in Santman-Berends et al. (2016). In short: the incidence rate of CM (**IRCM**) was calculated as the number of cases per 100 cows per year at risk in 2013. Clinical mastitis was defined as every abnormality of udder and/or milk as observed by the farmer. Abnormalities included alteration in color or texture of the milk, swollen or red quarters with or without systemic clinical signs in cows. Cows could have more than 1 case of CM in the same lactation, but a CM case in the same quarter within 14 days after a previous case, was considered to be the same case. Each observed CM case was recorded by the farmers on a form and was reported on a monthly base. To ensure high data quality and reduce bias, farmers were reminded by e-mail and telephone to return the forms at the end of each month.

A case of subclinical mastitis (**SCM**) was defined as a high composite SCC (**CSCC**) after 2 previous consecutive low composite SCC values, irrespective of the dry period. Threshold values were 150,000 cells/mL for primiparous and 250,000 cells/mL for multiparous cows (de Haas et al., 2008). Cows could have had more than 1 case of SCM in the same lactation. The incidence rate of SCM (**IRSCM**) was based on the number of days cows were at risk of developing SCM, and was expressed as cases per 100 cows at risk per year in 2013.

Bulk tank SCC was measured on all farms on a 2-weekly basis. These data were used to calculate the average BTSCC for 2013 for each of the farms.

Data were available on all antimicrobials delivered by veterinarians to each of the herds from January 1 to December 31, 2013. The average Animal Defined Daily Dose of AMU per year (**ADDD/Y**) i.e., the average number of days a cow receives antimicrobial treatment, was calculated per herd for 2013 according to the definitions provided by the Dutch Veterinary Medicines Authority (**SDa**) (SDa, 2014), as described by Santman-Berends et al. (2015). Antimicrobial use for DCT was calculated as 1 ADDD/Y per quarter treated with antibiotics at drying off, as defined by SDa (Scherpenzeel et al., 2014).

Statistical analysis

The herds were divided in 3 groups, based on the information on the percentage of cows dried off with antibiotics in 2013 as provided during the interviews. The first group applied BDCT i.e., used DCT on all cows at drying off. Herds that applied SDCT were split in 2 equally sized groups based on the percentage of cows dried off with antibiotics as indicated by the farmer. The SDCT group with more than median use of dry cow antibiotics was the SDCT high use (**$SDCT_{HU}$**) group and the SDCT group with less than median use of dry cow antibiotics, was the SDCT low use (**$SDCT_{LU}$**) group.

Descriptive statistics such as means, medians, and percentages were used to describe the complete study population and the 3 study groups (BDCT, $SDCT_{HU}$, $SDCT_{LU}$). Parameters that were evaluated include herd demographics, the mindset and udder health parameters (IRSCM, IRCM and BTSCC) in the year 2013. Descriptive statistics and univariable non-parametric tests such as Kruskal-Wallis (Kruskal and Wallis, 1952) and proportion tests were used to evaluate the association between the applied drying-off strategy, the AMU and udder health parameters. Differences between groups with $P \leq 0.05$ were considered significant and differences of groups with a *P*-value between 0.05 and 0.10 were described as a trend.

In addition, we evaluated whether the farmers' mindset regarding application of DCT was associated with their DCT strategy. For this evaluation, the mindset of the farmers that applied SDCT (groups $SDCT_{HU}$ and $SDCT_{LU}$ together) were compared with the mindset of farmers that applied BDCT in 2013. Logistic regression models with a logit link function were used for this analysis. Here, the group status was the dependent variable and parameters with regard to the attitude and management of the farmer were included as independent variables. First, the association between group status (BDCT vs. SDCT) and attitude or management variables were pre-screened using univariable regression techniques. Variables with a *P*-value<0.25 were considered to be potentially associated with the group status and were entered in the multivariable model. The best multivariable model was selected using a stepwise backward selection and elimination procedure. Because of the low number of observations, it was decided to include all parameters with an overall *P*-value<0.10 in the final model. The best model was deemed the model with the Akaike's information criterion closest to 0 (Akaike, 1974). During the selection and elimination procedure, confounding was monitored, where a variable was considered a confounder if an estimate of another variable changed by >20% after inclusion or exclusion of the (non-significant) confounder variable. The amount of variance explained by the final model was evaluated using the pseudo R^2. Stata 13.1® (Statacorp, 2014) was used for the analysis.

RESULTS

Descriptive results

Of 233 farmers that enrolled in the study, 177 farmers delivered all requested data and completed the questionnaire. In total 56 farmers did not participate in the interview, because they had stopped farming or had switched to organic farming during the study period (n=3), could not be reached to conduct the questionnaire (n=29), did not want to cooperate (n=19) or did not finish the questionnaire (n=5). The median herd size of the 177 participating herds was 90 lactating cows and varied between 16 and 386 lactating cows. The herds were slightly larger than the average Dutch dairy herd, were representative with regard to their location, purchased slightly more antimicrobials compared with the Dutch average, and showed a slightly better udder health based on SCC data (Santman-Berends et al., 2015, 2016).

The median aplication of DCT was 80% of cows (mean 72%) and varied between all cows (BDCT, n=44 herds) and none of the cows (n=2 herds) in 2013 (Figure 1). The percentage of cows that were dried off with DCT as indicated by the 177 farmers was highest in the first quarter of 2013 (median 95%) and declined thereafter (Q2: median 82% and Q3 and Q4: median 80%).

Of 177 participants, 44 farmers (25%) indicated that they applied BDCT throughout 2013. In the 133 herds in which SDCT was applied, the median percentage of cows that were dried off with antibiotics was indicated at 67% (mean 63%; interquartile range (**ICR**): 50-87%). This resulted in 67 herds in the $SDCT_{HU}$-group (> 67% of cows dried off with antibiotics) and 66 herds in the $SDCT_{LU}$-group ($\leq$ 67% of the cows dried off with antibiotics).

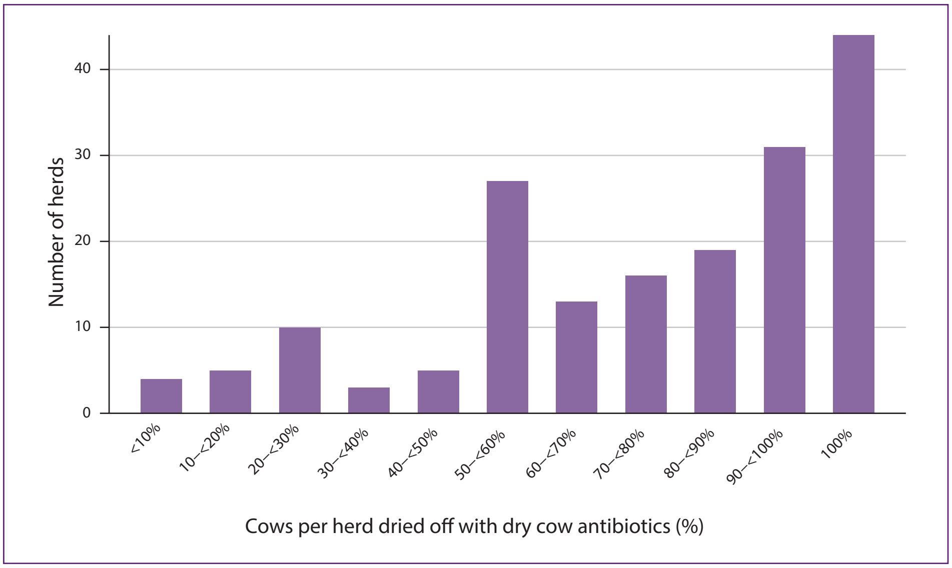

Figure 1. Distribution of the application of dry cow therapy in 177 Dutch dairy herds in 2013

The farmers in the SDCT groups used different criteria to select cows for DCT. Often, more than 1 criterium was used. On 93 farms (70%) SCC-history during the complete previous lactation was used, among which 48 farms (36%) used SCC at the last milk recording before drying off. On 36 farms (27%) clinical mastitis history in the previous lactation was used, and on 18 farms (14%) milk yield at the day of dry-off was used as criterium to select cows for DCT.

When farmers decided to use antimicrobials at drying-off, application of DCT was applied in all 4 quarters by 167 farmers (94%), whereas 10 farmers (6%) decided on DCT application at quarter level. In 114 of the 177 herds (64%), internal teat sealants were used. Among these 114 herds, 52 farmers (46%) used teatsealants in all cows, 22 farmers (19%) in more than 50% and 40 farmers (35%) in less than 50% of the cows.

Table 1. Udder health parameters and antimicrobial use for 3 groups of dairy herds with different proportions of cows dried off with antibiotics. Farmers are categorized in groups with blanket dry cow therapy (BDCT, 100% DCT), selective dry cow therapy high use ($SDCT_{HU}$, >67% DCT <100%) and selective dry cow therapy low use ($SDCT_{LU}$, ≤67% DCT)

	BDCT (n=44)	$SDCT_{HU}$ (n=67)	$SDCT_{LU}$ (n=66)
Incidence rate of clinical mastitis per 100 cows per year[1]	28 (22-44)	30 (21-44)	30 (19-42)
Incidence rate of subclinical mastitis per 100 cows per year[1]	64 (49-86)	73 (54-87)	72 (54-86)
Bulk tank somatic cell count (*1,000 cells/mL)[1]	170 (140-205)	169 (147-208)	199 (156-231)
ADDD/Y total (cows >2 years old)[3]	4.48[a]	4.09[b]	3.16[c]
ADDD/Y dry cow treatment	1.98[a]	1.65[b]	0.92[c]
ADDD/Y intramammary treatment[2]	0.70	0.52	0.63
ADDD/Y parenteral applied antibiotics	0.67	0.66	0.56

[1] *Values are median (medians (25-75th percentile).*
[2] *Intramammary treatment other than dry cow treatment*
[3] *ADDD/Y = Animal defined daily dose of antimicrobial use per year*
[a-c] Percentages within a row with different superscript are statistically different ($P \leq 0.05$)

Internal teat sealants at drying off were more often applied in $SDCT_{LU}$ herds (73%; 95%CI: 60-83%) compared with herds of which the farmer applied BDCT (48%; 95%CI: 32-63%) (*P*-value=0.008). From the $SDCT_{HU}$ group, 64% (95%CI: 52-76%) of the farmers applied internal teat sealants at drying off. This percentage was not different from the $SDCT_{LU}$ group and tended to be lower when compared to the BDCT group (*P*-value=0.10).

Udder health parameters were available for 175 of the 177 herds. The median IRCM in these herds was 29.1 cases per 100 cows per year (IQR: 21-44; mean 33.7), the median IRSCM was 70.9 cases per 100 cows per year (IQR: 52-86; mean 71.0) and the median BTSCC was 174,000 cells/mL (IQR: 147,000-221,000; mean 183,000) in 2013.

Association between dry cow therapy, mastitis and antimicrobial usage

The IRCM and IRSCM were comparable between the groups BDCT, $SDCT_{HU}$ and $SDCT_{LU}$ (*P >0.05*; Table 1) while BTSCC tended to be higher in the $SDCT_{LU}$ group when compared with the $SDCT_{HU}$ group (*P=0.08*) and the BDCT group (*P=0.09*). Between groups BDCT, $SDCT_{HU}$ and $SDCT_{LU}$ a significant difference in total AMU was found, obviously due to a difference in use of dry cow antimicrobials. Group BDCT had 4.48 ADDD/Y, where group $SDCT_{HU}$ and $SDCT_{LU}$ had 4.09 ADDD/Y and 3.16 ADDD/Y respectively. No significant difference in AMU for intramammary or parenteral treatment between the 3 groups was found, although group $SDCT_{LU}$ tended to have a lower ADDD/Y for parenterally applied antimicrobials as compared to BDCT (Table 1).

Table 2. Opinions of 177 dairy farmers on statements toward antibiotic usage in the animal industry and towards dry cow therapy

	Strongly disagree	Disagree	Neither agree nor disagree	Agree	Strongly agree
It is important that the usage of antibiotics in the animal industry is restricted	7 (4%)	2 (1%)	13 (7%)	24 (13%)	133 (74%)
With less antibiotics, I can still be a good farmer	8 (5%)	6 (3%)	10 (6%)	27 (15%)	128 (72%)
My veterinarian encourages me to reduce antibiotic usage on my farm	18 (10%)	9 (5%)	26 (15%)	23 (13%)	103 (58%)
I do not have a problem with the (potential) negative consequences of selective dry cow therapy	66 (37%)	28 (16%)	21 (12%)	20 (11%)	44 (25%)
I select cows for dry cow therapy in the correct way	10 (6%)	2 (1%)	27 (15%)	34 (19%)	106 (59%)
When I have questions about dry cow therapy, the veterinarian is my main advisor	13 (7%)	3 (2%)	10 (6%)	20 (11%)	133 (74%)
Other dairy farmers I know are positive about selective dry cow therapy	28 (16%)	17 (10%)	89 (50%)	18 (10%)	27 (15%)

Attitude

The majority (87%) of farmers agreed or strongly agreed that it is important that the use of antimicrobials in the animal industry is restricted, and 87% considered they can still be a good farmer when they use less antimicrobials (Table 2). Most of the 177 farmers think they apply DCT in the correct way (78% agreed or strongly agreed). Among the interviewed farmers, 53% indicated to have problems with the (potential) negative consequences of SDCT. Most farmers (85% agreed or strongly agreed) saw their veterinary practitioner as the main advisor with regard to (S)DCT and stated that their veterinarian encourages them to reduce AMU on their farms (71% agreed or strongly agreed). Finally, opinions on the experiences of other farmers toward SDCT vary among the interviewees.

Most farmers cited 'financial consequences' and 'improving public health' within the top three most positive aspects of reduction of AMU (Table 3). There were no significant differences in the most important positive aspects of reduction of AMU between the 3 groups.

With respect to the negative consequences of reduction of AMU, there were significant differences in the indicators between the 3 evaluated groups of herds. Eleven percent of the farmers could not name a single negative aspect of the reduction of AMU. Overall, 25% of the farmers considered 'uncertainty whether a cow will recover without antimicrobials' and a 'higher risk of sick cows' as the most important negative aspects of reduction of AMU, followed by farmers who indicated that 'cows suffer without antimicrobials' (17%). Some farmers answered that they believed that reduction of AMU would lead to additional labor (14%) or had the feeling they were pushed to follow rules they do not agree with (14%).

Table 3. The most important (top 3) of positive aspects of the reduction of antimicrobial usage according to 177 Dutch dairy farmers, expressed in percentages (95% CI). Farmers are categorized in groups with blanket dry cow therapy (BDCT, 100% DCT), selective dry cow therapy high use ($SDCT_{HU}$, >67% DCT <100%) and selective dry cow therapy low use ($SDCT_{LU}$, ≤ 67% DCT).

Item	Overall (n=177)	BDCT (n=44)	$SDCT_{HU}$ (n=67)	$SDCT_{LU}$ (n=66)
Financial consequences	46 (38-53)	52 (37-68)	40 (29-53)	48 (36-61)
Improving public health	36 (29-44)	43 (28-59)	34 (23-47)	35 (24-48)
Improving the image of the dairy industry	27 (21-34)	20 (10-35)	31 (21-44)	27 (17-40)
Easier to take care of my dairy herd	13 (8-19)	16 (7-30)	7 (3-17)	17 (9-28)
Creating resilient cows	13 (8-19)	7(1-19)[a]	10 (4-20)[ab]	20 (11-31)[b]
Less withholding of milk and meat	11 (7-16)	14 (5-27)	9 (3-19)	12 (5-23)
Improving general cattle health	10 (6-15)	7 (2-17)	7 (1-19)	14 (6-24)
Increased awareness of managing animal health and usage of veterinary medicines	6 (3-10)	7 (1-9)	4 (0-13)	6 (2-15)

[a-b] Percentages within a row with different superscript are statistically different (P < 0.10)

Farmers that applied BDCT or $SDCT_{HU}$ were significantly more often insecure whether a cow would cure without antimicrobials as compared to farmers in the group $SDCT_{LU}$ (41% and 30% vs. 9%; *P*-value <0.001 and 0.003, respectively). In addition, farmers in the group $SDCT_{HU}$ (4%) and $SDCT_{LU}$ (6%) frequently considered 'financial consequences' significantly less as one of the most important negative aspects of reduction of AMU as compared with the BDCT group (18%) (*P*-value 0.05 and 0.02, respectively). Finally, farmers of the $SDCT_{H}$ group indicated worries about animal health as one of the most important negative aspects of AMU significantly more often (9%) when compared to $SDCT_{LU}$ (0%) herds (*P*-value 0.01) (Table 4).

Table 4. The most important (top 3) of negative aspects of the reduction of antimicrobial usage according to 177 Dutch dairy farmers, expressed in percentages (95% CI). Farmers are categorized in groups with blanket dry cow therapy (BDCT, 100% DCT), selective dry cow therapy high use ($SDCT_{HU}$, >67% DCT <100%) and selective dry cow therapy low use ($SDCT_{LU}$, ≤ 67% DCT).

Item	Overall (n=177)	BDCT (n=44)	$SDCT_{HU}$ (n=67)	$SDCT_{LU}$ (n=66)
Uncertainty whether a cow will recover without antimicrobials	25 (19-32)	41 (26-57)[a]	30 (19-42)[a]	9 (3-19)[b]
Higher risk of sick cows	25 (19-33)	32 (19-48)	25 (16-37)	21 (12-33)
Cows suffer without antibiotics	17 (12-23)	23 (11-38)	16 (8-27)	14 (6-24)
Extra labor	14 (9-20)	16 (7-30)	16 (8-27)	9 (3-19)
Pushed to follow the rules, although I do not agree with the policy	14 (9-20)	9 (3-22)	16 (8-27)	14 (6-24)
Risk of making the wrong choice about whether to treat	10 (6-15)	11 (4-25)	10 (4-20)	8 (3-17)
Financial consequences	8 (5-14)	18 (8-33)[a]	4 (1-13)[b]	6 (2-15)[b]
Lack of clarity improvement public health	8 (4-13)	5 (1-15)	10 (4-20)	8 (3-17)
More worries about animal health	4 (2-8)	2 (0-12)[ab]	9 (3-18)[a]	0 (0-4)[b]
Harder to take care of my dairy herd	2 (1-6)	2 (0-12)	1 (0-8)	3 (0-11)

[a-b] Percentages within a row with different superscript are statistically different ($P \leq 0.05$)

Multivariable analysis

Of the 29 variables that were evaluated (28 variables related to attitude and 1 management variable related to usage of internal teat sealants), 9 variables had a *P*-value<0.25 in the univariable pre-screening. These variables showed potential to be associated to DCT and therefore entered the multivariable model (BDCT versus SDCT).

The final multivariable model contained 3 variables based on the mindset of the farmer and 1 on the usage of internal teat sealants. The final model had the lowest AIC possible (178) and explained 19% of the variation in application of BDCT and $SDCT_{L}$ (pseudo R^2=0.19). Farmers who indicated that financial consequences was one of the most important negative aspects of reduction of AMU had a 4.7 times higher odds (95% CI: 1.4-16.0, *P*-value=0.01) to apply BDCT instead of SDCT as compared to farmers that did not indicate this negative aspect. In addition, farmers that indicated the uncertainty whether a cow will recover without antimicrobials as one of the most important negative aspects of reduction of AMU had a 3.0 times higher odds (95% CI: 1.3-7.0; *P*-value=0.009) to apply BDCT instead of SDCT. Farmers that either strongly disagreed or were neutral with regard to the statement 'I do not have a problem with the (potential) negative consequences of selective dry cow therapy' had a significantly higher odds to apply BDCT as compared to farmers that strongly agreed with this statement (OR=4.1, 95% CI:1.1-15.7 and OR=10.5, 95% CI:2.3-48.2, respectively). Finally, usage of internal teat sealants at drying of was associated with a 2.1 times lower odds (95% CI: 0.9-4.5, *P*-value=0.07) to apply BDCT as compared to no use of teat sealants at drying off.

DISCUSSION

The aim of this study was to provide insight into the level and methods used to implement SDCT in 2013 in the Netherlands. Furthermore, SDCT in relation to udder health indicators, AMU, and the attitude and motivation of farmers toward SDCT were evaluated. The results showed that the Dutch farmers took up SDCT progressively, with 75% of them implementing a form of SDCT in 2013. During this year, increasingly more farmers began with SDCT although there was no implementation guideline. Implementation of SDCT showed no dramatic increase in mastitis incidence and related AMU, although earlier work did show a possible increase in IRCM and SCM when SDCT was applied (Scherpenzeel et al., 2014; Cameron et al., 2015). This difference may be due to the fact that these studies used more stringent criteria for DCT, like SCC at the last milk recording before drying off and on-farm culturing as criteria to select cows for DCT. Additionally, in the earlier studies only low SCC cows were considered whereas, in the current study, all cows were included. Farmers may be aware of this greater risk on CM and may have changed their udder health management as well.

Our study showed that the farmers selected their cows mostly based on SCC history and CM-history. These criteria are in line with findings that were described earlier by Torres et al. (2008) and Rajala-Schultz et al. (2011) and are considered as useful parameters in practice.

The belief of a farmer whether SDCT will result in an increased risk for CM or not, will influence the farmer's choice to apply either BDCT or SDCT. It is obvious that individual positive or negative experiences with the use of SDCT are of great importance for their believes. In our study we found that farmers attitude explained 19% of the variation to apply BDCT or SDCT, which is remarkable, because it is higher than the percentage of explained variance in udder health based on management parameters (van den Borne et al., 2010; Santman-Berends et al., 2016). This finding has earlier been described by Jansen et al. (2010), who found that farmers' mindset is highly associated with udder health. Furthermore, a study on prudent antibiotic use in South Carolina showed that mindset related factors such as limited economic benefits and lack of time were barriers to follow proper antibiotic procedures (Friedman et al., 2007). These factors appeared to influence the mindset of Dutch dairy farmers as well, because the financial consequences were mentioned as one of the most important positive aspects. Besides factors related to farmers' attitude we also found that application of teat sealants at drying off were applied more often in herds of which the farmer applied $SDCT_L$ as compared to herds of which the farmer applied BDCT. Usage of internal teat sealants were previously found to have a protective effect on the incidence of new CM cases as teat sealants help prevent colonisation of quarters with bacteria during the dry period (Rabiee and Lean, 2013).

This questionnaire, executed in April and May 2014, included questions regarding the attitude of the farmer and the management of the herd in 2013. Hence, there could therefore be some recall bias, as interviewees were maybe not able to remember the decisions they made regarding dry cow management. However, the attitude of farmers wil not change quickly (Hardeman et al., 2002) so it can be assumed that the attitude has not changed tremendously between the year 2013 and the moment the questionnaire was conducted.

In our study, farmers indicated that on average 72% of the cows were dried off with dry cow antibiotics. This percentage is higher than the 61% estimated in the study of Santman-Berends et al. (2016). The difference between these percentages can be explained based on the differences in data that were used in both studies. In our current study, we used the information from the farmers on usage of antimicrobials for DCT as indicated in the questionnaire, while Santman-Berends et al. (2016) used the data on supplies of antimicrobials for DCT. Both estimates are imperfect. In the earlier report (Santman-Berends et al., 2016), antimicrobial supplies from the veterinarian to the farmer were used, which is a proxy for AMU and does not provide data on the actual usage. In addition, the percentage as described by Santman-Berends et al. (2016) will slightly underestimate the percentage of cows in which DCT is applied, because here it was assumed that antimicrobials are applied in all four quarters. In this study it was shown that 6% of the farmers do not treat all quarters when they use antimicrobials at drying off.

In this study, the herds that indicated to have used BDCT likely reported that correctly. However, in herds that used SDCT the percentage of cows in which DCT is applied is likely imperfect due to recall bias. Additionally, we observed that farmers tended to round the percentage of cows in which DCT was applied on a multiplication of five percent, which was most obvious for the 50% answer.

Multivariable analysis was carried out to find significant differences between groups BDCT and SDCT. Farmers that either strongly disagreed or were neutral with regard to the statement 'I do not have a problem with the (potential) negative consequences of SDCT' had a significantly higher odds to apply BDCT as compared to farmers that strongly agreed with this statement (OR= 4.1, 95% CI: 1.1-15.7). If the $SDCT_H$ would not be taken into account in the multivariable analysis, the odds would be much higher and increase to 13.7 when comparing BDCT to $SDCT_{LU}$. We chose to keep the $SDCT_{HU}$ group in the analysis to compare all three groups over all aspects. Our results show that the application of SDCT is highly associated with farmers' attitude. Specific attention given to SDCT in education, training and specific campaigns seems important to change farmers' attitude towards mastitis management (Lam et al., 2013). Additionally, efforts need to be made to support the farmer in reducing the risk on mastitis by improving mastitis management in general and providing effective measures for mastitis prevention.

CONCLUSIONS

Selective DCT was quickly adopted by the farmers in our study, with 75% of them implementing SDCT in 2013. The main criterion used to select cows for DCT was the SCC history during the complete previous lactation. There were no significant differences in udder health parameters between herds that applied BDCT or SDCT, nor between SDCT herds with high or low DCT use. Overall, AMU was higher in herds that applied BDCT, although there were no significant differences in intramammary use of antimicrobials. Although application of SDCT appeared highly associated with farmers' attitude, the mindset of farmers in general with respect to reduction of AMU and the implementation of SDCT seemed positive.

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Chapter 6

Veterinarians' attitude towards antimicrobial use and selective dry cow treatment

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SUMMARY

In the Netherlands antimicrobial use (AMU) in animal husbandry including the dairy industry became subject of public debate around 2008. This debate led to regulations with respect to decreasing AMU, including a ban on preventive use of antimicrobials, as for instance is practised when applying blanket dry cow treatment in dairy cows. Both, farmers and veterinarians play an important role in implementing these measures and have a shared responsibility with respect to prudent AMU. The attitude of Dutch dairy veterinarians towards restricted AMU and towards selective dry cow treatment (SDCT) is unknown, while a favorable attitude towards this approach seems crucial for successful implementation.

In 2015, a questionnaire was conducted in a group of 181 veterinarians and included questions with regard to their attitude and behavior towards reduction of AMU and towards SDCT. Descriptive statistics were used to describe the data and multivariable logistic regression models with a logit link function were applied to evaluate potential associations between veterinarians' attitude towards AMU and SDCT and the rationale behind their mindset, based on positive and negative aspects of reduction in AMU. The veterinarians were divided into three groups based on their opinion on four statements with regard to AMU and SDCT; veterinarians with an unfavorable, a neutral, and a favorable attitude towards reduction of AMU and towards SDCT. For the multivariable logistic regression analysis the first two groups were combined and compared to the veterinarians with a favorable attitude.

Dutch dairy veterinarians were found to generally have a positive attitude towards reduction of AMU, and most of them considered that they can still be a good veterinarian when they prescribe less antimicrobials. Selective DCT was progressively promoted by them since 2013. Most veterinarians see the advice they provide to the farmer on SDCT as the best possible approach and are convinced that their farmers apply this SDCT approach. Results of the multivariable model showed that having a favorable or an unfavorable attitude towards reduction of AMU and towards SDCT is mainly based on mindset issues indicated by quotes such as "*Farmers have increased consciousness of animal health and usage of veterinary medicines*" (favorable) and *"I have the feeling that the committee that determines which antimicrobials can be used is paid by the industry, they do not care about integrity, and lack practical experience"* (unfavorable).

INTRODUCTION

Prudent antimicrobial use (**AMU**) is of major importance in order to reduce the risk of development of antimicrobial resistance (**AMR**) (Chantziaras et al., 2014). Several European countries closely monitor human as well as veterinary AMU. In the Netherlands, AMU in animal husbandry became subject of public debate around 2008. This debate led to regulations with respect to decreasing AMU. Eversince AMU in animal husbandry is monitored not only at the national level, but also at the individual farm level, and at the level of veterinary practices, with for each specific targets (Bos et al., 2015). Nowadays, in most western countries the majority of the antimicrobials in the dairy sector are applied by farmers. The veterinarian subsequently has an advisory role towards AMU, with different responsibilities in different countries, based on national legislation. Irrespective of legislation, however, farmers and veterinarians both have a role with respect to AMU and AMR and ought to share the accountability for prudent on farm AMU.

In the Netherlands, preventive use of antimicrobials in animal husbandry was prohibited since november 2012 and farmers and veterinarians were encouraged to restrict curative AMU, specifically of antimicrobials that are critical in human medicine. For many years, approximately 60% of AMU in dairy cattle was related to mastitis, of which roughly two third could be assigned to dry cow treatment (**DCT**) (Kuipers et al., 2016). Since the ban on preventive use of antimicrobials, blanket DCT (**BDCT**) has been replaced by selective DCT (**SDCT**) (Santman-Berends et al., 2016). In order to optimize AMU in the Netherlands, including the introduction of SDCT, farmers and veterinarians have a shared responsibility that is reflected in a compulsory one-on-one relationship between them (Speksnijder et al., 2015b). Together they have to make a herd health plan and a herd treatment plan, which is based on the actual herd situation. The herd health plan contains the main points of disease monitoring and prevention at the herd level. The herd treatment plan contains the therapies for diseases such as mastitis and lameness that are treated by the farmer himself or herself.

This type of rules and regulations are an important cue to change human behavior, besides other factors like education, social pressure, economics and tools that are part of the RESET Mindset Model as described by Lam et al. (2017). Apart from the actual behavior of dairy farmers and veterinarians with respect to AMU and DCT, the veterinarians' behavior is also of importance with respect to influencing farmers' behavior (De Briyne et al., 2013, Postma et al., 2016, Higgins et al., 2017).

At the time when BDCT was prohibited in the Netherlands, it was unclear how to select cows for SDCT, which complicated implementation. Additionally, given the fact that BDCT had been fiercely promoted until then (Lam et al., 2013), implementation of SDCT was perceived to be quite a challenge, specifically for veterinary practitioners as the primary advisors for farmers in this field. At the end of 2012 when SDCT became the standard, no guidelines were available on how to interprete and implement SDCT. Nevertheless in 2013, most farmers implemented some form of SDCT according to their own comprehension (Santman-Berends et al., 2016). In January 2014, the Royal Dutch Veterinary Association launched a guideline for veterinary practitioners on how to select cows for DCT (KNMvD, 2014).

Since the introduction of SDCT a major change in the farmers' approach towards the use of dry cow antimicrobials has taken place. In general, farmers have had a positive attitude towards reducing AMU and towards SDCT (Scherpenzeel et al., 2016). Understanding the attitude of the veterinarian towards AMU and specifically towards SDCT, seems crucial in order to maintain and support responsible use of antimicrobials in dairy practice. That attitude, however, is unknown. Therefore, the objective of this study was to obtain insight into the attitude of Dutch dairy veterinarians towards reduction of AMU and towards SDCT.

MATERIALS AND METHODS

Study population

In March 2015, all 648 Dutch dairy veterinary practitioners that were officially registrered as qualified cattle veterinarian in the Dutch database 'Geborgde Rundveedierenarts' (SGD, 2015) were contacted by email, requesting them to participate in an online questionnaire. The questionnaire was subsequently distributed to all replicants who agreed to participate.

Survey Questionnaire

A detailed questionnaire was sent by email, to collect data on the opinion of veterinarians on SDCT as compared to BDCT, their attitude towards AMU and SDCT, their experiences with SDCT, and experienced positive and negative aspects of reduction of AMU in general. The survey also contained generic questions about demographics of the veterinarian and his or her veterinary practice.

Open questions, multiple choice questions with pre-defined answer categories and statements that had to be filled in on a 5-point Likert scale (Likert, 1932) were included. The veterinarians were asked how they assessed their attitude and knowledge towards AMU and SDCT, as well as their self-reported prescribing practices, the interaction with farmers and their perceived role in advicing on reduction of AMU and specifically on SDCT. To study which aspects of SDCT and reduction of AMU were perceived as most important, veterinarians were asked which positive and negative aspects they considered most important and were ranked as top 3 aspects.

The questionnaire was pre-tested for completeness, wording and time needed to answer all questions by three veterinary practitioners and their feedback was incorporated in the final version. At the start of the questionnaire, it was clearly stated that the answers provided would remain anonymous. The questionnaire was distributed online through SurveyMonkey (SurveyMonkey.com, LLC, Palo Alto, California, USA) on 24 March 2015 and was open for reply until 23 April 2015. Email reminders were sent on 4 April and on 18 April 2015.

Classifications and definitions

The respondents were classified in three groups, based on their answers on four statements asking for their attitude towards reduction of AMU in general, and specifically on SDCT. The four statements were:

- '*It is a good thing that antimicrobials are no longer used for preventive reasons in animal husbandry*';
- '*It is a good thing that antimicrobials are no longer allowed for preventive use in dry cow treatment*';
- '*It is commendable that a guideline for selective dry cow treatment has been developed*';
- '*I am positive about selective instead of blanket dry cow treatment*'.

The statements were answered on a Likert scale with five answer categories and points were allocated to each answer category, varying from strongly disagree (zero points) via neutral (two points) to strongly agree (four points). The maximum number of points was 16 per respondent (four statements times four points per statement). The first group had a score of less than eight points and was considered to generally have an unfavorable (**UNF**) attitude towards SDCT and reduction of AMU. Veterinarians that had a score of eight to 11 points were assigned to the second group, which was defined as a neutral (**NEU**) attitude. The group of veterinarians that was classified as having a favorable (**FAV**) attitude scored at least 12 points on the 4 statements and were regarded as generally agreeing with the statements.

Statistical analysis

Descriptive statistics were used to describe the study population. Univariable non-parametric tests such as Kruskal-Wallis (Kruskal and Wallis, 1952) and proportion tests were used to evaluate the association between the attitude of the veterinarian towards AMU and SDCT (UNF, NEU, FAV) and factors such as age, size of the veterinary practice, years since graduation, employer/employee and geographic location (North, Central, South of the Netherlands) of the veterinary practice. Differences between groups with $P \leq 0.05$ were considered significant and differences between groups with a *P*-value between 0.05 and 0.10 were described as a trend.

Positive and negative aspects of reduction of AMU and SDCT that were mentioned by the respondents were described for the three groups of veterinarians. For each respondent the three most important positive and three most important negative aspects that were answered were included in the analysis.

In addition, we evaluated whether the veterinarians' attitude towards the changed approach of AMU, was associated with their perceived top three of positive and negative aspects of reduction of AMU and SDCT. For this evaluation, the answers of the veterinarians that were not favorable towards SDCT (groups UNF and NEU together) (n=94, 52%) were compared to the answers of veterinarians that had a favorable attitude (FAV) towards SDCT (n=87, 48%) in 2015. Logistic regression models with a logit link function in Stata 14® (Statacorp, 2014) were used for this analysis, where the group status (UNF/NEU versus FAV) was included as dependent variable. The positive and negative aspects of reduction of AMU and SDCT that were mentioned, were included as independent variables. The association between group status and attitude variables were pre-screened using univariable regression techniques. Variables with a *P*-value < 0.25 were considered to be potentially associated with the group status and were included in the multivariable model. The best multivariable model was selected using a backward selection procedure. Because of the relative small number of observations, all parameters with an overall *P*-value < 0.10 were retained in the final model. The best model was deemed the model with the AIC closest to 0 (Akaike, 1974). During the selection and elimination procedure, confounding was monitored, where a variable was considered a confounder if an estimate of another variable changed > 25% after inclusion or exclusion of the (non-significant) confounder variable. The amount of variance explained by the final model was evaluated using the pseudo R^2. A pearson goodness-of-fit test was used to evaluate whether the final fitted model was correct.

RESULTS

Survey response and respondents' characteristics

Of 648 veterinarians that received the online questionnaire, 207 participated. Data from 26 veterinarians were excluded from analysis, because of incomplete results. Eventually, 181 dairy veterinarians (28%) completed the questionnaire and their results were included for further analysis. These 181 veterinarians were subsequently categorized, into UNF (n = 39), NEU (n = 55) and FAV (n = 87) (Figure 1). The characteristics of the respondents for each of the groups are shown in table 1.

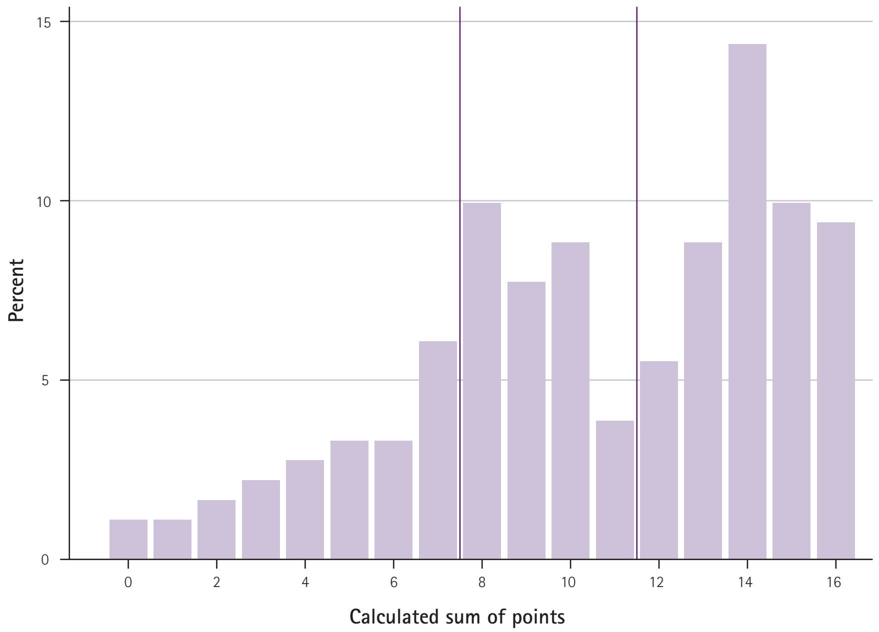

Figure 1. Distribution of the calculated sum of points, based on answers on 4 statements about the attitude of veterinarians towards antimicrobial use and selective dry cow treatment with for every answer 0-4 points (=16 points maximum per respondent) from 181 dairy veterinarians in 2015.

The median age and number of years since graduation of the participating veterinarians was 43 years and 16 years, respectively. There were no significant differences between the three groups with regard to the gender (roughly two third of the respondents was male) or location in the Netherlands. Significant differences between the groups were the number of dairy veterinarians and the number of dairy farms in the practices as well as being employer or employee. Veterinarians in the UNF group worked in practices with significantly less veterinarians, that had significantly less dairy farms as clients and were significantly more often employer as compared to veterinarians in the FAV group.

Table 1. Respondents' characteristics for 3 groups of dairy veterinarians with a favorable, a neutral and an unfavorable attitude towards antimicrobial use and selective dry cow treatment in the Netherlands

	Unfavorable (n=39)		Neutral (n=55)		Favorable (n=87)		Total (n=181)	
	no.	median or %	no.	median or %	no.	median or %	no.	median or %
Age[1]	35	50 (33-55)	41	43 (34-55)	81	39 (32-48)	157	42 (33-53)
Years since graduation[1]	35	22 (6-28)	45	15 (8-28)	82	13 (5-20)	162	15 (6-26)
Gender (male/female, %)	35	77/23	44	77/23	82	63/37	161	70/30
Region (north/central/south, %)	28	14/54/32	46	30/44/26	82	39/45/16	181	31/47/22
Number of dairy vets in the practice[1]	39	4 (3-5)[a] (mean: 4.1)	53	4 (3-6)[ab] (mean: 5.1)	86	4 (4-6)[b] (mean: 5.0)	178	4 (3-6) (mean: 5.1)
Number of dairy farms in the practice[1]	37	90 (60-150)[a]	50	90 (50-150)[a]	81	120 (80-180)[b]	168	110 (60-160)
Employer/employee (%)	35	66 / 34[a]	45	56 / 44[ab]	82	49 / 51[b]	162	55/45

[1] Values are medians (P25-P75)

[a-b] Percentages within a row with different superscript are statistically different ($P \leq 0.05$)

Attitude

The majority (92%) of the veterinarians agreed or partly agreed that it is important that AMU in the animal industry is restricted, and 89% considered that they can still be a good veterinarian when they use less antimicrobials (Table 2). Most of the 181 veterinarians believe that their farmers can still be a good farmer when using less antimicrobials (90% agreed or partly agreed). Of the respondents, 88% indicated that they actively encouraged their farmers to reduce AMU. Only 8% of the veterinarians (partly) agreed with the statement '*Since the introduction of SDCT, udder health has improved on the farms in my practice*'. Most veterinarians (89% agreed or partly agreed) see the advice they provided the farmers on SDCT as the best possible approach and are convinced that their farmers apply this SDCT approach (68% agreed or partly agreed). The opinions of veterinarians about the attitude of other veterinarians towards SDCT varied but was generally considered to be neutral to positive.

A substantial number of veterinarians indicated that '*Further increased consciousness of animal health and usage of veterinary medicines*', '*Chance to add value for the dairy farmer*', and '*Improving public health*' were among their perceived most positive aspects of reduction of AMU (Table 3). There were some significant differences with regard to positive aspects of reduction of AMU between the three groups. Veterinarians in the FAV group indicated '*Further increased consciousness of animal health and usage of veterinary medicines*', and '*Farmers have increased consciousness of animal health and usage of veterinary medicines*' significantly more often as a positive aspect of reduction of AMU compared to veterinarians in the UNF group (Table 3). The UNF group indicated '*Financial consequences for my farmers*', '*Improving animal health*', '*Improving the image of the dairy industry*', and '*Reducing antimicrobial resistance*' significantly more often as one of the top three of positive aspects of reduction of AMU as compared to the FAV group.

Table 2. Opinions of 181 dairy veterinarians on statements towards antimicrobial usage (AMU) in the animal industry and towards selective dry cow treatment (SDCT) in the Netherlands

	Disagree	Partly disagree	Ambivalent	Partly agree	Agree
It is important that AMU in the animal industry is restricted	1 (1%)	7 (4%)	6 (3%)	62 (34%)	105 (58%)
With less antimicrobials, I can still be a good veterinarian	2 (1%)	8 (4%)	10 (6%)	47 (26%)	114 (63%)
With less antimicrobials, my farmers can still be a good farmer	2 (1%)	10 (6%)	6 (3%)	55 (30%)	108 (60%)
I actively encouraged my farmers to reduce AMU on their farms	1 (1%)	5 (3%)	14 (8%)	50 (28%)	111 (60%)
I used the best possible approach in advicing my farmers on SDCT	4 (2%)	2 (1%)	15 (8%)	57 (32%)	103 (57%)
Since the introduction of SDCT, udder health has improved on the farms in my practice	1 (1%)	42 (23%)	124 (68%)	14 (8%)	0 (0%)
My farmers use the best possible approach on SDCT	2 (1%)	30 (17%)	26 (14%)	102 (56%)	21 (12%)
Other dairy veterinarians have a positive attitude towards SDCT	10 (6%)	28 (15%)	57 (32%)	64 (35%)	22 (12%)

With respect to the negative aspects of reduction of AMU, there were also some significant differences between the three evaluated groups. Two percent of the total group of veterinarians could not name a single negative aspect of the reduction of AMU. Overall, 73% of the veterinarians considered a '*Higher risk of sick cows*' as the most important negative aspect of reduction of AMU, followed by '*Limited choice of antimicrobials*' (60%). Some veterinarians answered that '*Lack of clarity about improvement of public health*' (36%) or '*Uncertainty whether a sick cow will recover without using antimicrobials*' (29%).

Table 3. The most important (top 3) positive aspects of the reduction of antimicrobial usage according to 181 dairy veterinarians in 2015 in the Netherlands. Veterinarians are categorized in unfavorable, neutral and favorable attitude towards reduction of antimicrobial use and selective dry cow treatment

Item	Unfavorable n=39	Neutral n=55	Favorable n=87	Total n=181
	% (95%CI)	% (95%CI)	% (95%CI)	% (95%CI)
Further increased consciousness of animal health and usage of veterinary medicines	69 (52-83)[a]	74 (60-85)[a]	89 (80-94)[b]	80 (73-86)
Chance to add value for the farmer	59 (42-74)	61 (47-74)	55 (44-66)	58 (50-65)
Improving public health	33 (19-50)	35 (23-49)	46 (35-57)	40 (33-48)
Farmers have increased consciousness of animal health and usage of veterinary medicines	18 (8-34)[a]	39 (26-53)[b]	51 (40-62)[b]	40 (33-48)
Improving animal health	39 (23-55)[a]	41 (28-55)[a]	21 (13-31)[b]	31 (24-38)
Improving farm management	13 (4-27)	6 (1-15)	16 (9-26)	12 (8-18)
Creating resilient cows	8 (2-21)	13 (5-25)	12 (6-20)	11 (7-17)
Less withholding of milk and meat	5 (1-17)	9 (3-20)	6 (2-13)	7 (4-11)
Reducing antimicrobial resistance	23 (11-39)[a]	0 (0-7)[b]	1 (0-6)[b]	6 (3-10)
Improving the image of the dairy industry	10 (3-24)[a]	6 (1-15)[a]	0 (0-4)[b]	4 (2-8)
Financial consequences for my farmers	5 (1-17)[a]	4 (1-13)[ab]	0 (0-4)[b]	2 (1-6)
Financial consequences for my veterinary practice	0 (0-9)	4 (1-13)	0 (0-4)	1 (0-4)

[a-b] Percentages within a row with different superscript are statistically different ($P \leq 0.05$)

Veterinarians with an UNF attitude significantly more often answered 'I feel pushed to follow the rules, although I do not agree with the policy' as compared to veterinarians in the FAV group. In addition, veterinarians with a FAV attitude significantly more often considered 'Risk of making the wrong choice about treatment of sick cows' as one of the most important negative aspects of reduction of AMU compared to the UNF group (Table 4).

Table 4. The most important (top 3) negative aspects of the reduction of antimicrobial usage according to 181 dairy veterinarians in the Netherlands. Veterinarians are categorized in unfavorable, neutral and favorable attitude towards reduction of antimicrobial use and selective dry cow treatment

	Unfavorable	Neutral	Favorable	Total
Item	n=39 % (95%CI)	n=55 % (95%CI)	n=87 % (95%CI)	n=181 % (95%CI)
Higher risk of sick cows	74 (58-87)	81 (68-91)	67 (56-76)	73 (66-79)
Limited choice of antimicrobials	56 (40-72)	57 (42-70)	64 (53-74)	60 (53-68)
Lack of clarity about improvement of public health	41 (26-58)	38 (25-52)	33 (24-44)	36 (29-44)
Uncertainty whether a sick cow will recover without using antimicrobials	15 (6-31)[a]	36 (23-50)[b]	30 (21-41)[ab]	29 (22-36)
Worries about animal health	26 (13-42)	26 (15-40)	14 (7-23)	20 (15-27)
Harder for farmers to take care of their dairy cows	13 (4-27)[ab]	21 (11-34)[a]	8 (3-16)[b]	13 (8-19)
I feel pushed to follow the rules, although I do not agree with the policy	28 (15-45)[a]	9 (3-21)[b]	2 (0-8)[b]	10 (6-15)
Risk of making the wrong choice about treatment of sick cows	0 (0-9)[a]	6 (1-16)[ab]	13 (7-22)[b]	8 (4-13)
Extra labor for the farmer	5 (1-17)	13 (6-25)	5 (1-11)	7 (4-12)
Financial consequences for my veterinary practice	10 (3-24)[a]	0 (0-7)[b]	7 (3-14)[ab]	6 (3-10)
No negative aspect at all	3 (0-14)	0 (0-7)	3 (1-10)	2 (1-6)
Changes in added value for me as veterinarian	0 (0-9)	0 (0-7)	2 (0-8)	1 (0-4)

[a-b] Percentages within a row with different superscript are statistically different ($P \leq 0.05$)

Multivariable analysis

In the univariable pre-screening model of the multivariable analysis, 12 of 25 parameters that were evaluated for their association with the veterinarians' attitude had a *P*-value < 0.25 and subsequently entered the multivariable model (FAV versus NEU/UNF).

The final multivariable model contained three positive and three negative aspects of reduction of AMU. The final model had the lowest possible AIC, showed no evidence of incorrectness of the fitted model (*P*-value = 0.20) and explained 20% of the variation in attitude of veterinarians (pseudo R^2 = 0.20). Veterinarians who indicated "*Farmers have increased consciousness of animal health and usage of veterinary medicines*" as one of the most important positive aspects of reduction of AMU and SDCT had a 5.7 times higher odds to belong to the FAV group compared to veterinarians that did not indicate this positive aspect. In addition, veterinarians who indicated "*Reducing AMR*" as one of the most important positive aspects of reduction of AMU and SDCT had a 5 times higher odds to belong to the FAV group. Veterinarians who indicated "*I feel pushed to follow the rules, although I do not agree with the policy*" as one of the most important negative aspects of reduction of AMU and SDCT had a 10 times lower odds to belong to the FAV group as compared to veterinarians that did not indicate this negative aspect (Table 5).

Table 5. Results of a multivariable logistic regression analysis of the association between the attitude of veterinarians and the most positive and negative aspects indicated by them on the changed approach of antimicrobial usage and selective dry cow treatment in the Netherlands. Veterinarians that had a favorable attitude towards this change (n=87) were compared to those that did not have a favorable attitude (n=94)

	Multivariable OR[1] (95% CI)	P-value
Positive aspects		
Chance to add value for the farmer	3.2 (1.5;6.8)	0.002
Reducing antimicrobial resistance	5.0 (2.2;11.6)	0.000
Farmers have increased consciousness of animal health and usage of veterinary medicines	5.7 (2.1;15.3)	0.001
Negative aspects		
Pushed to follow the rules, although I do not agree with the policy	0.1 (0.0;0.4)	0.002
Worries about animal health	0.3 (0.1;0.8)	0.016
Higher risk of sick cows	0.4 (0.2;1.0)	0.039

[1] OR = odds ratio

DISCUSSION

The aim of this study was to provide insight into the attitude of Dutch dairy veterinarians towards reduction of AMU and towards SDCT. The results showed that Dutch veterinarians in general had a positive attitude towards reduction of AMU and towards SDCT. Selective DCT was taken up progressively, with 92% of the veterinarians expressing they considered reducing AMU as important and 88% claiming to have actively encouraged their farmers to reduce AMU on their farms. Thus, the majority of veterinarians seemed to have a positive attitude towards the changed AMU policy, which was reflected by quotes, such as *"I am positive about the [changed antibiotic] policy. For me the antibiotic policy may even be more strict, because there are still dairy farmers and veterinarians that could improve by implementing certain preventive measures rather than using antibiotics."* Nevertheless, we must realize that a number of respondents were reluctant about the changed policies. This was reflected by their answers and subsequently illustrated by quotes as *"I am annoyed by the army of profiting auditors* *who think they have an important task by checking veterinarians. The dairy farmers believe this serves only the employment of the auditors, which they have to pay."* and *"I have the feeling that the committee that determines which antimicrobials can be used is paid by the industry, they do not care about integrity, and lack practical experience."* In addition to these reactions, there are also veterinarians that generally endorsed the policy but nevertheless showed concerns which was reflected by quotes like *"I fully support the reduction of antimicrobials and completely endorse the guideline on SDCT. However, the way in which the Dutch Food and Consumer Product Safety Authority (NVWA) maintains this policy and tightens the norms and rules is not good. The possibility of being sued or fined while you honestly and sincerely do your job annoys me."*. Whether or not this is rightly so, it indicates that for succesfull adoption of rules and regulations and implementation of changed behavior, proper communication to all involved parties is crucial.

In our study, we classified veterinarians into three groups based on their opinion with regard to four statements on AMU and SDCT. Veterinarians in the FAV group seemed to be more focussed on the importance of being conscious of animal health and on optimizing usage of veterinary medicines by both, themselves and their farmers, compared to veterinarians that were less favorable. Several studies have stressed the importance of farmers' compliance to implement preventive strategies on the farm to reduce diseases and AMU in livestock animals, and the important role of veterinarians as advisors for farmers herein (Friedman et al., 2007, Cattaneo et al., 2009). Our findings on differences between veterinarians in the FAV and the UNF group, show that the former seem to have a mindset in which long term consequences for farmers and society play a more important role as compared to short term effects. With this attitude they are likely to have a positive effect on their farmers as well, with a higher probability of success in further implementation of prudent AMU. Veterinarians with a FAV attitude were more proactive and willing to keep their farmers engaged to the changed antimicrobial policy, whereas the veterinarians with an UNF attitude were mainly complaining and focusing on the negative effects of reducing AMU. With respect to the consequences of the changed approach of AMU for animal diseases, individual positive and negative experiences with the use of SDCT may have influenced the veterinarians' attitude.

Earlier work of Higgins et al. (2014) described that it is important for veterinarians to be homogenous in clinical beliefs (expectations and demands) in order to optimize their influence on disease control and mastitis management. As Jansen et al. (2010) showed, there are different types of farmers based on their trust in external information sources regarding mastitis management, and their orientation toward the outside world. To effectively change mastitis management and DCT decisions it is important for veterinarians to approach different types of farmers in a different way and through different canals, which asks a proactive approach.

In theory, veterinarians are the ideal advisors on udder health and dry cow management including DCT. In daily practice, however, there seems room for improvement. Although most veterinarians have the intention of working proactively on reducing AMU, feel that a constructive approach of this issue comes within their professional remit, and consider encouraging their farmers is an important task, their actual behavior is sometimes different.

This ambiguity between their intentions and the actual behavior is described in earlier work from Lam et al. (2011). Given the apparent influence of veterinarians on the attitude of farmers and the differences found between the attitude of veterinarians, different types of veterinarians also seem to need different approaches from program organizers, to effectively improve prudent AMU on dairy farms.

Our questionnaire was executed in March and April 2015 and included questions on the attitude of the veterinarians in 2013 with respect to their advice on herd health management and on SDCT. Hence, some recall bias may have occurred. However, behavior and attitude does not change easily (Hardeman et al., 2002), and we assumed the attitudes measured had not changed tremendously between 2013 and the moment the questionnaire was conducted.

Our results did not show significant differences between the veterinarians with an UNF and FAV attitude towards reduction of AMU and SDCT with regard to the demographic parameters 'age' and 'years since graduation', although a trend can be recognized that veterinarians in the FAV group seemed to be younger and had less working experience. We did find that veterinarians working in larger practices generally were more positive on the changed policy than those working in smaller practices. Recent work by Higgins et al. (2017) proposed that when considering how to best facilitate a change from BDCT to SDCT, a multifaceted approach should be used that clearly recognizes that the issues hampering this change are markedly different between veterinarians at different stages of their career. Subsequently, it seems recommendable for veterinarians to work in groups, with senior veterinarians in a leading role, in order to change their own and their farmers' behavior with respect to issues such as AMU. We found, however, indications that younger veterinarians are more favorable to change than the older generation, as was earlier described by (Speksnijder et al., 2015a). From the perspective of the work of Higgins et al. (2017) composition of groups of veterinarians needs explicit thought with an important role for senior veterinarians, which therefore may need specific attention. How veterinary practices are organized is up to the veterinarians, but it may be of interest for program organizers at a regional or national level to take this effect into account.

The multivariable analysis showed that the most important negative aspect, contributing to an UNF attitude towards reduction in AMU and towards SDCT, was the perception that they were forced to follow the rules while they did not agree with the policy. This indicates that there is a group of veterinarians that has a negative mindset towards the chancing policy on AMU and is not willing to change their behavior related to the subject. This mindset seems comparable to that of the 'reclusive traditionalist' among dairy farmers, as described by Jansen et al. (2010). These are mainly inward oriented people, that generally do not like interference of externals and do not seek alliance with others. Specific attention needs to be given to this group of veterinarians by program organizers, to change their attitude towards reduction of AMU and towards SDCT or to compensate that effect in another way, in order to make those programs successful.

CONCLUSIONS

The attitude of Dutch dairy veterinarians with respect to the reduction of AMU and specifically to SDCT was found to be generally positive, although there was a small group of veterinarians that was negative about these changes. Veterinarians working in larger practices generally had a more positive attitude towards the changed AMU policy than those working in smaller practices. Given the influence veterinarians potentially have on the attitude of farmers, and given the variability found in their attitude and behavior, veterinarians need specific attention by program organizers trying to encourage prudent AMU and SDCT.

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Chapter 7

General Discussion

INTRODUCTION

Worldwide, dry cow management and the use of dry cow treatment (**DCT**), often with antimicrobials, is an essential part of the dairy farmer's routine to ensure health and welfare of the dairy cow in the dry period, which is a high risk time for acquisition of new bacterial infections. The periods directly following drying-off and before calving are associated with an increased susceptibility to new intramammary infections (**IMI**) (Oliver and Mitchell, 1983; Smith et al., 1985). This period of non-lactation allows producers to use dry cow antimicrobials, without needing to discard milk due to antibiotic residues, in an attempt to eliminate existing IMI and provide protection against new IMI during the early dry period (Natzke, 1981).

Drying-off a cow actually means the cessation of milking which can be done in an abrupt or gradual way. After milking has stopped, the intramammary pressure increases, milk products accumulate in the gland, and further milk secretion is inhibited. In the dairy industry, over the years, the blanket DCT (**BDCT**) approach, treating all cows with antimicrobials at drying-off, made that 'drying-off' became synonymous with infusion of long-acting antimicrobials, the so called dry-cow tubes. Insertion of these dry-cow tubes does, in spite of what sometimes is thought, not stop the cow from producing milk. In this thesis the term drying-off is used in its actual meaning, independent of whether or not antimicrobials are used. If antimicrobials are applied at drying-off, this is described as dry cow treatment.

Dry cow antimicrobial therapy was first used in the early 1950s to prevent *Trueperella* (formerly *Corynebacterium*) *pyogenes* infections, known as summer mastitis (Pearson, 1950; 1951). These infections were common during the dry period and often resulted in the death of affected animals or lead to a non-productive quarter with obvious economic consequences. Earlier research had highlighted the dry period as a risk in terms of acquisition of many new IMI including coliforms and *T. pyogenes* (Neave et al., 1950).

The dry period is a time of big changes for the dairy cow, not in the least for the mammary gland. Generally speaking, there are 3 stages in the mammary gland during the dry period, 2 of which are periods of increased susceptibility to infection. The first of these occurs immediately following drying-off in the first 3 weeks of the dry period (involution) and the second period is immediately prior to and just after calving (colostrogenesis) (Figure 1). IMI that occur during the dry period may lead to clinical mastitis (**CM**) cases during the subsequent lactation as do IMI that occur during the post-calving period.

During the past decades, BDCT was adopted as one of the recommendations in the mastitis control plan (later called the 'Five Point Plan') of the National Institute for Research in Dairying (NIRD) / Central Veterinary Laboratory in the United Kingdom (Neave et al., 1966; Smith et al., 1967). In a short period of time, BDCT resulted in a substantial reduction in subclinically infected quarters. From that time, antibiotic formulations in a long-acting oil base in tubes to be inserted into the teat further improved quality and were used in many countries, specifically in Europe, Oceania and Northern America. The Nordic countries, however, took a different approach by only treating cows known to have IMI, i.e., therapeutic use only instead of preventive use, which nowadays is described as selective DCT (**SDCT**). In the Nordic countries concerns were raised with respect to administering antimicrobials to all cows, because it may lead to the development of antimicrobial resistance (**AMR**) in both animal and human populations (Bratlie, 1972). From that time, more research was initiated to study the effects of selecting cows for DCT.

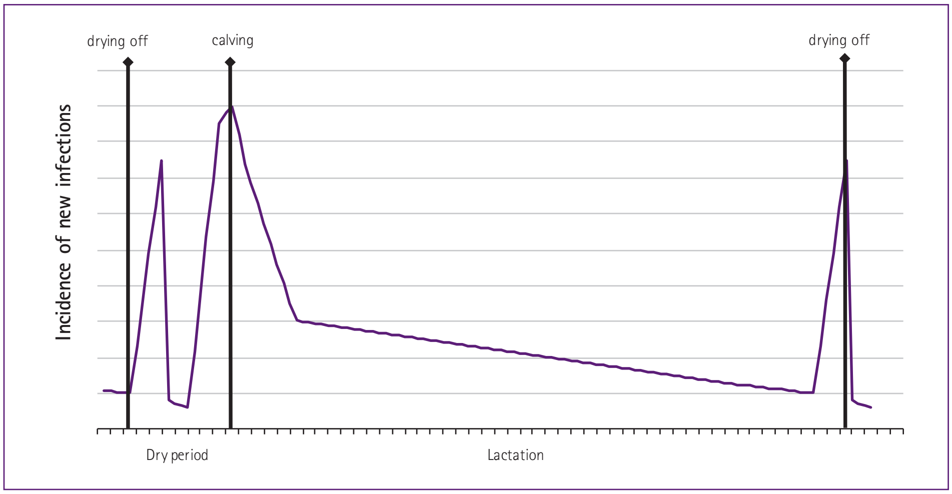

Figure 1. Incidence of new intramammary infections during the dry period (Adapted from Green et al., 2002).

In many other countries SDCT was also evaluated (Table 1), generally based on the infection status at the time of drying-off. In these studies generally 2 types of study designs were used to evaluate the curative and preventive effects of selecting cows for DCT. The curative effect was evaluated using a design that treated only those cows that were identified to have an IMI (Bratlie, 1973; Rindsig et al., 1978). The infection rate of new IMI was determined in not treated, as well as in treated cows. In the latter group the cure rate was also evaluated. The preventive effect was evaluated in studies using a design in which all cows with an identified IMI were treated with antimicrobials, while the non-infected cows were randomly dried-off with or without DCT (Browning et al., 1994). An example is the study from Norway, where treatment was randomly assigned to cows with an identified IMI (Osteras et al., 1994). This study design was specifically used in the Nordic countries, because in these countries, not only the use of DCT in uninfected cows, but also in infected cows lead to concerns (Whist et al., 2007).

An overview of the studies on SDCT done in the period 1973-2011 is presented in Table 1. In the briefly described study designs criteria for cows to be assigned to the case or the control group are presented, being mostly the infection status of the cow or the quarter at the time of drying-off.

Table 1. Chronologic overview of literature on selective dry cow therapy with different approaches for selection of cows for dry cow therapy from 1973-2011

Study (year)	Origin[1]	Number of herds/cows	Type I[2]	Type II[3]	Conclusion(s)
Bratlie, 1973	UK	48/746	+		BDCT gives better cure rate than noDCT
Rindsig et al., 1978	USA	1/232	+		SDCT did not improve udder health
Robinson et al., 1988	UK	6/1800	+	+	SDCT gives more infections after calving
Browning et al., 1994	Australia	12/1044	+		No difference in cure rate between BDCT and SDCT
Østerås et al., 1994	Norway	288/684	+		It is important to treat identified IMI at drying-off
Williamson et al., 1995	New Zealand	4/378		+	BDCT protects better against *S. uberis* than noDCT
Hassan et al., 1999	Australia	3/150		+	BDCT protects better than no DCT
Berry et al., 2002	UK	4/290		+	BDCT protects better than no DCT
Whist et al., 2007	Norway	178	+		BDCT gives better cure rate than noDCT
Rajala-Schultz et al., 2011	USA	4/1937		+	BDCT protects better than SDCT

[1]UK = United Kingdom, USA = United States of America
[2]Type I design = study on curative effect of DCT
[3]Type II design = study on preventive effect of DCT

Every country or region has its own type of dairy industry, its own udder health situation and its own approach of mastitis management and antimicrobial use (**AMU**). A lot of factors contribute to the dynamics of IMI, such as housing, hygiene, production level, pasture based grazing, herd size, season and weather circumstances, calving season, et cetera. Comparing different countries, their udder health epidemiology, and the effect of approaches such as selective or blanket DCT, may therefore lead to biases. Additionally, at the herd-level effects such as herd immunity and type of predominant pathogen should also be taken into account when evaluating SDCT. These findings indicate that conclusions from different studies and in different countries cannot simply be extrapolated. Each country, and probably each herd needs to give specific attention to its own specific situation.
The objectives of this thesis were to quantify the effects of SDCT on clinical and subclinical mastitis, AMU and economics in the Netherlands. Additionally the effect of different SCC threshold-scenarios for selecting cows for DCT on these parameters has been evaluated. The

economic consequences of using different levels of AMU in DCT has been evaluated as well as the attitude of the dairy farmer and the veterinarian with respect to reduction of AMU and of SDCT. During the execution of this study BDCT changed to SDCT in the Netherlands and all of the aforementioned aspects were evaluated in the perspective of this transition.

SOCIETAL AND POLITICAL BACKGROUND IN THE NETHERLANDS; DEVELOPMENTS UNTIL 2013

In the Netherlands AMU in animal husbandry has been subject of political debate for quite some time. In 1998 a national surveillance program on AMU and AMR in animal husbandry in the Netherlands was started and in 2006 the use of antibiotic growth promoters was prohibited. Parallel with the prohibition of the use of antibiotic growth promoters, veterinary AMU in the Netherlands increased markedly. During the same period, AMR problems, such as methicillin resistant *Staphylococcus aureus* (MRSA) (de Neeling et al., 2007) and extended spectrum beta-lactamase producing bacteria (ESBLs) (Leverstein-van Hall et al., 2011) occurred and subsequently the political debate increased. In 2008, the Dutch parliament decided that the national veterinary AMU had to decrease to the level of 1999. A goal was set to reduce veterinary AMU with 20% in 2011 and with 50% in 2013, as compared to 2009 (Speksnijder et al., 2015b). It was indicated that the livestock sector itself had the responsibility to realize this reduction. Thus, a taskforce on AMR in animal husbandry was established for the major livestock production sectors, in which the major stakeholders in these sectors, participated. Although the dairy sector was not the sector in which most antimicrobials were used or that seemed to have a big AMR problem, there were some issues there too that had to be solved (MARAN, 2008) and a specific working group on reducing and optimizing AMU in cattle was initiated (ABRES Rund). The efforts of this taskforce resulted in a first reduction in AMU (MARAN, 2011). Additionally, in June 2011 an independent Veterinary Drug Authority (SDa) was founded with the task to monitor and judge national trends in AMU in animal husbandry.

PRUDENT USE OF ANTIMICROBIALS

Prudent AMU requires evidence based justification of DCT protocols. This thesis, specifically Chapter 2 and 3, underlines that BDCT cannot be interpreted as prudent use and that DCT is only indicated for specific cows with a proven infection at drying-off.

A correlation between quantities of AMU at the country level, and development of AMR has been described in food producing animals (Chantziaras et al., 2014) as well as in human medicine (Bronzwaer et al., 2002). These studies show a clear correlation between AMU and AMR, indicating that prudent antimicrobial use should lead to the use of as little antimicrobials as possible which is in accordance with the current status of the World Health Organization. Although for the use of DCT in the dairy industry, evidence is lacking to support a widespread, emerging resistance among mastitis pathogens to antimicrobials due to DCT (Erskine et al., 2002; Barlow, 2011), prudent AMU also asks for restricted AMU in this subject.

Rethinking the AMU in animals in general and specifically the use of dry cow antimicrobials in treating subclinical infection in cows at drying-off is essential for farmers and veterinarians to maintain a society provided 'license to produce'. Thus, further studies on the rationality of AMU at drying-off are warranted, focusing on minimizing AMU at the national level, while leaving room for necessary treatment at the individual level. This should lead to a practical approach for farmers in specific herd-situations, including attention for quarter-, cow- and herd-level factors in order to be broadly implemented. The Nordic countries, however, showed that it is possible not to apply BDCT without deteriorating the udder health situation. Based on the experience, the given political situation and the principles of prudent AMU in the Netherlands, a new situation with respect to AMU at drying-off had to be developed.

SELECTING COWS FOR DRY COW TREATMENT

In daily practice different criteria can be used to select cows for DCT. Decision-making can be done on herd level (e.g. bulk tank somatic cell count (**BTSCC**)), cow level (e.g. somatic cell count (**SCC**), CM history, parity) or quarter level (e.g. SCC, teat end condition). Often used are bacteriological culture (Robinson et al., 1988; Browning et al., 1990), SCC and/or CM history (Rindsig et al., 1978; Torres et al., 2008; Rajala-Schultz et al., 2011). Additionally, the California Mastitis Test (Rindsig et al., 1978; Bhutto et al., 2012), N-acetyl-ß-D-glucosaminidase (Hassan et al., 1999) and conductivity can be used, all with a different accuracies in identification of infected cows. Bacteriological culture can be used to get more insight in the infection status at drying-off and is routinely available in the Netherlands. Most Dutch dairy farmers (85%), however, do not use bacteriological culturing at drying-off, mainly because of the long time to result (Griffioen et al., 2016). For optimal decision-making, the dairy farmer has a need for a diagnostic test to determine the infection status at drying-off that preferably is cheap, easy to use, accurate, and has a quick result. When used to diagnose IMI in cows with a low SCC (< 200,000 cells/mL) before drying off in low-BTSCC herds (< 250,000 cells/mL), a Petrifilm-based on-farm culture system for SDCT performed well, with a sensitivity of 85% and specificity of 73% (Cameron et al., 2013). Selecting cows for DCT with Petrifilm did not affect the risk of IMI at calving or the risk of a first case of clinical mastitis in the first 120 days of lactation when compared with BDCT (Cameron et al., 2014).

Selection of cows for treatment with dry cow antibiotics, based on their SCC on the last milk recording before drying-off, was evaluated in a large field trial using a split-udder design in low-SCC cows (**Chapter 2**). A substantial reduction in antibiotic use was found, with an increase in CM, subclinical mastitis and culture positive quarters. In this study the last available SCC value before drying-off was evaluated as a diagnostic tool for selection for DCT. In practice, measuring SCC is widely adopted in the Netherlands, and the application of SCC is easily available for selecting cows for DCT. This may conflict with situations in other countries, where data on SCC on cow-level are not routinely available. In our study as well as in daily practice, using the theoretical optimal approach, bacteriological culturing was not realistic, both from a logistical, as well as a financial perspective.

Diagnostic sensitivity of a single SCC measurement to diagnose an IMI has been reported to range between 57.4% and 74.5% (Schepers et al., 1997; Sargeant et al., 2001), meaning that between 42.6% and 25.5% of infected cows in a SCC-based SDCT program would go undetected and untreated at drying-off. The sensitivity of using a SCC cut-off of < 200,000 cells/mL to identify infected cows or quarters has been reported to be 69.7% and 62,4% respectively (Torres et al., 2008; Pantoja et al., 2009). Thus, because monitoring udder health performance and making decisions on treatments is impossible without reliable and affordable diagnostic methods we used SCC based on DHI in this study.

THE EFFECT OF SDCT ON UDDER HEALTH

In quarters from cows with a low-SCC at drying-off that were not treated with DCT, the incidence rate of CM (**IRCM**) was 1.7 times higher than in quarters dried off with antibiotics. The highest IRCM was found during the first 100 days of lactation, with *S. uberis* as the predominant organism causing CM. This is similar to previous work on the incidence of new IMI and prevalence of *S. uberis* in the dry period (Williamson et al., 1995; Berry and Hillerton, 2002). Somatic cell count and the percentage of quarters with an SCC >200,000 cells/mL at dry-off and 14 DIM were significantly higher in quarters dried off without antibiotics. An elevated SCC or being culture positive for major pathogens at drying-off was associated with a higher percentage of quarters with an elevated SCC at 14 days in lactation. Being culture positive for major pathogens at drying-off was neither significantly associated with clinical and subclinical mastitis during the period of study.

Results from the field study revealed a high IRCM in the dry period. From all CM cases in the study period (from dry-off until 100 DIM), 19% and 8% of the CM cases were manifest in the dry period in quarters that were treated without and with dry cow antimicrobials, respectively. This may be due to the intensive observations of the farmers during the field phase which probably is not reflecting what is commonly done in daily practice. There may therefore, be a diagnostic basis, either in our study or in daily practice by underestimating the incidence of CM during the dry period because of a lack of attention and observations of dry cows.

In this field study, variation in the treatment groups due to herd or cow factors was considered to be minimal because of the split-udder design. The benefit of a split-udder design is that cow- and herd-level factors are the same for both groups and cannot influence the results. Both groups of quarters have the same genetic background, have the same ration, are milked by the same farmer and milking machine, experience the same environmental circumstances and so on. A disadvantage of the split-udder design is that quarters dried off with or without antibiotics may influence each other, possibly leading to an underestimation of effect (Lam et al., 1996). Due to the advantages mentioned, however, a within-cow comparison is an often used approach in these types of studies (Schukken et al., 1993; Bradley et al., 2010). Additionally, the financial aspect of performing field studies should be taken into account as well. The budget allowed a split udder design, based on which we build a model which was parameterized with field data from this large trial. Making a power calculation for a trial with a between-cow comparison or a between-herd comparison lead to numbers of herds and cows that were not affordable and could not have been executed.

EFFECT OF DIFFERENT SCC-SCENARIOS FOR SDCT AT HERD LEVEL

Because different age groups have different characteristics with regard to the dry period and udder health, cows in first and later lactation need to be judged separately. The youngest group is the group of animals after their first calving. At the end of their first lactation these animals are dried off. Mastitis in their first dry period, and 100 DIM after (their second) calving is related to the DCT at the end of their first lactation. Multiparous cows are animals that had calved at least twice. Although different terms were used throughout this thesis, in the general discussion, terminology related to parity was considered as parity at drying off.

The impact of SDCT as compared to BDCT on udder health, antimicrobial usage and economics is influenced by the SCC criteria used to select cows for DCT (**Chapter 3**). The SCC criteria chosen for heifers and cows not only affect quantifiable parameters, such as udder health, AMU and economics, but also non-quantifiable parameters, such as welfare and practical achievability. Dependent on the weight given to these parameters optimal selection criteria should be chosen when implementing SDCT. Our findings showed that for the different scenarios chosen, the herd-level IRCM as well as the prevalence of SCM at 14 DIM did not vary extremely. Although literature shows that the effect of SDCT is bigger in multiparous than in primiparous cows (Fox, 2009; Santman-Berends et al., 2012), these findings seems to indicate that with respect to udder health and the associated costs, how exactly cows are selected for DCT is not very important. Over the scenarios, total AMU, including CM treatment, however, varied substantially, leading to a maximum difference in AMU of 60% when compared to BDCT.

Herds may differ in their udder health management and pathogen prevalence and thus the effects of DCT can be very different between herds (Hassan et al., 1999; Rajala-Schultz et al., 2011). Recalculating the effect of CM and SCM from quarter to cow and herd level of our data, that were based on the within cow comparison in the field trial, probably may lead to an underestimation of effect. Because these biases likely are equal for the different scenarios evaluated, comparison of different scenarios is possible, and the relative ranking seems robust. We chose a deterministic approach for our model and thus cannot claim statistical differences between scenarios.

The herd-level effect of SDCT on CM was also evaluated in another study, in which the percentage of cows with CM in the first 90 DIM for BDCT-herds (**BCT**), SDCT-herds with high DCT use (**SCT_HU**) and SDCT-herds with low DCT use (**SCT_LU**) was compared (Santman-Berends et al., 2015; Santman-Berends et al., 2016). Herd-level evaluation of AMU for DCT and CM-incidence indicated that IRCM in early lactation did not significantly differ between the three groups (figure 2), underlining that the effect of applying different approaches of SDCT does have a limited effect on udder health as compared to applying BDCT, whereas there is a substantial effect on AMU (Santman-Berends et al., 2016).

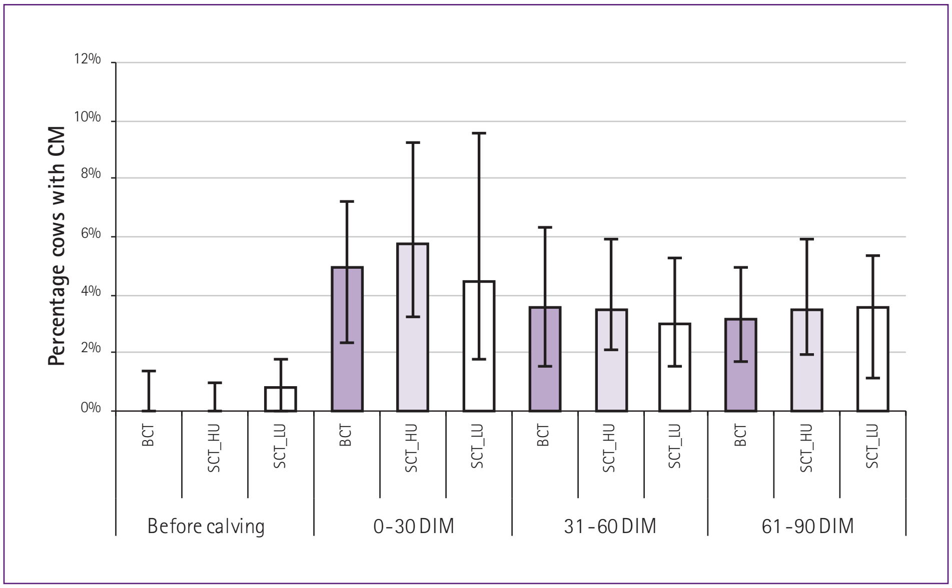

Figure 2. Median percentage of cows with clinical mastitis per DCT-approach.

ECONOMIC CONSEQUENCES OF SDCT

For many years applying BDCT was seen in daily practice as an ideal way to prevent mastitis problems and the related economic consequences. Although differences between different DCT approaches were small and differ per BTSCC level, SDCT was found to be economically beneficial over BDCT, with greater economic profits in herds with a lower IRCM and lower BTSCC (**Chapter 4**). In all types of herds, however, the use of dry cow antimicrobials can be reduced without economic consequences. In herds with low IRCM, using no dry cow antimicrobials at all is cheaper than BDCT, with SDCT being the optimum. The economic impact of improvement of udder health, both the IRCM and the BTSCC, is bigger than the effect of the DCT approach. Altogether, economics is not an argument against reduction of the use of dry cow antimicrobials by applying SDCT, while it is an argument to improve udder health.

FARMER' AND VETERINARIANS' ATTITUDE

Selective DCT was taken up quickly by Dutch farmers, with 75% of them implementing SDCT in 2013 (**Chapter 5**). Farmers that either strongly disagreed or were neutral with regard to the statement 'I do not have a problem with the (potential) negative consequences of SDCT' had a significantly higher odds to apply BDCT as compared to farmers that strongly agreed with this statement. This underlines the finding that application of SDCT was found to be highly associated with farmers' attitude. Nevertheless, the mindset of farmers in general with respect to reduction of AMU and the implementation of SDCT was positive.

The attitude of Dutch dairy veterinarians with respect to the reduction of AMU and specifically to SDCT was found to be generally positive, although there was a small group of veterinarians that was very negative about these changes (**Chapter 6**). Selective DCT was taken up progressively, with 92% of the veterinarians indicating they considered reducing AMU as important and 88% claiming to have actively stimulated their farmers to reduce AMU on their farms. Veterinarians working in larger practices generally had a more positive attitude towards the changed AMU policy than those working in smaller practices. Given the influence veterinarians potentially have on the attitude of farmers, and given the variability found in their attitude and behavior, veterinarians need specific attention by program organizers trying to stimulate prudent AMU and SDCT.

As described by Lam et al. (2017) both, the mindset of farmers and veterinarians are important to change actual behavior of farmers. The veterinarians' attitude may give rational arguments as well as influences social pressure. That, together with rules and regulations from the government and tools provided by the taskforce on AMU in cattle may have an important effect on actual behavior.

In the studies described in this thesis, the mindset of both, farmers and veterinarian was evaluated. A remarkable finding was that farmers seemed to be more adaptable to change than expected by veterinarians (Table 3).

The comparison of the survey results from the dairy farmers with the results of the survey of dairy veterinarians (Table 3) shows that considerably more dairy farms selected cows for DCT in 2013 already (75%) than the dairy veterinarians thought (37%). It appears that dairy farmers are much more positive towards the changed policy of restricted AMU than the veterinarians expected. Dairy farmers expected fewer problems due to SDCT than the veterinarians thought they did. For example, veterinarians estimated 35% of dairy farmers experienced a (strong) deterioration of udder health, while in fact only 14% of dairy farmers experienced this. It should, however, be kept in mind that the veterinarians were asked to estimate the answers of the Dutch dairy farmer 'in general', and not their own customers. Nevertheless, differences found are remarkably large, indicating veterinarians are not fully aware of the opinions of dairy farmers with respect to AMU and DCT.

The surveys also showed that veterinarians are aware of their own important role in farmers' AMU, but that they may do not properly assess the attitude of dairy farmers, or exactly understand the considerations that farmers take into account selecting cows for DCT. Veterinarians estimated that 70% and 50% of dairy farmers took CM history and milk production at drying-off into account when selecting cows for DCT respectively, while in fact this was 20% respectively 10%. These findings indicate veterinarians may improve their knowledge on what farmers actually think on issues such as AMU.

Table 3. A number of important findings from a survey of dairy farmers' attitude towards antibiotic use in dairy cows and the estimation of dairy veterinarians about what these dairy farmers would answer.

	Percentage of dairy farmers that (partially) agrees with the statement or carries out the measurement	Estimation of dairy veterinarians of the percentage of dairy farmers that (partially) agrees with the statement or carries out the measurement
It is important that the usage of antimicrobials in the animal industry is restricted	87	85
I do not have a problem with the (potential) negative consequences of selective dry cow treatment	36	20
I applied selective dry cow therapy 2013	75	37
When I have questions about dry cow therapy, the veterinarian is my main advisor	85	85
I cannot name a single negative aspect of reducing AMU	11	5
Reduction of AMU leads to a higher risk of sick cows	10	50
Criteria to select cows for dry cow treatment:		
All SCC-records from previous lactation	52	40
Last SCC-record before dry-off	27	30
Clinical mastitis history	20	70
Milk yield at dry-off	10	50
Since the introduction of SDCT on my farm, udder health has:		
Improved	21	10
Remained the same	61	50
Deteriorated	10	25
Strongly deteriorated	4	10

DEVELOPMENTS OVER TIME IN REAL LIFE

ANTIMICROBIAL SALES DATA

Based on data supplied by FIDIN, representing the veterinary pharmaceutical industry in the Netherlands, the percentage of cows treated with antibiotics at drying off was calculated, thereby using the actual number of dairy cows >2 years in the Netherlands. It was assumed the calving interval (410 days) was constant over the years and that when a cow was dried-off, 4 antimicrobial tubes were applied per cow. During 2008-2016 the percentage of cows that were dried-off with antibiotics decreased with 48%, from 77% in 2008 to 29% in 2015 (Figure 3).

Figure 3. Percentage of cows dried-off with antimicrobial dry cow treatment from 2008-2016

UDDER HEALTH IN THE NETHERLANDS

In April 2015, the milk quota were abolished and the number of dairy cows increased in 2016 with 6% as compared to 2015. To prevent an increase in the phosphate surplus of the dairy sector a new legislation was introduced in the Netherlands in 2017: the dairy farming act. Since the introduction of this act, growth is only possible when it is bound to land. In addition, each farmer in the Netherlands is allocated a certain amount of phosphate rights, based on the total number of dairy cows that were present on the farm in 2014, and, therefore, some more cows were culled as compared to the averages of other years. These dynamics in the Dutch dairy sector were taken into account by the Dutch Animal Health Monitor, that combines routinely collected cattle census data (Santman-Berends et al., 2016).

In the period 2013-2016, the trend in the percentage of herds with >25% new infections in fresh multiparous cows increased with 2%, varying from 7% in 2013 to 9% in 2016 (figure 4). Over these years, AMU for DCT decreased remarkably. The preventive effect of DCT on new IMI in the dry period was affected, however, not as much as the substantial decrease in AMU at drying-off. Apparently, this was compensated differently. Much attention, however, is needed for other preventive measurements in (the environment of) the dry period, such as immunology of the cow, housing and hygiene in order to break this trend.

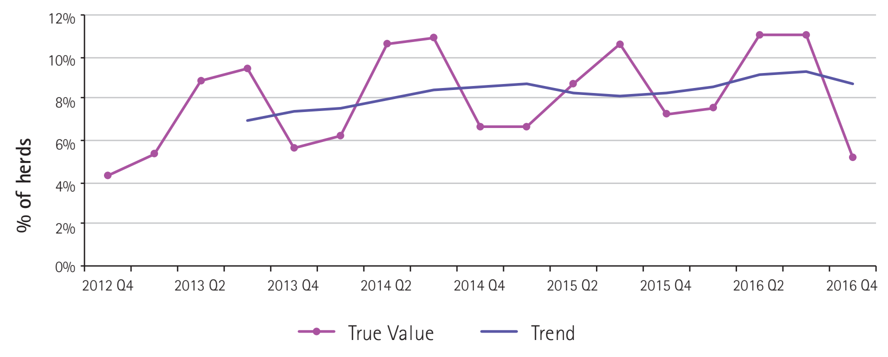

Figure 4. Herds with > 25% new intramammary infections in fresh multiparous cows from 2012-2016 in the Netherlands (Source: GD Diergezondheidsmonitoring)

In spite of a substantial decrease in AMU at drying-off and in general in dairy, udder health based on BTSCC and cows with elevated SCC improved rather than deteriorated (figure 5 and 6). The BTSCC decreased from 220,000 cells/mL in 2007 to 185,000 cells/mL in 2016 and the percentage of cows with an elevated SCC decreased from 24% in 2007 to 18% in 2016. This indicates that, although AMU at drying-off decreased substantially, farmers progressively found alternatives for AMU at drying-off to prevent IMI during the subsequent lactation in their cows.

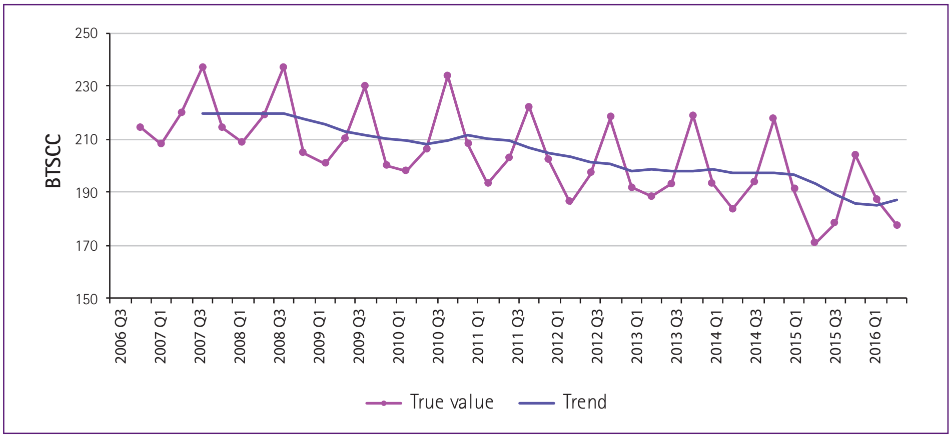

Figure 5. Bulk tank somatic cell count (BTSCC) from 2006-2016 in the Netherlands (Source: GD Diergezondheidsmonitoring)

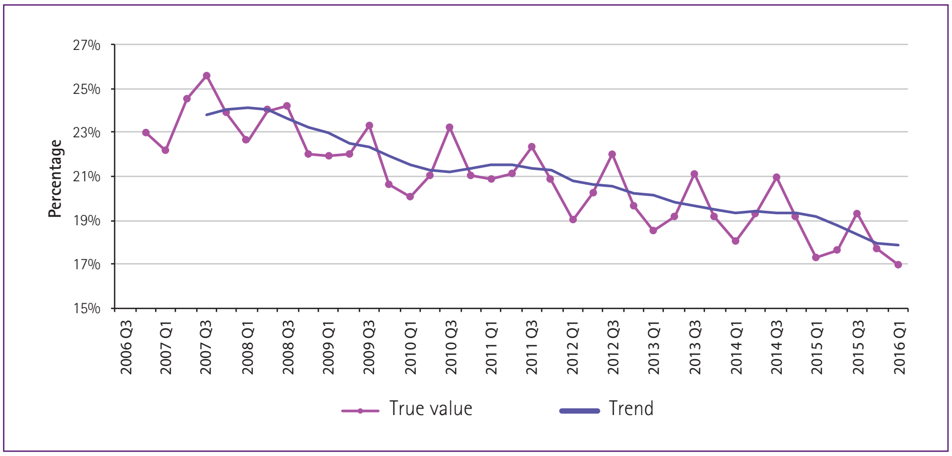

Figure 6. Percentage of cows with an elevated cow-level somatic cell count from 2006-2016 in the Netherlands (Source: GD Diergezondheidsmonitoring)

SELECTIVE DRY COW TREATMENT THROUGHOUT THE EU

It seems that in the Netherlands, a large proportion of farmers apply SDCT. As described above, over the years, DCT was evaluated in several European countries. In order to have an idea on developments in Europe in recent years, 13 experts in the field of mastitis from different European countries were asked about DCT approaches in their country, with respect to the percentage of farms that applies SDCT, whether selection for DCT is made on cow- or quarter-level, what the most used selection criteria for selection of cows for DCT were, and what percentage of herds is able to manage a successful selection of cows for SDCT. Except for the Nordic countries and the Netherlands, BDCT was found to be the most used approach in Europe (Table 2).

Table 2. Estimates of approaches of dry cow treatment in different European countries based on expert opinions; Belgium (B), Switzerland (CH), Germany (D), Denmark (DK), Spain (E), Finland (FIN), Hungary (H), Italy (I), the Netherlands (NL), Portugal (P), Poland (PL), Sweden (S), and the United Kingdom (UK).

	B	CH	D	DK	E	FIN	H	I	NL	P	PL	S	UK
Distribution DCT approach													
% farms with BDCT-approach	81	63	70	0*	95	10	95	95	5	70	90	0	80
% farms with SDCT-approach	16	35	20	70	5	80	5	1	85	25	5	30	18
% farms using no DCT	3	2	10	20	0	10	0	4	10	5	5	70	2
Selection level for DCT													
Selection at quarter-level	--	2	15	0	0	10	0	0	10	5	--	0	<1
Selection at cow-level	--	70	85	100	100	90	100	100	90	95	--	100	99
Selection criteria for DCT													
Mastitis history of the cow	89	70	60	40	100	50	100	99	40	80	45	20	80
Individual SCC at dry-off	9	95	15	40	0	20	0	1	50	10	45	65	15
Bacteriology at dry-off	2	30	25	10	0	0	0	0	5	10	10	10	5
PCR at dry off	0	20	0	10	0	30	0	0	5	0	0	5	<1
Succes rate of SDCT													
% farms with succesfull SDCT	--	50	70	50	70		5	--	75	40	--	--	--

As though these data reflect opinions rather than hard data, they indicate that, despite a mounting pressure to reduce the use of antibiotics throughout the EU, DCT is still a blanket approach. If SDCT is applied, it basically is always at the cow-level and based on the mastitis history of the cow. In countries in which SDCT is applied at a national level, such as Sweden, Denmark, Finland and the Netherlands, the selection method based on mastitis history seems to be replaced by more practical and easily applicable methods such as SCC at drying-off.

FUTURE RESEARCH

It is very important that farmer and veterinarian are aware of the necessity to reduce AMU, as much as reasonably is possible. As veterinarians are the prescribers of antimicrobials on the dairy farm, more research is needed on the role of risk perception and uncertainty avoidance in AMU of both, farmers and veterinarians. More insight into the differences in attitude, mindset, risk perception, social influences and decision making on AMU between farmers that have a high and low use of DCT is urgently needed to identify their drivers and incentives to do so and to develop specific interventions.

In order to judge the importance of reduction in AMU, the effect on AMR has to be estimated, which was, however, not evaluated in this study. Future studies should focus on whether a reduction of the use of dry cow antibiotics has an effect on selective pressure and thus on the risk on development of AMR. There is a need to set up a uniform monitoring system of AMR-development in the world, with uniform thresholds to distinguish sensitive from resistant strains.

A way to further optimize AMU at drying-off is potentially drying-off at quarter-level. One concern that could theoretically compromise the success of such an approach is the interdependence of quarters for acquiring new IMI during the dry period (Berry et al., 2003; Robert et al., 2006). This could result in increased risk for infection in uninfected, untreated quarters adjacent to infected quarters. More research is needed on the possibilities for making dry-off decisions on quarter-level and the consecutive herd-level consequences.

In mastitis control strategies, optimal management of the dry cows and their transition to a subsequent lactation is crucial, although considerable progress in the understanding of epidemiology, immunology, diagnostics and pathogenesis of IMI in the dry period has been made over the years. The management of risk on IMI in the dry period is often underestimated in daily practice. Modern molecular biological methods may help to study the epidemiological and virulence aspects of bacteria further, which may help in building-up specific mastitis control strategies for dairy herds. Studies on the host response and relationship between SCC and susceptibility to IMI offer many tools for farmer and veterinarian. Biotechnological approaches, sensory data and interventions for mastitis prevention are developing quickly, like vaccination, and immunostimulation of dairy cows. Different methods of immunomodulation and dry-off facilitation for the prevention of mastitis were found promising in experimental trials, like the role of granulocyte colony-stimulating factor (McDougall et al., 2017) and the role of cabergoline (Bertulat et al., 2017) respectively.

More research on big-data from milking technique, including robotic milking, may provide better possibility for proper milking, improved teat condition, udder health and therefore optimal decision making on DCT.

The challenge for veterinarians is in effectively guiding the farmer with advices that address the farmers' values, beliefs, risk perceptions and needs (Speksnijder et al., 2015a). Optimal advise for the farmer about topics like abrupt or gradual cessation of milking, production level at dry-off and prevention of milk leakage are essential as well as advise on internal and external teat sealants. Internal teat sealants have been shown to be as effective as dry cow antimicrobials in preventing new IMI during the dry period (Huxley et al., 2002). They do not have any therapeutic effect, so any existing infections would not resolve unless there was a self-cure. External teat sealants are not as effective and require frequent reapplication (Hemling et al., 2000). There is an urgent need for more research on the herd-level effects of the internal teat sealant, when an SDCT-approach is used.

Future research should be focused on the alternatives for AMU in the dry period to prevent the cow from new IMI, with regard to development of immune stimulants, seal systems, multivalent vaccines, dry-off facilitation and teat-canal support, in order to create an optimal dry cow management. This should always be part of modern herd health management, because dry cow therapy does not only consist of antimicrobial dry cow treatment.

CONCLUSIONS

This thesis shows that reduction of AMU at drying-off leads to more mastitis at the individual level, however, this effect was much smaller at the herd level. The effect of SDCT compared with BDCT on udder health was not extremely influenced by the SCC criteria used to select cows for DCT. The effect of the SCC criteria used on AMU, however, was substantial. Economics is not an argument against reduction of the use of dry cow antimicrobials by applying SDCT, whereas in most scenarios SDCT was economically beneficial. SDCT appeared to be associated with farmers' and veterinarians' attitude and their mindset on reduction of AMU is crucial for successful implementation of an SDCT-approach.

Antimicrobial use in the dairy industry in the Netherlands changed within a relatively short time, which included the introduction of SDCT. Those changes were generally supported by both, dairy farmers and veterinarians, and did not lead to dramatic changes in animal health. Although reduction of AMU at drying-off leads to more mastitis at the individual level, it was successfully implemented in the Netherlands without dramatic effects on udder health.

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Summary

Udder health is associated with mastitis management, of which blanket dry cow treatment (BDCT) has been an important part for decades to prevent the udder from new intramammary infections (IMI) during the dry period. The use of BDCT, as part of the five-point mastitis prevention program, has been advocated for more than 50 years. The goal of DCT is to reduce the prevalence of IMI by eliminating infections already present at drying off and by preventing new IMI from occurring during the dry period. Since 2012, preventive use of antimicrobials in veterinary medicine is prohibited in the Netherlands. Therefore BDCT has been replaced by exclusive antimicrobial treatment at drying off of cows suspected of IMI, known as selective dry cow treatment (SDCT). Although selection of cows is an important part of SDCT and likely has a great effect on the consequences with respect to antimicrobial use and udder health, not much research been done in this field. Thus, SDCT had to be applied by all approximately 18,000 dairy farmers in the Netherlands, while little was known on how to execute it.
In order to smoothen the transition from BDCT to SDCT, it was considered important to come up with a cow selection approach that was not too complicated to execute, and to know what the consequences of that approach would be. Therefore the effect of various approaches to select cows for DCT on udder health, antimicrobial use, and economics was evaluated. Understanding and balancing these effects was considered to be beneficial for an optimal introduction and execution of SDCT and for prudent antimicrobial use in the dairy industry in the Netherlands.
The aims of this thesis were to quantify the effects of SDCT on clinical mastitis (CM) and subclinical mastitis (SCM), antimicrobial use and economics. The effect of different scenarios to select cows for SDCT were evaluated that were, for reasons of applicability, all based on a single somatic cell count (SCC) measurement before drying off. The effect of different SDCT scenarios on udder health, antimicrobial use and economics was evaluated. Additionally the economic consequences of treating different numbers of dairy cows with antimicrobials at drying off were evaluated as was the attitude of the dairy farmer and the veterinarian with respect to SDCT and to reduction of antimicrobial use on dairy farms in general. During the execution of this study BDCT changed to SDCT in the Netherlands and all of the aforementioned aspects were evaluated in the perspective of that transition.

In Chapter 2 SDCT was evaluated in 1,657 cows in 97 Dutch dairy herds, that all had a low SCC at the last milk recording before drying off. A split-udder design was used in which two quarters of each cow were treated with dry cow antimicrobials and the other two quarters remained as untreated controls. Low SCC was defined as <150,000 cells/mL for primiparous and <250,000 cells/mL for multiparous cows. The effect of DCT on CM, bacteriological status, SCC and antibiotic

use were determined at quarter level using logistic regression and chi-square tests.
The incidence rate of CM was found to be 1.7 times higher in quarters dried off without antimicrobials as compared to quarters that were dried off with antimicrobials. *Streptococcus uberis* was the predominant organism causing CM in both groups. Somatic cell count at calving and at 14 days in milk was significantly higher in quarters dried off without antimicrobials (772,000 cells/mL and 46,000 cells/mL respectively) as compared to the quarters dried off with antibiotics (578,000 cells/mL and 30,000 cells/mL respectively). Quarters with an elevated SCC or a positive culture for major pathogens at drying off had a higher risk for a SCC above 200,000 cells/mL at 14 days in milk as compared to quarters with a low SCC and a negative culture for major pathogens at drying off. For quarters that were culture positive for major pathogens at drying off also a trend for a higher risk of CM was found.
Selective DCT, not using dry cow antimicrobials in cows that had a low SCC at the last milk recording before drying off, significantly increased the incidence rate of CM and the SCC after calving. The decrease in antimicrobial use by not applying DCT was not compensated by an increase in antimicrobial use for treating CM. The total antimicrobial use related to mastitis was reduced by 85% in these quarters.

In Chapter 3 the effects of eight scenarios for selecting animals for DCT were studied, taking into account variation in parity and cow-level SCC at drying off. The aim of this study was to evaluate udder health (CM and SCM), antimicrobial usage and economics at the herd level when using different scenarios for selecting cows for DCT. The parameters mentioned were evaluated in an average 'example herd' consisting of 100 dairy cows, during the dry period and the first 100 days in lactation, when the biggest effect of DCT is expected. In addition to a BDCT-scenario, seven scenarios to select cows for DCT based on SCC were evaluated. These scenarios were all based on the cow level SCC on the last milk recording before drying off, and cover a range of possible approaches to select cows for DCT. The incidence rate of CM in the example herd varied from 11.6 to 14.5 cases of CM per 10,000 cow-days at risk in the different scenarios, and the prevalence of SCM varied from 38.8% to 48.3%. Total antimicrobial usage for dry cow and mastitis treatment varied over the scenarios from 1.27 to 3.15 animal daily dosages, leading to a maximum reduction in antimicrobial usage of 60%. The total costs for each of the scenarios showed little variation, varying from 4,893 to 5,383 per herd per year. The consequences of SDCT as compared to BDCT on udder health, antimicrobial usage and economics was found to be influenced by the SCC criteria used to select cows for DCT. The SCC criteria chosen not only affect quantifiable parameters, such as CM, SCM, antimicrobial usage and economics, but also non-quantifiable parameters, such as welfare and practical achievability. Dependent on the weight given to these parameters optimal selection criteria should be chosen when implementing SDCT.

In Chapter 4 a mathematical model to identify a scenario with the lowest costs for mastitis associated with the dry period was developed, while restricting the percentage of cows to be dried off with dry cow antimicrobials. Costs of CM, SCM and antimicrobial use were quantified.

Based on data derived from the field trial described in chapter 2, a linear programming model was built with the goal to minimize the costs associated with antimicrobial use at drying off. To enable calculations on minimizing costs of DCT on herd-level by drying off decisions, again an average 'example' herd was used. Cows were projected on three different types of herds, based on bulk milk SCC, and were categorized in groups based on parity and SCC at the last test milk recording before drying-off. Economically optimal use of antimicrobials was determined while restricting the maximum percentage of cows dried of with antimicrobials from 100% to 0%. This restriction reveals the relationship between the maximum percentage of cows to be dried off with antibiotics and the economic consequences. A sensitivity analysis was performed to evaluate the effect of variation in the most important input variables on the total economic costs, being the effect of dry cow antimicrobials on the occurrence of CM and SCM, and the milk price.

Although differences were small, BDCT was, from an economical perspective, not the optimal DCT approach. It was found that in herds with a lower bulk milk SCC, more dry cow antimicrobials can be omitted without economic consequences, thus leading to lower costs. The economic impact of reducing the percentage of CM was found to be much larger than that of reducing the bulk milk SCC. The optimal percentage of cows to be dried off with antimicrobials depends on the udder health situation, indicated by the bulk milk SCC and the incidence of CM. For all evaluated types of herds SDCT was economically more beneficial than BDCT. Economic profits of SDCT are greater if bulk milk SCC and CM incidence are lower. Economics was found not to be an argument not to change the BDCT routine to reduction of dry cow antimicrobials by applying SDCT.

In Chapter 5 insight into the level of implementation of SDCT in 2013 in the Netherlands was provided. The methods used by farmers for selection of cows for DCT, the relation between SDCT and udder health and antimicrobial use in 2013, and the mindset of farmers towards SDCT were evaluated. In 2014, a questionnaire was conducted in a group of 177 farmers that participated in a large scale udder health study in 2013 and recorded all CM cases during that year. In addition, data on SCC parameters and antimicrobial use was available from these herds. The questionnaire included questions with regard to DCT with special emphasis on farmers attitude and mindset to application of DCT in 2013. The data that was obtained from the questionnaire was combined with the available data on CM, SCC and antimicrobial use. Descriptive statistics were used to evaluate the data and to study the association between DCT, udder health and antimicrobial use.

Selective DCT was taken up quickly by the farmers in our study, with 75% of them implementing SDCT in 2013. The main criterium indicated by the farmers to be used to select cows for DCT was the SCC history during the complete previous lactation. There were no significant differences in udder health parameters between herds that applied BDCT or SDCT, nor between SDCT herds with high or low use of dry cow antimicrobials. Overall, antimicrobial use was higher in herds that applied BDCT, although there were no significant differences in intramammary treatment with antimicrobials other than DCT. Although application of SDCT appeared to be associated with farmers' attitude, the mindset of farmers with respect to reduction of antimicrobial use in general and to the implementation of SDCT was generally found to be positive.

In Chapter 6 the attitude of Dutch dairy veterinarians towards restricted antimicrobial use and towards SDCT was studied. A questionnaire was conducted in a group of 181 veterinarians in 2015, that included questions with regard to their attitude and behavior towards reduction of antimicrobial use and towards SDCT. Descriptive statistics were used to describe the data and multivariable logistic regression models with a logit link function were applied to evaluate potential associations between veterinarians' attitude towards antimicrobial use and SDCT and the rationale behind their mindset, based on positive and negative aspects of reduction in antimicrobial use. The veterinarians were subdivided into three groups based on their opinion (unfavorable, neutral or favorable) towards four statements with regard to antimicrobial use and SDCT. For the multivariable logistic regression analysis the first two groups were combined and compared to the veterinarians with a favorable attitude.
The attitude of Dutch dairy veterinarians with respect to the reduction of antimicrobial use and specifically to SDCT was found to be generally positive, although there was a small group of veterinarians that was negative about these changes. Veterinarians working in larger practices generally had a more positive attitude towards the changed antimicrobial use policy than those working in smaller practices. Given the variability found in their attitude and behavior, and the influence veterinarians potentially have on the attitude of farmers, veterinarians need specific attention by program organizers trying to stimulate prudent antimicrobial use and SDCT.

In Chapter 7 finally, the previous chapters were discussed in the light of practical implications for the dairy farmer and the veterinary practitioner, in the current situation in the Netherlands. Reduction of antimicrobial use at drying off leads to more mastitis at the individual cow level. The effect was much smaller at the herd level. The effect of SDCT as compared with BDCT on udder health was influenced by the SCC criteria used to select cows for DCT, but changes were limited. The effect of the SCC criteria used on antimicrobial use, however, was substantial. Economics was found not to be an argument against reduction of the use of dry cow antimicrobials by applying SDCT, whereas in most scenarios SDCT was economically beneficial.

Application of SDCT appeared to be associated with farmers' and veterinarians' attitude. Their mindset towards reduction of antimicrobial use is crucial for successful implementation of SDCT. During the last years antimicrobial use in the dairy industry in the Netherlands decreased enormously, in which the introduction of SDCT played an important role. These changes were generally supported by both, dairy farmers and veterinarians, and did not lead to dramatic changes in animal health. Although reduction of antimicrobial use at drying off leads to more mastitis at the individual level, it was successfully implemented in the Netherlands without dramatic effects on udder health. These changes were realized by constructive cooperation between farmers and veterinary practitioners in the field, supported by the main stakeholders in the dairy industry.

Samenvatting

Het voorkomen van mastitis op het melkveebedrijf wordt beïnvloed door het uiergezondheidsmanagement, waarvan het behandelen van alle koeien met antibiotica ('droogzetters') bij het droogzetten, de zogenoemde *blanket dry cow treatment* (BDCT) decennia lang een standaard onderdeel was. Het toepassen van BDCT, als onderdeel van het 5-puntenplan dat in de '60-er jaren van de vorige eeuw is ontwikkeld, wordt daarmee al meer dan 50 jaar bepleit. Het doel van het behandelen van koeien met antibiotica in de droogstand is enerzijds om bestaande intramammaire infecties te genezen en anderzijds om de uier te beschermen tegen nieuwe infecties in de droogstandsperiode. Sinds 2012 is in Nederland het preventief gebruik van antimicrobiële middelen in dieren echter verboden. Om die reden is het standaard droogzetten van alle dieren met antibiotica vervangen door het selectief behandelen van koeien die op het moment van droogzetten verdacht worden van een intramammaire infectie. Deze methode heet selectief droogzetten, ofwel *selective dry cow treatment* (SDCT). Hoewel de selectie van de juiste koeien voor een droogzetbehandeling een belangrijk onderdeel is van selectief droogzetten en potentieel grote gevolgen kan hebben op antibioticumgebruik en uiergezondheid, is er niet veel onderzoek gedaan naar het selecteren van de juiste koeien in het kader van SDCT. Tegelijkertijd was duidelijk dat het selectief droogzetten voor alle ongeveer 18.000 melkveehouders in Nederland wettelijk verplicht werd, terwijl relatief weinig bekend was over hoe SDCT uit te voeren en wat de gevolgen ervan zouden zijn. Om de overgang van BDCT naar SDCT soepel te laten verlopen leek het belangrijk om een selectiemethode te vinden die praktisch en gemakkelijk uit te voeren is terwijl de gevolgen van een dergelijke aanpak zo goed mogelijk in beeld zijn. Om die reden werd het effect van verschillende methoden om koeien te selecteren voor een droogzetbehandeling met antibiotica geëvalueerd, op uiergezondheid, antibioticumgebruik en op economische consequenties. Het goed kunnen doorgronden en interpreteren van de effecten van verschillende droogzetstrategieën is cruciaal voor een succesvolle introductie, implementatie en uitvoering van selectief droogzetten en daarmee voor terughoudend en verantwoord antibioticagebruik in de Nederlandse melkveehouderij.

Het doel van de onderzoeken beschreven in dit proefschrift is om de effecten van selectief droogzetten op klinische en subklinische mastitis, antibioticumgebruik en economie te kwantificeren. Daarnaast werd het effect van verschillende scenario's om koeien te selecteren voor behandeling met droogzetantibiotica geëvalueerd die, om redenen van praktische toepasbaarheid, allemaal gebaseerd waren op een enkelvoudige bepaling van het koecelgetal op de laatste melkproductie registratie (MPR) voor droogzetten. Ook het effect van deze verschillende scenario's op uiergezondheid, antibioticumgebruik en economische consequenties werd geëvalueerd. Bovendien werden de economische gevolgen van het behandelen van verschillende

aantallen melkkoeien met antibiotica bij droogzetten geëvalueerd, evenals de attitude van de melkveehouder en de dierenarts met betrekking tot antibioticareductie in het algemeen en selectief droogzetten in het bijzonder. Tijdens de uitvoering van deze studie veranderde in Nederland het standaard droogzetten van alle dieren met antibiotica naar selectief droogzetten. Alle bovengenoemde aspecten werden geëvalueerd in het perspectief van deze overgang.
In hoofdstuk 2 werd het effect van selectief droogzetten geëvalueerd in 1.657 koeien afkomstig van 97 Nederlandse melkveebedrijven, met een laag koecelgetal op de laatste MPR voor droogzetten. Het onderzoek was opgezet op basis van een split-udder design, waarbij de linker of de rechter twee kwartieren van elke koe werden behandeld met droogzetantibiotica en de overige twee kwartieren als onbehandelde controle dienden. Een laag koecelgetal op het moment van droogzetten werd gedefinieerd als <150.000 cellen/ml voor vaarzen en <250.000 cellen/ml voor ouderekalfs koeien. Het effect van droogzetantibiotica op klinische mastitis, de bacteriologische status van de kwartieren, het celgetal en het antibioticumgebruik werd bepaald op kwartierniveau met behulp van logistische regressie en chi-kwadraat testen.
De incidentie van klinische mastitis bleek 1,7 maal hoger in onbehandelde kwartieren dan in behandelde kwartieren. *Streptococcus uberis* was de meest voorkomende verwekker van klinische mastitis in beide groepen. Het celgetal bij afkalven en op 14 dagen in lactatie was significant hoger in onbehandelde kwartieren (respectievelijk 772.000 cellen/ml en 46.000 cellen/ml) dan in behandelde kwartieren (respectievelijk 578.000 cellen/ml en 30.000 cellen/ml). Kwartieren met een verhoogd celgetal of een positief bacteriologisch onderzoek met een major mastitisverwekker op het moment van droogzetten, hadden een hoger risico op een celgetal boven de 200.000 cellen/ml op 14 dagen in lactatie dan kwartieren met een laag celgetal en een negatief bacteriologisch onderzoek met een major mastitisverwekker op het moment van droogzetten. Voor bacteriologisch positieve kwartieren met een major mastitisverwekker op het moment van droogzetten werd ook een trend voor een hoger risico op klinische mastitis gevonden. Selectief droogzetten, waarbij koeien met een laag celgetal op de laatste MPR voor droogzetten niet behandeld worden met antibiotica, leidt tot een significante verhoging van de incidentie van klinische en subklinische mastitis na afkalven. De daarbij optredende substantiële afname van het antibioticumgebruik door een verminderd gebruik van droogzetantibiotica werd geenszins gecompenseerd door een toename van het antibioticumgebruik voor het behandelen van klinische mastitis. Het totale antibioticumgebruik in relatie tot uiergezondheid is in deze kwartieren met 85% afgenomen.

In hoofdstuk 3 werden de effecten van acht scenario's voor het selecteren van koeien voor behandeling met droogzetantibiotica bestudeerd, waarbij rekening werd gehouden met variatie in pariteit en koecelgetal op het moment van droogzetten. Het doel van dit onderzoek was om uiergezondheid (klinische en subklinische mastitis), antibioticumgebruik en economische consequenties op koppelniveau te beoordelen bij gebruik van verschillende scenario's voor het selecteren van koeien voor behandeling met droogzetantibiotica. De genoemde parameters werden geëvalueerd in een gemiddelde 'voorbeeldkoppel' bestaande uit 100 melkkoeien, tijdens de droogstand en de eerste 100 dagen in lactatie, de periode waarin het grootste

effect van droogzetantibiotica te verwachten is. Naast een BDCT-scenario werden zeven SDCT scenario's geëvalueerd waarbij op verschillende manieren koeien werden geselecteerd voor behandeling met droogzetantibiotica. Deze scenario's waren allemaal gebaseerd op basis van het koecelgetal tijdens de laatste MPR voor droogzetten De incidentie van klinische mastitis in de voorbeeldkoppel varieerde over de verschillende scenario's van 11,6 tot 14,5 gevallen van klinische mastitis per 10.000 koedagen-at-risk, en de prevalentie van subklinische mastitis varieerde van 38,8% tot 48,3%. Het totale antibioticumgebruik voor droogzetbehandeling en behandeling van mastitis varieerde over de scenario's van 1,27 tot 3,15 dierdagdosering, wat resulteerde in een maximale antibioticareductie van 60%. De totale kosten voor elk van de scenario's lieten slechts een kleine variatie zien, variërend van 4.893 tot 5.383 per koppel van 100 koeien per jaar.
De gevolgen van selectief droogzetten ten opzichte van het standaard behandelen van alle koeien met antibiotica bij het droogzetten op uiergezondheid, antibioticumgebruik en economie bleken wel degelijk beïnvloed te worden door de koecelgetal-criteria die werden gebruikt om koeien te selecteren voor behandeling met droogzetantibiotica. De geselecteerde criteria beïnvloeden niet alleen kwantificeerbare parameters zoals klinische en subklinische mastitis, antibioticumgebruik en economische kengetallen, maar ook moeilijker kwantificeerbare parameters zoals welzijn en praktische haalbaarheid. Afhankelijk van het belang dat aan deze afzonderlijke parameters wordt gegeven, kunnen optimale selectiecriteria gekozen worden bij het vaststellen van een beleid ten aanzien van selectief droogzetten.

In hoofdstuk 4 is een wiskundig model beschreven dat werd gebruikt om een scenario te identificeren met de laagste totale kosten ten gevolge van mastitis (klinische mastitis, subklinische mastitis en antimicrobiële behandeling) voortvloeiend uit (behandeling in) de droogstandsperiode, waarbij het percentage koeien dat behandeld werd met antibiotica bij droogzetten stapsgewijs werd begrensd. Gebaseerd op data vanuit van de veldproef die beschreven is in hoofdstuk 2, werd een lineair programmeringsmodel gebouwd met als doel de kosten die geassocieerd zijn met uiergezondheid te minimaliseren. Om de berekening van de kosten ten gevolge van mastitis rond de droogstandsperiode op bedrijfsniveau mogelijk te maken werd opnieuw een gemiddelde 'voorbeeldkoppel' van 100 melkkoeien gebruikt. De situatie op drie verschillende soorten bedrijven gebaseerd op het tankmelkcelgetal werd gemodelleerd, waarbij koeien werden gecategoriseerd in groepen op basis van de pariteit en het celgetal op de laatste MPR voor droogzetten. Het economisch optimale gebruik van behandelingen met droogzetantibiotica werd bepaald, terwijl het maximale percentage koeien dat mocht worden behandeld met antibiotica bij droogzetten stapsgewijs werd beperkt van 100 naar 0%. Door deze restrictie wordt de relatie tussen het maximale percentage koeien dat bij het droogzetten met antibiotica mag worden behandeld en de economische gevolgen daarvan in de voorbeeldkoppel vastgesteld. Hierbij is tevens een sensitiviteitsanalyse uitgevoerd om het effect van variatie in de belangrijkste inputvariabelen, namelijk het effect van het gebruik van droogzetantibiotica op het voorkomen van klinische en subklinische mastitis en het effect van de melkprijs, te evalueren.

Hoewel de verschillen klein waren, was het standaard behandelen van alle koeien met antibiotica bij droogzetten vanuit economisch oogpunt niet de beste strategie. Als bedrijven een lager tankmelkcelgetal hebben, kunnen meer koeien zonder antibiotica worden drooggezet, zonder dat dat economische gevolgen heeft. Hierdoor worden de totale kosten ten gevolge van uiergezondheid lager. Reductie van het percentage klinische mastitis blijkt een veel groter economisch effect te hebben dan het verlagen van het tankmelkcelgetal. Het optimale percentage met droogzetantibiotica te behandelen koeien is afhankelijk van de uiergezondheidssituatie op het bedrijf zoals weerspiegeld in het tankmelkcelgetal en de klinische mastitis incidentie. Voor alle geëvalueerde soorten bedrijven was SDCT economisch gunstiger dan BDCT. De economische winst van selectief droogzetten is groter als het tankmelkcelgetal en de incidentie van klinische mastitis op een bedrijf lager zijn. Economie bleek in geen geval een valide argument om het standaard behandelen van alle koeien met antibiotica bij droogzetten niet te vervangen door selectief droogzetten.

In hoofdstuk 5 is de mate van implementatie van selectief droogzetten door melkveehouders in Nederland in 2013 beschreven. De methoden die de melkveehouders gebruikten voor de selectie van koeien voor een behandeling met droogzetantibiotica werden geëvalueerd, evenals de relatie tussen selectief droogzetten, uiergezondheid en antibioticumgebruik en de mindset van melkveehouders ten opzichte van selectief droogzetten. In 2014 is een enquête afgenomen onder een groep van 177 melkveehouders die in 2013 aan een grootschalige uiergezondheidsstudie deelnamen en alle gevallen van klinische mastitis in dat jaar hadden geregistreerd. Daarnaast waren celgetal-gegevens van de MPR van deze bedrijven beschikbaar, evenals het antibioticumgebruik. De vragenlijst omvatte vragen met betrekking tot de behandeling met antibiotica bij droogzetten, met speciale aandacht voor de attitude en mindset van de melkveehouders ten aanzien van droogzetantibiotica. De gegevens die werden verkregen uit de vragenlijst werden gecombineerd met de beschikbare gegevens over klinische mastitis, celgetal en antibioticumgebruik. Beschrijvende statistiek werd gebruikt om de gegevens te evalueren en de associatie tussen de strategie ten aanzien van droogzetten, uiergezondheid en antibioticumgebruik te bestuderen.
Uit dit onderzoek bleek dat selectief droogzetten snel door de melkveehouders is opgepakt, waarbij 75% van de melkveehouders al in 2013 SDCT toepaste. De melkveehouders gaven aan dat het belangrijkste selectiecriterium dat zij gebruikten om koeien te selecteren voor een behandeling met droogzetantibiotica de celgetalhistorie van de volledige vorige lactatie was. Er waren geen significante verschillen in de uiergezondheidsparameters tussen bedrijven die standaard alle koeien met antibiotica behandelen bij droogzetten of bedrijven die selectief droogzetten toepasten. Ook was er geen verschil tussen bedrijven die selectief droogzetten met een hoog of laag gebruik van droogzetantibiotica. Wel was het antibioticumgebruik hoger op bedrijven die standaard alle koeien met droogzetantibiotica behandelden. Er bleek een associatie te bestaan tussen de toepassing van selectief droogzetten en de attitude van de melkveehouder ten aanzien van de vermindering van het antibioticumgebruik in het algemeen.

Desalniettemin bleek de houding van melkveehouders ten aanzien van de vermindering van het antibioticum gebruik en de implementatie van selectief droogzetten positief te zijn.

In hoofdstuk 6 werd de houding van Nederlandse rundveedierenarts ten opzichte van antibioticareductie in het algemeen en selectief droogzetten in het bijzonder bestudeerd. In 2015 werd een complete vragenlijst afgenomen van een groep van 181 dierenartsen, die items bevatte over hun houding en gedrag ten opzichte van vermindering van antibioticumgebruik en selectief droogzetten. Met behulp van beschrijvende statistiek zijn de data beschreven, waarna multivariabele logistische regressiemodellen met een logit linkfunctie werden gebruikt om potentiële associaties te vinden tussen de attitude van dierenartsen ten opzichte van antibioticumgebruik en hun beleving van de positieve en negatieve aspecten van antibioticareductie en selectief droogzetten. De dierenartsen werden ingedeeld in drie groepen op basis van hun mening (ongunstig, neutraal of gunstig) over vier statements met betrekking tot antibioticumgebruik en selectief droogzetten. Voor de multivariabele logistische regressieanalyse werden de eerste twee groepen gecombineerd en vergeleken met de dierenartsen met een gunstige attitude. De houding van Nederlandse rundveedierenartsen met betrekking tot de vermindering van het antibioticumgebruik in het algemeen en selectief droogzetten in het bijzonder bleek over het algemeen positief te zijn, hoewel er een kleine groep dierenartsen was die uitgesproken negatief was over deze veranderingen. Dierenartsen die in grotere praktijken werken, hadden in het algemeen een positievere attitude ten aanzien van het veranderde antibioticumbeleid dan zij die in kleiner praktijken werkten. Gezien de variabiliteit die werd gevonden in hun attitude, en de invloed die dierenartsen hebben op de attitude van melkveehouders, is het belangrijk om specifieke aandacht te geven aan dierenartsen om prudent antibioticumgebruik en selectief droogzetten te stimuleren.

In hoofdstuk 7 zijn de voorgaande hoofdstukken in het licht van de praktische implicaties voor melkveehouder en dierenarts in Nederland besproken. Vermindering van behandeling met antibiotica bij droogzetten leidt tot meer mastitis op individueel koeniveau. Op bedrijfsniveau was het effect echter veel kleiner. Het effect van selectief droogzetten in vergelijking met het standaard behandelen met antibiotica van alle koeien bij droogzetten op uiergezondheid werd slechts zeer beperkt beïnvloed door de gebruikte celgetal criteria om koeien te selecteren voor behandeling met droogzetantibiotica. Het effect van de verschillende celgetal criteria op het antibioticumgebruik echter was substantieel. Economie bleek in geen geval een valide argument om het standaard behandelen van alle koeien met antibiotica bij droogzetten niet te vervangen door selectief droogzetten, aangezien selectief droogzetten in de meeste scenario's economisch gunstiger uitpakt. Toepassing van selectief droogzetten blijkt geassocieerd te zijn met de attitude van melkveehouders en dierenartsen. Hun houding ten opzichte van vermindering van het antibioticumgebruik is van groot belang voor het succesvol implementeren van selectief droogzetten. In de afgelopen jaren is het antibioticumgebruik in de melkveehouderij in Nederland sterk gedaald, waarbij de introductie van selectief droogzetten een belangrijke rol heeft gespeeld. Deze veranderingen werden over ondersteund door melkveehouders en dierenartsen en leidden niet tot dramatische veranderingen in de diergezondheid. Hoewel de vermindering van het antibioticumgebruik bij droogzetten tot meer mastitis op individueel niveau kan leiden, is SDCT in Nederland succesvol geïmplementeerd zonder dat het dramatische effecten op de uiergezondheid had. Deze verandering is gerealiseerd door een constructieve samenwerking tussen melkveehouders en dierenartsen in het veld, die werd ondersteund door de belangrijkste stakeholders in de melkveehouderij.

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Curriculum vitae

Christian Scherpenzeel is geboren op 9 september 1980 te Amsterdam. Na het behalen van zijn diploma op het voortgezet wetenschappelijk onderwijs op Scholengemeenschap De Rietlanden te Lelystad in 1999, studeerde hij twee jaar diergeneeskunde aan de Rijksuniversiteit Gent in België. In 2001 werd hij via decentrale selectie toegelaten tot de opleiding diergeneeskunde aan de Universiteit Utrecht, die in 2008 afgesloten werd met de differentiatie Landbouwhuisdieren. Tijdens de studie besteedde hij zijn onderzoeksstage aan regionale diergezondheid; 'IBR in de Buitenpraktijk Utrecht', in samenwerking met de Gezondheidsdienst voor Dieren en was hij bestuurlijk actief in het faculteitsbestuur van de faculteit diergeneeskunde en in meerdere commissies van de Diergeneeskundige Studenten Kring.
Na zijn afstuderen was Christian werkzaam als dierenarts bij Dierenartsenpraktijk Veenendaal waar hij zich voornamelijk bezighield met rundvee. Vervolgens heeft hij gewerkt als docent/onderzoeker bij de faculteit diergeneeskunde, Departement Landbouwhuisdieren in Utrecht waar hij een bijdrage heeft geleverd aan diersoort overschrijdend onderwijs in de klinische pathofysiologie en de ziekteleer en aan verschillende (internationale) onderzoeksprojecten.
Sinds 2011 is Christian werkzaam bij de Gezondheidsdienst voor dieren op de afdeling herkauwergezondheidszorg als senior veterinair medewerker, waar hij zich als onderdeel van het UGA-team heeft toegelegd op de aandachtsgebieden uiergezondheid, melkkwaliteit en ontwikkeling van antibioticaresistentie. In 2012 is hij begonnen met het promotieonderzoek dat heeft geleid tot dit proefschrift.

About the author

Christian Scherpenzeel was born on 9 September 1980 in Amsterdam, the Netherlands. After graduating from secondary school at Scholengemeenschap De Rietlanden in Lelystad in 1999, he started to study veterinary medicine at Ghent University in Belgium. In 2001, he was admitted to study veterinary medicine at Utrecht University via an application procedure, where he graduated in 2008 with the differentiation of farm animal health. During his studies he did his research thesis on regional animal health; 'Infectious Bovine Rhinotracheitis in the the University practice Utrecht University', in collaboration with GD Animal Health, and was active in the faculty board of the Faculty of Veterinary Medicine and in several committees of the Dutch Veterinary Student Association.

After graduation, Christian worked as a dairy veterinarian in a large veterinary practice in Veenendaal, where he mainly worked with dairy cows. After dairy practice, he went back to the veterinary school in Utrecht, where he was employed as lecturer/researcher at the Department of Farm Animal Health, where he contributed to cross-disciplinary education in clinical pathophysiology and to various (international) research projects.

Since 2011 Christian works as senior dairy veterinarian at the Ruminant Health Department of GD Animal Health in Deventer, the Netherlands. In this job, his challenge is to integrate state-of-the-art scientific udder health expertise with the implementation of practical expertise, working closely together with dairy farmers and associated veterinarians. His research activities focus on udder health, antimicrobial resistance and social aspects of modern herd health management.

Together with his team, carrying out the 'Udder Health Approach', the combination of scientific and practical expertise on udder health management triggers a lot of farm visits each year and resulted in major experience in dairy consultancy and veterinary communication skills. In 2012 he started his PhD-track that led to this thesis.

Publications

PEER REVIEWED PUBLICATIONS

C.G.M. Scherpenzeel, H. Hogeveen, L. Maas, and T.J.G.M. Lam. 2018. Economic optimization of selective dry cow therapy. Journal of Dairy Science *In Press*

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CONTRIBUTION TO BOOK CHAPTERS

Co-authored chapters 2, 17, and 19 (Mastitis bacteria; Milker and milking; Treatment) in Handbook udder health in dairy cattle (*Handboek Uiergezondheid Rund; pp. 333*), edited by Theo Lam and Sarne DeVliegher. Communication in Practice, Nijmegen.