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Invited review: Selective use of antimicrobials in dairy cattle at drying-off

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ABSTRACT

Administering intramammary antimicrobials to all mammary quarters of dairy cows at drying-off [i.e., blanket dry cow therapy (BDCT)] has been a mainstay of mastitis prevention and control. However, as udder health has considerably improved over recent decades with reductions in intramammary infection prevalence at drying-off and the introduction of teat sealants, BDCT may no longer be necessary on all dairy farms, thereby supporting antimicrobial stewardship efforts. This narrative review summarizes available literature regarding current dry cow therapy practices and associated impacts of selective dry cow therapy (SDCT) on udder health, milk production, economics, antimicrobial use, and antimicrobial resistance. Various methods to identify infections at drying-off that could benefit from antimicrobial treatment are described for selecting cows or mammary quarters for treatment, including utilizing somatic cell count thresholds, pathogen identification, previous clinical mastitis history, or a combination of criteria. Selection methods may be enacted at the herd, cow, or quarter levels. Producers' and veterinarians' motivations for antimicrobial use are discussed. Based on review findings, SDCT can be adopted without negative consequences for udder health and milk production, and concurrent teat sealant use is recommended, especially in udder quarters receiving no intramammary antimicrobials. Furthermore, herd selection should be considered for SDCT implementation in addition to cow or quarter selection, as BDCT may still be temporarily necessary in some herds for optimal mastitis control. Costs and benefits of SDCT vary among herds, whereas impacts on antimicrobial resistance remain unclear. In summary, SDCT is a viable management option for maintaining udder health and milk production while improving antimicrobial stewardship in the dairy industry.

Key words: dry cow therapy, antimicrobial stewardship, dairy cow, mastitis

INTRODUCTION

Intramammary (**IMM**) administration of antimicrobials to all quarters of all dairy cows at drying-off, termed blanket dry cow therapy (**BDCT**), is a key component of the National Mastitis Council (**NMC**) Recommended Mastitis 10-point Control Program (NMC, 2020). This program is the successor to the 5-point mastitis control plan originally focused on prevention and treatment of contagious IMI (Neave et al., 1969; Ruegg, 2017). Consequently, it is the most widely used dry cow therapy (**DCT**) approach in many countries (Bertulat et al., 2015; USDA-APHIS, 2016; Bauman et al., 2018). In contrast, selective DCT (**SDCT**) involves selecting only cows or mammary quarters with existing IMI to be treated with IMM antimicrobials at drying-off (Cameron et al., 2015; Scherpenzeel et al., 2016a; Lhermie et al., 2018).

The majority of antimicrobial use (**AMU**) on dairy farms is for mastitis treatment and prevention (Saini et al., 2012a; Stevens et al., 2016; Ruegg, 2017), and

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DCT uses long-acting antimicrobials (Rowe et al., 2020a; Rowe et al., 2021a). Owing to pressure to reduce overall AMU, including in food production animals, and to phase out preventive antimicrobial treatments, SDCT is being considered in lieu of BDCT to improve prudent AMU in the dairy industry (Rajala-Schultz et al., 2021; Santman-Berends et al., 2021). Reducing livestock-associated AMU has the potential to reduce the prevalence of antimicrobial resistance (**AMR**), with expected benefits for both animal and public health. In addition to reducing overall AMU, the dairy industry signals it is engaged in antimicrobial stewardship and promoting sustainability (Barkema et al., 2015). Since the introduction of a mandatory ban on BDCT in the Netherlands, DCT AMU has declined by 36% and overall IMM AMU (including treatments during lactation) has declined by 15% between 2013 and 2017 (Santman-Berends et al., 2021).

A large proportion of producers have adopted BDCT, owing to the demonstrated efficacy of treating existing IMI and mitigating the risk of new IMI development, which is highest at the beginning of the dry period and at the start of the subsequent lactation (Neave et al., 1950; Smith et al., 1985; Bradley and Green, 2001; Nitz et al., 2021). Dry period IMI incidence is associated with several factors, including milking cessation, accumulation of milk in the udder, potential milk leakage, teat-end condition, environmental hygiene, and the delay or absence of keratin plug formation (Williamson et al., 1995; Dingwell et al., 2004; Pyörälä, 2008; Dufour et al., 2019; Vilar and Rajala-Schultz, 2020). Furthermore, around calving, immunosuppression occurs, hormone concentrations change, and colostrum formation may lead to milk leakage resulting in opening of teat orifices (Oliver and Sordillo, 1988; Pyörälä, 2008; Dufour et al., 2019), increasing new IMI risk.

Although SDCT has been done in Scandinavian countries for decades (Niemi et al., 2020; Niemi et al., 2021), it has only recently been considered in national policies in many other countries. This change has been motivated and justified by or due to changes in mastitis epidemiology, including considerable decreases in IMI prevalence at drying-off (du Preez and Greeff, 1985; Pantoja et al., 2009; Rowe et al., 2019), reduced prevalence of contagious mastitis pathogens such as *Streptococcus agalactiae* and *Staphylococcus aureus* (Cameron et al., 2014; Scherpenzeel et al., 2014; Ruegg, 2017), and reductions in bulk milk SCC (Hillerton et al., 1995; Ekman and Østerås, 2003; Agriculture and Horticulture Development Board, 2017). In addition, reliable and affordable diagnostics have been developed and teat sealants (**TSL**) are now available. With these improvements, the opportunity—or arguably the obligation—exists to reduce or perhaps completely phase out prophylactic AMU in the dry period (Rajala-Schultz et al., 2011).

Research regarding udder health impacts of SDCT has included various approaches to selection methods for SDCT (e.g., SCC thresholds and bacteriological culture), including the level of selection (i.e., herd, cow, quarter) and whether TSL are used in SDCT protocols. As a consequence, comparing studies is complicated. Therefore, it is important to know which selection methods were used, as well as the effectiveness of these criteria in relation to udder health and production. Consensus regarding appropriate herd and cow selection criteria for SDCT has not been achieved, perhaps in part because of insufficient comparable scientific research, differences in regulations, the structure of the dairy industry, attitudes of key stakeholders toward DCT, and pathogen distributions among countries and regions (Erskine et al., 1988; Bradley et al., 2007; Olde Riekerink et al., 2008, Lam et al., 2017). Due to differences among regions in availability and formulations of DCT products, the primary focus of this narrative review is on selection criteria and associated outcomes rather than specific antimicrobial products when antimicrobials are part of the dry cow management strategy.

Furthermore, parenteral rather than IMM administration of DCT is considered, whereby parenteral antimicrobials are administered in combination with or in lieu of IMM antimicrobials. Despite evidence that systemic antimicrobial administration can be effective against IMI (Contreras B et al., 2013; Bolourchi et al., 1995; Janosi and Huszenicza, 2001), IMM antimicrobial DCT is far more common and remains the focus of this review.

Clearly, SDCT is a management practice for which farm-specific benefits and risks are difficult to quantify. Therefore, a comprehensive review of SDCT implementation and subsequent farm-level outcomes is required to appropriately evaluate SDCT as a management strategy to enhance antimicrobial stewardship. This narrative review aims to summarize current drying-off practices and their results, specifically referring to antimicrobial treatment of existing IMI at drying-off and prevention of new IMI during the dry period, to provide an overview of trends worldwide, including associations with udder health, production, economics, and AMR. Discussion of SDCT and BDCT comparisons is limited to field trials and excludes studies comparing BDCT and no antimicrobials.

DRY COW THERAPY PRACTICES

Adoption of DCT and selection methods vary considerably among countries (Table 1) (Ekman and Østerås,

2003; Vilar et al., 2018). In North America, BDCT is practiced widely, on 80 and 84% of surveyed operations in the United States and Canada, respectively (USDA-APHIS, 2016; Bauman et al., 2018), whereas in Nordic European countries and the Netherlands, routine prophylactic AMU at drying-off is not permitted (Scherpenzeel et al., 2016b; Rajala-Schultz et al., 2021; Santman-Berends et al., 2021). Further, veterinary prophylactic AMU, other than in exceptional cases, has been forbidden in the European Union since January 28, 2022 (Official Journal of the European Union, 2019). In New Zealand, SDCT has been recommended since the 1990s (McDougall, 2003; Blackwell and Lacy-Hulbert, 2013), although veterinarians may prescribe BDCT (Bryan and Hea, 2017). In some countries, regulatory violations can result in monetary fines for dairy farmers, whereas veterinarians could either temporarily or permanently lose their licenses with repeat offenses, although loss of license is rare (Rajala-Schultz et al., 2021). In all Nordic countries, cow or quarter bacteriologic diagnosis before DCT AMU is encouraged, or the herd mastitis pathogen profile and antimicrobial susceptibility profile should at least be known (Rajala-Schultz et al., 2021). In the Netherlands, veterinary guidelines for selection of cows eligible for antimicrobial DCT primarily based on SCC levels at drying-off were developed by the Royal Dutch Veterinary Association, although most farmers, in consultation with their veterinarian, use specific selection methods for their own herd (Santman-Berends et al., 2016). Selection criteria must optimize sensitivity and specificity for IMI identification while remaining feasible, both logistically and financially.

HERD CHARACTERISTICS AND SDCT

Optimization of herd screening for SDCT eligibility and management changes required before SDCT implementation have not been fully evaluated. Despite some general guidelines, robust data to direct herd-level selections are lacking. Regardless, before implementation of SDCT, a review and optimization of herd and udder general hygiene and health characteristics should be undertaken, including bulk milk SCC (**BMSCC**) thresholds (e.g., <250,000 cells/mL), clinical mastitis (**CM**) incidence, and factors that influence them, such as hygienic drying-off practices and mastitis pathogen profiles (Schukken et al., 1993; Berry et al., 1997; Cameron et al., 2014; Bradley et al., 2018). It is important that major pathogen IMI prevalence at drying-off and new major pathogen IMI incidence in the dry period are minimized. Additional considerations include adequate record keeping (CM cases, antimicrobial treatments, etc.), so that producers know whether cows have had CM during lactation or additional negative health consequences (CM recurrence, culling, etc.). Such record keeping also enables identifying whether a SDCT protocol was successful based on, for example, maintained milk production and BMSCC and no increase in major pathogen IMI. As herd selection criteria were not always stated, the external validity of SDCT studies also needs to be considered because the DCT approaches may differ based on herd characteristics. For example, in Finland, BDCT adoption was greater in larger herds and in those using automated milking systems (Vilar et al., 2018).

When BDCT was banned in the Netherlands, only minor negative outcomes followed (slight increase in percentage of cows with high SCC and new high SCC), providing evidence that SDCT can be initiated in most herds without major negative udder health consequences (Santman-Berends et al., 2021). A Finnish analysis of DHIA records over 5 yr compared herd milk production and SCC among farms implementing various DCT approaches (SDCT, BDCT, or no DCT) (Niemi et al., 2020). The authors stated it was possible to maintain low herd average BMSCC and high milk production while employing SDCT. Regarding SCC, production and management skills varied greatly among herds (Niemi et al., 2020); therefore, udder health management is likely crucial to successfully implement SDCT.

In studies on DCT, herd characteristics were variable and often unreported (Table 2). Herd characteristics that may contribute to improved SDCT outcomes include a relatively low BMSCC, low contagious mastitis prevalence (absence of *Strep. agalactiae* and controlled *Staph. aureus* IMI) (Cameron et al., 2014; Bradley et al., 2018), hygienic drying-off practices (e.g., minimizing risk of introducing bacteria into the teat canal, dry and clean bedding after drying-off) (McDougall et al., 2009), good record keeping, veterinary support, and ongoing monitoring for potential unintended consequences. Although most herds can adopt SDCT without major udder health consequences (Santman-Berends et al., 2021), herds with deficiencies in any of the preceding criteria should improve mastitis management before considering adopting SDCT to improve overall mastitis management and optimize SDCT implementation.

SELECTION OF COWS

The IMM administration of antimicrobials at drying-off is associated with higher bacteriological cure rates compared with no DCT (Halasa et al., 2009a; Winder et al., 2019a); therefore, failure to treat quarters infected with major pathogens has negative udder health consequences (Østerås and Sandvik, 1996; Winder et al., 2019a). Consequently, the main

Table 1. Summary of most recent reported country-specific selective dry cow therapy (SDCT) practices[1]

Country	Reference	Drying-off practice		DCT regulation
		Antimicrobial	TSL	
Austria	Wittek et al. (2018) n = 1,657 herd records	- 31.3% dried off using antimicrobials - 68.7% dried off without antimicrobials	- Unknown	None
Canada	Bauman et al. (2018) n = 374 participants	- 84% BDCT	- Unknown	None
Finland	Vilar et al. (2018) n = 715 participants	- 13% BDCT, 78% SDCT, 9% no DCT - Drying-off microbiological milk testing was the most common selection method (81.9%) of SDCT farms (also conducted on 64.2% of BDCT farms). - Milk from all cows was examined on 33.9% of SDCT farms; significantly, this was done more frequently on pipeline farms (51.9%) than on parlor (25.4%) or AMS (22.7%) farms. - CM history and high SCC (61.3%) second most common criteria - 71.5% of SDCT farms treated up to 25% of cows - BDCT higher in AMS, larger farms, and with increasing milk production	- Larger herds more likely to use internal TSL, 44.5% of TSL farms applied it to up to one-fourth of cows and 34.6% to all cows - Differences between internal TSL with AMS (49.0%), milking parlor (40.7%), or pipeline (24.8%) - Internal TSL alone or in combination with antimicrobial DCT on 35% of farms	Nordic countries do not permit routine prophylactic AMU at drying-off
France	Poizat et al. (2017) n = 24 participants	- 58.3% BDCT - 41.7% SDCT	- Some used it, details not specified	None
Germany	Bertulat et al. (2015) n = 93 participants	- 79.6% BDCT, SDCT not mentioned by any producer, 9.7% did not use DCT - Bacteriological examination of milk before drying-off on 31.0% of farms, with bacteriological examinations of all cows on 6.6% of farms, whereas 24.4% were for selected cases (e.g., high-yielding cows) - 64.9% of all antimicrobial DCT conducted without bacteriological examination	- Internal TSL used by 33.3% of farms - Farms using antimicrobial DCT 2.8 times as likely to use internal TSL - 22.6% of farms used internal TSL and antimicrobials	None
Ireland	More et al. (2017) n = ~85% of all sales (2003–2015)	- Estimated national coverage of DCT (2003–2015), increased by 2.9–3.2% (each year from 2003 to 2015), reaching ~100% coverage during last 6 yr of the study period	- 64–67% of teat sealant of total numbers of antimicrobial tubes sold (2011–2015)	None
The Netherlands	Santman-Berends et al. (2016) n = 224 herds, 220 for TSL use	- 16 (7.1%) treated ≤25% of cows with antimicrobials at drying-off - 26 (11.6%) treated 26–50% of cows - 27 (12.1%) treated 51–75% of cows - 155 (69.2%) treated ≥76% of cows	- 60 herds (27.2%) indicated "yes" (>90% of cows) 47 (21.4%) said "sometimes" (11–89% of cows), and 113 (51.4%) said "no" (<10% of cows)	Preventive AMU in animal husbandry prohibited since 2013
United States	USDA-APHIS (2016) n = 1,261 herds	- 93.0% treated with IMM antimicrobials at drying-off, no DCT used on 9.2% of farms - BDCT used in 94.2% of farms with >500 cows versus 77.5% with <100 cows	- Internal TSL used in some cows on 36.9% - 33.9% used internal TSL on all cows, 14.0% used external TSL	None
United Kingdom	Fujiwara et al. (2018) n = 146 participants	- Drying-off IMM antimicrobials used on 95.9% of farms	- 82.2% using antimicrobials with TSL - TSL used by 84.9% of farms, with 86.3% using internal TSL, 3.2% using external, and 9.5% using both	None

[1]AMS = automatic milking system; AMU = antimicrobial usage; BDCT = blanket dry cow therapy; DCT = dry cow therapy; IMM = intramammary; TSL = teat sealant.

challenge for SDCT implementation is deciding which cows or quarters should be treated with antimicrobials and which could be left untreated. For prudent AMU, the objective is to accurately identify cattle likely to have a major pathogen IMI that would potentially benefit from antimicrobial treatment. If antimicrobi-

Table 2. A summary of reported blanket and selective dry cow therapy (SDCT) comparisons primarily using SCC or pathogen identification-based selection methods, limited to field studies (controlled trials), sorted by reference[1]

Reference	Region/ country	Herd BMSCC	Cow selection	Selection level	Teat sealant	Outcome
SCC-based selection						
Rindsig et al. (1978) - 232 cows - 1 herd	University of Illinois, United States	Not listed	- CMT ≥2 in any quarter, or SCC (membrane filter-DNA procedure) >500,000 cells/mL antimicrobial treated - Controlled trial	Cow	No	- Similar quarter IMI elimination rate (*Staphylococcus aureus*, *Streptococcus agalactiae*, other streptococci, and gram-negative rod) in BDCT (85.4%) and SDCT (88.2%) - New quarter IMI slightly higher in SDCT (6.5%) compared with BDCT (3.1%) - Lower CM incidence with BDCT (4.6%) compared with SDCT (7.8%) - Lower SCC with BDCT
Østerås et al. (1991) - 703 cows - 291 herds	Norway	Not listed	- >100,000 cells/mL in last 2 SCC tests, and positive CMT or major pathogen in 1+ quarters at first screening (1–6 wk before drying-off) - Randomized controlled trial: Group A = control (no treatment); Group B = placebo (infected quarters treated); Group C = only treated infected quarters; Group D = IMM AMU in infected quarters every second day for 6 d at drying-off	Quarter (except if ≥3 quarters infected, all treated) Drying-off CM treated with antimicrobials (groups B/C/D)	No	- Quarter-based SDCT using samples taken 1–6 wk before drying-off provided inadequate diagnostics for SDCT (i.e., culture results before drying-off were not well correlated with drying-off culture results) - When using long-acting IMM antimicrobials, all quarters of an infected cow should be treated, whereas treating only infected quarters may be possible with short-acting IMM antimicrobials
Østerås et al. (1994) - 684 cows - 288 herds	Norway	Not listed	- Cows >100,000 cells/mL in last 2 tests, and mastitis present (positive CMT) or bacteriological finding of major pathogen in 1+ quarters at first screening (45 ± 32 d before drying-off) - Randomized controlled trial: group A = control (no treatment), group B = placebo, group C = long-acting AMU in each infected quarter, group D = short-acting AMU, every second day for 8 d in infected quarters	Quarter (except if ≥3 quarters infected, all treated) CM treated at drying-off with antimicrobials (groups B/C/D)	No	- More healthy cows in treatment groups (C+D) than control groups (A+B), and more cows with major pathogens in control groups mid-lactation - More healthy quarters with short than long-acting AMU in mid-lactation, and for cows with major pathogens both before and at drying-off (higher cure rate than long-acting AMU) - In quarters with *Staph. aureus* IMI both before and at drying-off, no difference between groups at calving - Short-acting AMU had significantly fewer new IMI (*Staph. aureus* or *Streptococcus dysgalactiae*) in untreated healthy quarters in cows with <3 infected quarters - Differences between long-acting AMU and controls were present at calving but decreased later in lactation to a level that was not significant
Østerås and Sandvik (1996) - 608 cows - 268 herds	Norway	Not listed	- Refer to Østerås et al. (1994)	Refer to Østerås et al. (1994)	No	- No effect on culling rate - Control cows had higher incidence of CM, higher SCC, and lower mean milk yield per lactation

Continued

Table 2 (Continued). A summary of reported blanket and selective dry cow therapy (SDCT) comparisons primarily using SCC or pathogen identification-based selection methods, limited to field studies (controlled trials), sorted by reference[1]

Reference	Region/ country	Herd BMSCC	Cow selection	Selection level	Teat sealant	Outcome
Bradley et al. (2010) - 839 and 810 cows - 6 herds	Somerset and Wiltshire, England	<250,000 cells/mL	- Uninfected (last 3 SCC <200,000 cells/mL, no CM within that period) → TSL alone or with antimicrobials - All other animals: infected → antimicrobial alone or with internal TSL - Controlled trial	Quarter	Internal	- Combination treatment (TSL and AMU) in infected cows increased likelihood of being pathogen free after calving and decreased likelihood of developing CM in first 100 DIM compared with AMU alone - No difference between TSL alone and in combination with AMU in uninfected cows, except for IMI prevalence at calving with coagulase-positive staphylococci and *Streptococcus* spp. combined - No significant differences in cure rates and new IMI rates for major or minor pathogens - In uninfected cows, no significant difference in CM; however, combination treated quarters were more likely to develop CM caused by *Escherichia coli* or an enterobacterial pathogen
Rajala-Schultz et al. (2011) - 723 cows - 4 herds	Ohio, United States (2 herds were institutional)	Mean BTSCC = 162,000–340,000 cells/mL	- Randomized controlled trial: low-risk cows randomly assigned to antimicrobial DCT or no DCT (1) if <200,000 cells/mL and no CM, (2) if CM during first 90 DIM, but <100,000 cells/mL for rest of lactation	Cow	No	- No significant difference between milk yield or IMI at calving of treated and untreated low-risk cows during following lactation - Treated low-risk cows had 16% lower SCC than untreated cows during following lactation - Milk yield and SCC effects were variable in different herds
Scherpenzeel et al. (2014) - 1,657 cows - 97 herds	Netherlands	BMSCC = 41,000–387,000 cells/mL (mean 184,000)	- Primiparous <150,000 cells/mL - Multiparous <250,000 cells/mL - No CM present - Split-udder controlled trial	Split-udder	No	- SCC at calving and 14 DIM significantly higher without AMU - CM incidence rate 1.7 times higher without AMU - Highest CM incidence rate occurred during first 21 DIM - Dry period → CM 3.7 times higher odds to acquire CM without AMU
Vasquez et al. (2018) - 565 cows - 1 herd	New York, United States	Mean BMSCC = 201,000 cells/mL	- Low risk = <200,000 cells/mL at last test, mean <200,000 cells/mL over last 3 tests, no CM at drying-off and ≤1 CM case during lactation - Blinded randomized controlled trial	Cow	External, all cows	- No statistical differences for new IMI risk, milk production, linear scores, culling events, or CM events - Cows treated with antimicrobials had slightly higher IMI cures than cows that did not receive antimicrobials

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Table 2 (Continued). A summary of reported blanket and selective dry cow therapy (SDCT) comparisons primarily using SCC or pathogen identification-based selection methods, limited to field studies (controlled trials), sorted by reference[1]

Reference	Region/ country	Herd BMSCC	Cow selection	Selection level	Teat sealant	Outcome
McParland et al. (2019) - 654 cows - 3 herds	Cork, Ireland (research herds)	BMSCC <200,000 cells/mL, exceeded only in Jan and Feb (n = 2)	- Randomized controlled trial: SCC <200,000 cells/mL, and no CM (low SCC) in previous lactation assigned to internal TSL alone or antimicrobials and TSL (high SCC = >200,000 cells/mL or CM during lactation)	Cow	Internal, all cows	- Cows with internal TSL alone → higher daily milk yield (0.67 kg/d) over lactation and higher SCC (not considered problematic) in early, up to mid-, and throughout lactation compared with low-SCC cows with internal TSL and antimicrobials - No difference → weekly SCC of cows with internal TSL alone and high-SCC cows - Odds of internal TSL alone cows having bacteria present in foremilk across lactation was 2.7 and 1.6 times the odds of low-SCC cows with internal TSL and antimicrobials and of high-SCC cows, respectively
Zecconi et al. (2020) - 516 cows - 5 herds	Lombardy, Italy	BMSCC 175,000–220,000 cells/mL	- AMU if SCC at last test before drying-off >100,000 cells/mL (primiparous), >200,000 cells/mL (multiparous) - Controlled trial (randomized for treatment group for 2 antimicrobial products)	Cow	Internal, all cows (3 herds)	- TSL significantly increased bacteriological cure, significantly decreased new IMI rate - New IMI rate significantly lower in negative untreated cows compared with treated cows - Proportion of negative (49.1 vs. 49.3%), transient (24.8 vs. 27.3%), or harbored IMI (26.1 vs. 23.5%) were very similar at drying-off and after calving, respectively - SDCT increased risks for IMI after calving
Pathogen identification-based selection						
Browning et al. (1990) - 1,044 cows - 12 herds	Victoria, Australia	Mean BMSCC = 100,000–400,000 cells/mL	- Laboratory culture-negative cows at drying-off randomly allocated to receive treatment (all quarters) or no treatment - Randomized controlled trial: Infected cows randomly allocated to all quarters treated or infected quarter only treatments	Cow/quarter	No	- New IMI rate during dry period almost 4 times higher for infected cows with quarter treatment compared with other treatment groups - Significantly higher *Staph. aureus* IMI rate in infected cow-level treatment group in early lactation compared with the uninfected, all treated group, but no overall difference for total pathogens between groups - Significantly higher *Streptococcus uberis* rate infected quarter-level treatment group, both at calving and mid-lactation, compared with the infected cow-level treatment - No significant difference in CM incidence, but in early lactation different between groups
Browning et al., (1994) - 1,044 cows - 12 herds	Refer to Browning et al. (1990)	Not listed	- Refer to Browning et al. (1990)	Cow/quarter	No	- Quarter SDCT resulted in a higher new dry period IMI rate - No significant difference; however, teat-level selected cows had more infected quarters at calving - No difference in IMI prevalence by mid-lactation - Low initial IMI prevalence → no difference between strategies - Medium initial IMI prevalence → new IMI rate with selective quarter therapy was higher than other strategies

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Table 2 (Continued). A summary of reported blanket and selective dry cow therapy (SDCT) comparisons primarily using SCC or pathogen identification-based selection methods, limited to field studies (controlled trials), sorted by reference[1]

Reference	Region/ country	Herd BMSCC	Cow selection	Selection level	Teat sealant	Outcome
Cameron et al. (2014) - 729 cows - 16 herds	Prince Edward Island and Québec, Canada	BMSCC <250,000 cells/mL	- Cultured cows: SCC <200,000 cells/mL on last 3 tests and no CM in same period - Randomized controlled trial: BDCT (with TSL) or SDCT - SDCT based on Petrifilm on-farm culture: culture (+) = antimicrobials and TSL, culture (−) = TSL only	Cow	Internal, all cows	- No difference observed between groups for quarter-level cure risk, new IMI risk over the dry period and at calving, and CM risk in first 120 DIM
Cameron et al. (2015) - 729 cows - 16 herds	Refer to Cameron et al. (2014)	BMSCC <250,000 cells/mL	- Refer to Cameron et al. (2014)	Cow	Internal, all cows	- No difference for natural logarithm of SCC or milk production over first 180 DIM
Patel et al. (2017) - 56 cows - 1 herd	University of Minnesota, United States	Not listed	- Randomized controlled trial: Cows without CM at drying-off assigned to BDCT (TSL and AMU) or SDCT - SDCT = rapid culture system, culture (−) = TSL, culture (+) = TSL and AMU	Quarter	Internal, all cows	- No difference in IMI risk after calving, bacteriological cures, or new IMI
Kabera et al. (2020) - 568 cows - 9 herds	Québec, Canada	BMSCC <250,000 cells/mL	- Randomized controlled trial - Petrifilm on-farm culture [culture (+) = infected, culture (−) = healthy] - SDCT groups; (1) AMU–infected, TSL–healthy, (2) AMU and TSL–infected, TSL–healthy - BDCT groups; AMU alone or AMU and TSL	Quarter	Internal	- No significant difference for new IMI or persistence of existing IMI over dry period, CM incidence, mean SCC, or mean daily milk production during first 120 DIM
Comparison of pathogen identification and SCC-based selection						
Rowe et al. (2020a) - 1,211 cows - 7 herds	California, Iowa, Minnesota, New York, and Wisconsin, United States	BMSCC <250,000 cells/mL	- Randomized controlled trial - Comparison between BDCT, culture-based SDCT (quarter level), and algorithm-based SDCT (cow level) - Culture SDCT, treating quarters culture (+) - Algorithm SDCT cows, AMU if any SCC >200,000 cells/mL or ≥2 CM cases during lactation	Both cow and quarter levels	Internal, all cows	- Both culture- and algorithm-based SDCT programs unlikely to increase CM risk or test-day $\log_e$SCC, risk of removal from herd and test-day milk yield. IMI dynamics (IMI cure risk, new IMI risk) and IMI prevalence postcalving similar between BDCT, culture-based SDCT, and algorithm-based SDCT

[1]AMU = antimicrobial use; BDCT = blanket dry cow therapy; BMSCC = bulk milk somatic cell count; CM = clinical mastitis; CMT = California mastitis test; IMM = intramammary; SDCT = selective dry cow therapy; TSL = teat sealant.

als are applied preventively, cows or quarters at high risk of acquiring a new major pathogen IMI during the dry period would need to be identified. However, TSL are also an effective IMI preventative in lieu of antimicrobials (Winder et al., 2019b; Kabera et al., 2021). Identification of IMI can be done using a variety of methods, including SCC at cow or quarter levels, pathogen identification-based methods, or other diagnostic procedures, such as the California Mastitis Test (**CMT**), milk leukocyte differential (**MLD**), conductivity testing, lactate dehydrogenase, and *N*-acetyl-β-D-glucosaminidase. A vast body of literature regarding selection using various SCC thresholds, bacteriological culture results, and their associated outcomes is summarized in Table 2.

Quarter-Level Versus Cow-Level Selection

Selection protocols can be employed at the cow or quarter level. Previous meta-analyses concluded that the success of SDCT protocols depended on whether they were implemented at the cow or quarter level (Robert et al., 2006a; Halasa et al., 2009b). This can be explained partly by interdependence of udder quarters (Barkema et al., 1997; Robert et al., 2006b; Paixão et al., 2017), meaning an IMI in 1 quarter is a risk factor for IMI development in other quarters of the same cow. Therefore, without TSL, quarter-level decisions could contribute to negative udder health outcomes (i.e., increased IMI prevalence). More recent studies with inclusion of TSL had success (i.e., no negative udder health impacts compared with BDCT) with cow- and quarter-level selection (Winder et al., 2019b; Rowe et al., 2020a; Kabera et al., 2021).

When using DHIA SCC reports as a basis for SDCT, only cow-level selection is possible, as composite milk samples are used, unless further quarter-level diagnostics are employed. However, a distinct advantage of quarter-level selection is the potential for additional AMU reduction. For example, with the inclusion of TSL, no negative udder health consequences were observed with a DCT AMU reduction of 22% using a cow-level culture-based method (Cameron et al., 2014), whereas a similar quarter-level SDCT protocol resulted in an AMU decline of 58% (Kabera et al., 2020). Rowe et al. (2020a), however, stated either a culture-guided quarter-level SDCT protocol or a cow-level algorithm-guided (SCC and CM history) SDCT protocol reduced AMU by 55%. To summarize, selection level (quarter versus cow) depends on the information available (i.e., composite milk samples versus information at quarter level), but SDCT can be successfully enacted at either level with a strong recommendation to use TSL to protect quarters not receiving IMM antimicrobials.

Pathogen Detection-Based Selection

Intramammary infection is defined based on culture of mastitis pathogens or detection of pathogen nucleic acid by PCR (Cameron et al., 2014; Vasquez et al., 2018; Vilar et al., 2018). Various mastitis pathogen detection-based SDCT protocols (e.g., rapid on-farm culture, PCR techniques, and laboratory culture methods at regional diagnostic facilities and veterinary clinics) have been studied (Cameron et al., 2014; Rowe et al., 2020a). However, their overall uptake in commercial herds is unknown (available information described in Table 1).

Pathogen detection-based SDCT methods aim to provide a direct diagnosis of IMI detection and thus more accurately identify cows that are infected and truly need antimicrobials, while also reducing negative udder health impacts associated with untreated IMI with targeted antimicrobial therapy against known infections. Sensitivity and specificity for diagnosing IMI are higher for pathogen detection-based methods compared with SCC-based approaches (Rowe et al., 2020b). Sensitivities, specificities, and positive and negative predictive values for IMI identification at drying-off are summarized in Table 3.

On-farm culture-based selection protocols [e.g., Petrifilm (Cameron et al., 2014; Cameron et al., 2015; Kabera et al., 2020) or rapid culture (Minnesota Easy 4Cast plate, University of Minnesota, St. Paul; Patel et al., 2017; Rowe et al., 2020a)] can be effectively used to select cows for SDCT (Table 2). However, culture-based selection has disadvantages compared with the use of SCC thresholds, including additional time, labor, and materials (Crispie et al., 2004; Vasquez et al., 2018, Rowe et al., 2021b). The goal of using a culture-based method is to collect milk samples from cows and culture them within a short interval, either on farm or through a veterinary clinic or other laboratory facility. However, costs are variable. For example, on-farm culture costs were estimated at 4 USD/cow (composite milk sample) (Rowe et al., 2021b), in addition to costs associated with training and maintaining skilled labor to perform cultures and interpret results. Further, culture-based methods may be less practical on smaller farms, owing to expiration dates of consumables and a lack of skilled labor. Costs associated with regular testing of milk for SCC (e.g., monthly DHIA testing) are also substantial and could exceed costs for conducting culture-based selection if used exclusively for SDCT.

Selection Based on SCC

A cow composite milk SCC >200,000 cells/mL is commonly used as an indicator of subclinical mastitis

Table 3. Summary of reported sensitivities and specificities for IMI identification at drying-off using SCC thresholds or culture results for selective dry cow therapy protocols from composite milk samples, sorted by reference[1]

Reference	Gold standard for IMI used	Method	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive predictive value, % (95% CI)	Negative predictive value, % (95% CI)
Torres et al. (2008), cow IMI prevalence 32.3%	- Culture/isolation of the same pathogen from paired samples (≥100 cfu/mL)	SCC <100,000 cells/mL and no CM	84.2 (78.8–88.8)	35.1 (30.5–39.8)	40.4 (35.9–45.0)	80.9 (74.6–86.4)
		(major pathogens only)	(88.4)	(31.0)	(not described)	
		SCC <200,000 cells/mL and no CM	69.8 (63.2–75.8)	50.6 (45.7–55.4)	42.5 (37.3–47.7)	76.2 (70.8–81.1)
		SCC <200,000 cells/mL (no CM in lactation) or <100,000 cells/mL (CM <90 DIM)	69.4 (62.9–75.4)	63.3 (58.5–67.9)	49.7 (43.9–55.4)	79.8 (75.1–83.9)
		(major pathogens only)	(79.1)	(56.9)	(not described)	
		SCC <300,000 cells/mL and no CM	62.2 (55.4–68.6)	55.3 (50.4–60.1)	42.1 (36.7–47.6)	73.7 (68.5–78.4)
Pantoja et al. (2009), cow IMI prevalence 34.6%	- ≥300 cfu/mL colonies of same type- 3+ dissimilar colony types = contaminated	<50,000 cells/mL	94	37	18	98
		<100,000 cells/mL	88	52	21	97
		<150,000 cells/mL	76	60	22	95
		<200,000 cells/mL	64	66	22	93
		<250,000 cells/mL	51	72	21	91
		<300,000 cells/mL	49	76	23	91
Cameron et al. (2013), cow IMI prevalence 43.4%	- ≥100 cfu/mL of any pathogenic organism of interest cultured, ≥200 cfu/mL for NAS - 3+ dissimilar colony types = contaminated	Petrifilm[2] on-farm culture negative (SCC <200,000 cells/mL)				
		>5 colonies	85.2 (78.5–90.5)	73.2 (66.4–79.3)	70.9	86.6
		>10 colonies	71.8 (63.9–78.9)	86.1 (80.4–90.6)	(not described)	(not described)
Kiesner et al. (2016), cow IMI prevalence 85.6%; only organic herds	- ≥100 cfu/mL of major contagious pathogens[3]	SCC <200,000 cells/mL	34.1 (27.8–40.5)	94.4 (87.0–100)	97.3	19.0
	- ≥500 cfu/mL of any other pathogen	SCC <100,000 cells/mL	70.5 (64.5–76.7)	80.5 (67.6–93.4)	95.6	31.5
	- 2 most numerous colony types identified	SCC <100,000 cells/mL + CM	72.9 (66.9–78.9)	78.0 (64.2–91.3)	95.1	32.6
		SCC <100,000 cells/mL + parity	78.5 (73.0–84.0)	61.0 (45.2–77.0)	92.3	32.4
		SCC <100,000 cells/mL + CMT >1	78.5 (73.0–84.0)	50.0 (33.6–66.3)	90.3	28.1
		Selection by farmers	36.3 (4.0–69.4)	91.6 (75.0–100)	96.7 (86.6–100)	20.0
Patel et al. (2017), quarter IMI prevalence of 34.8%	- ≥100 cfu/mL of any pathogenic organism of interest (except NAS set at ≥200 cfu/mL and *Bacillus* spp. ≥500 cfu/mL) - 3+ dissimilar colony types = contaminated	Rapid on-farm culture[4] (quarter level)	82.4 (73.3–91.4)	73.2 (65.5–80.9)	62.2 (52.2–72.2)	88.6 (82.5–94.7)

Continued

Table 3 (Continued). Summary of reported sensitivities and specificities for IMI identification at drying-off using SCC thresholds or culture results for selective dry cow therapy protocols from composite milk samples, sorted by reference[1]

Reference	Gold standard for IMI used	Method	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive predictive value, % (95% CI)	Negative predictive value, % (95% CI)
Lipkens et al. (2019), cow IMI prevalence 55.8%	- ≥300 cfu/mL colonies of same type - 3+ dissimilar colony types = contaminated (exception of NAS)	SCC at last test before drying-off				
		≥50,000	86.0 (82.8–89.3)	28.7 (24.5–33.0)	22.6 (18.7–26.5)	89.5 (86.6–92.3)
		≥100,000	68.6 (64.3–72.9)	52.4 (47.7–57.1)	25.9 (21.8–30.0)	87.3 (84.2–90.4)
		≥150,000	58.1 (53.5–62.7)	64.2 (59.8–68.7)	28.2 (24.0–32.5)	86.4 (83.2–89.6)
		≥200,000	41.9 (37.3–46.5)	74.4 (70.3–78.4)	28.3 (24.1–32.6)	84.1 (80.7–87.5)
		≥250,000	36.0 (31.6–40.5)	79.2 (75.4–82.9)	29.5 (25.3–33.8)	83.6 (80.2–87.1)
		≥500,000	20.9 (17.1–24.7)	93.8 (91.6–96.1)	45.0 (40.4–49.6)	83.0 (79.5–86.5)
		Geometric mean of last 3 SCC tests				
		≥50,000	82.4 (78.8–85.9)	32.5 (28.1–36.9)	23.0 (19.0–26.9)	88.3 (85.3–91.3)
		≥100,000	67.1 (62.6–71.5)	59.5 (54.9–64.1)	28.8 (24.5–33.1)	88.1 (85.0–91.1)
		≥150,000	49.4 (44.7–54.1)	71.6 (67.3–75.8)	29.8 (25.5–34.1)	85.3 (81.9–88.6)
		≥200,000	37.6 (33.1–42.4)	79.3 (75.5–83.1)	30.8 (26.4–35.1)	83.9 (80.4–87.4)
		≥250,000	32.9 (28.5–37.4)	85.3 (82.0–88.7)	35.4 (30.9–39.9)	83.9 (80.4–87.4)
		≥500,000	12.9 (9.8–16.1)	95.4 (93.4–97.4)	40.7 (36.1–45.4)	81.8 (78.1–85.4)
		Sum of last 3 SCC tests				
		≥50,000	89.4 (86.5–92.3)	20.1 (16.3–23.9)	21.5 (17.6–25.3)	88.6 (85.6–91.6)
		≥100,000	76.5 (72.5–80.5)	44.5 (39.9–49.2)	25.2 (21.1–29.3)	88.6 (85.6–91.6)
		≥150,000	68.2 (63.9–72.6)	57.2 (52.5–61.8)	28.0 (23.8–32.2)	88.1 (85.0–91.1)
		≥200,000	57.6 (53.0–62.3)	66.7 (62.2–71.1)	29.7 (25.4–34.0)	86.6 (83.4–89.8)
		≥250,000	49.4 (44.7–54.1)	72.4 (68.2–76.6)	30.4 (26.1–34.8)	85.4 (82.1–88.7)
		≥500,000	27.1 (22.9–31.2)	87.6 (84.5–90.7)	34.8 (30.4–39.3)	83.1 (79.6–86.6)
Rowe et al. (2020b),[5] quarter IMI prevalence of 25%	- "Significant growth" of any pathogen - NAS with <200 cfu/mL and *Bacillus* spp. <500 cfu/mL considered "nonsignificant growth" - 3+ dissimilar colony types = contaminated	SCC >200,000 cells/mL or 2+ CM cases during lactation	66 (61–71)	47 (44–50)	30 (27–33)	80 (77–83)
		(major pathogens only)	[72 (57–84)]	[44 (42–47)]	[4 (3–5)]	[98 (97–99)]
		Rapid on-farm culture, producer	72 (67–76)	55 (52–58)	35 (32–39)	85 (83–88)
		(major pathogens only)	[75 (59–86)]	[49 (46–52)]	[4 (3–5)]	[99 (97–99)]
		Quarter-level samples	72 (67–76)	61 (58–64)	39 (35–42)	87 (84–89)
		(major pathogens only)	[75 (59–86)]	[53 (51–56)]	[4 (3–6)]	[99 (98–99)]
		Rapid on-farm culture, technician	76 (72–81)	52 (49–55)	35 (32–38)	87 (84–89)
		(major pathogens only)	[72 (57–84)]	[45 (42–48)]	[4 (3–5)]	[98 (97–99)]
		Quarter-level samples	73 (68–77)	63 (60–66)	40 (36–44)	87 (85–89)
		(major pathogens only)	[70 (54–82)]	[54 (52–57)]	[4 (3–6)]	[98 (97–99)]
McDougall et al. (2021b),[6] cow IMI prevalence 7.2%, major pathogens	- Single *Staphylococcus aureus* colony present, or 2+ colonies of other species[7] - 2 colony types = mixed, 2+ types = contaminated	Last SCC report (>108,000 cells/mL)	86	71	20	98
		Maximum SCC (>152,000 cells/mL)	82	74	20	98
		Average SCC (>105,000 cells/mL)	76	80	24	98

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Table 3 (Continued). Summary of reported sensitivities and specificities for IMI identification at drying-off using SCC thresholds or culture results for selective dry cow therapy protocols from composite milk samples, sorted by reference[1]

Reference	Gold standard for IMI used	Method	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive predictive value, % (95% CI)	Negative predictive value, % (95% CI)
Rowe et al. (2021c), cow IMI prevalence 47.8%	- MALDI-TOF mass spectrometer, cows with 1+ infected quarters classified as positive for IMI - NAS with <200 cfu/mL and *Bacillus* spp. with <500 cfu/mL considered not infected	Primiparous, SCC <150,000 cells/mL at last test, Multiparous, SCC <50,000 cells/mL at last test	53 (47–58)	52 (47–57)	50 (45–55)	54 (51–58)
		(major pathogens only)	[62 (56–68)]	[52 (47–57)]	[20 (17–24)]	[88 (84–90)]
		Primiparous: SCC <120,000 cells/mL all tests; multiparous: SCC <150,000 cells/mL at all tests, no CM during whole lactation	69 (63–74)	44 (38–49)	53 (49–57)	61 (56–65)
		(major pathogens only)	[70 (64–76)]	[39 (33–45)]	[18 (15–22)]	[87 (83–90)]
		SCC <200,000 cells/mL for each of last 3 tests, no CM between third last test and drying-off	37 (32–43)	75 (69–79)	57 (52–62)	56 (53–60)
		(major pathogens only)	[44 (37–52)]	[71 (66–76)]	[23 (19–28)]	[87 (84–89)]
		SCC <200,000 cells/mL all tests, <2 CM cases during whole lactation	56 (50–63)	56 (50–62)	54 (50–58)	58 (54–63)
		(major pathogens only)	[59 (51–66)]	[59 (51–66)]	[19 (16–23)]	[87 (83–90)]

[1]CM = clinical mastitis; CMT = California mastitis test; NAS = non-*aureus* staphylococci.

[2]AC Petrifilm (3M Canada) and incubated on-farm at 35°C for 24 h in a TurboFan HovaBator (GQF Manufacturing).

[3]*Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, and *Trueperella pyogenes*.

[4]Minnesota Easy 4 Cast Plate.

[5]All tests conducted 2 d before drying-off.

[6]Identification for treatment instead of identification to leave cows untreated, major pathogens only.

[7]*Staphylococcus aureus*, *Streptococcus dysgalactiae*, *Streptococcus uberis*, *Streptococcus* spp. (i.e., streptococci other than *Strep. uberis* or *Strep. dysgalactiae*), *Escherichia coli*, or *Klebsiella* spp.

(Dohoo and Leslie, 1991). Although SCC is not perfectly correlated with IMI status, it is a practical and often easily accessible parameter to assess udder health for herds on a routine DHIA testing program (Schukken et al., 2003). However, some countries consider SCC thresholds other than >200,000 cells/mL or consider primiparous and multiparous cows separately (Table 2). Differential SCC (i.e., differentiating proportions of specific leukocyte types) has also been evaluated as an effective proxy for IMI status (Schwarz et al., 2019; Halasa and Kirkeby, 2020); however, application of differential SCC in practice is currently limited, and its value for SDCT has yet to be evaluated.

When establishing an optimal SCC threshold for SDCT selection, it is important to consider that lowering the threshold will increase the sensitivity of diagnosing an existing IMI, but concurrently increase the proportion of false positives (lower specificity and lower positive predictive value) and therefore result in more DCT AMU (Pantoja et al., 2009; Scherpenzeel et al., 2016a). Furthermore, pathogens vary in their effects on SCC after establishing an IMI and in their potential for identification at drying-off through the use of SCC records (Rowe et al., 2021c).

The ideal SDCT protocol will have an optimal sensitivity to identify cows with a major pathogen IMI that will benefit from antimicrobial treatment, but also be specific enough to limit the use of antimicrobials in udders or quarters unlikely to benefit from treatment. In the absence of a perfect diagnostic test, a balance must be struck between limiting untreated infected animals and administering unnecessary antimicrobial treatments; this balance may depend on the goal of AMU reduction (i.e., optimizing udder health versus limiting livestock-associated AMU for improving public health) (Scherpenzeel et al., 2016a; Rowe et al., 2021c).

Commonly, SCC-based SDCT protocols may include additional selection criteria such as CM history (no CM or ≤1 CM case during lactation, or no CM in a specific interval such as the previous 3 mo) (Rajala-Schultz et al., 2011; Vasquez et al., 2018; Rowe et al., 2020a). Although inclusion of CM history may not add additional benefit to selection criteria (McDougall et al., 2021b; Rowe et al., 2021c), these data may be readily accessible and could improve selection, specifically in herds with higher lactational CM incidence (Rowe et al., 2021c).

A threshold of >200,000 cells/mL is a conventional cutoff value for diagnosing an IMI, but sensitivity can be increased by considering more than a single SCC report (Torres et al., 2008; Lipkens et al., 2019) or lowering the threshold (McDougall et al., 2021b). Some authors suggested that SCC <200,000 cells/mL during the last 3 mo before drying-off provides the best balance of sensitivity and specificity for SCC-based identification of cows without IMI at drying-off, using bacteriological culturing as the gold standard (Torres et al., 2008; Lipkens et al., 2019). However, in a comparison of 4 SCC-based SDCT algorithms (Table 3), Rowe et al. (2021c) reported higher sensitivity through consideration of all SCC tests during lactation compared with using only the last 3 mo, although all algorithms had poor agreement with IMI status. Nevertheless, these algorithms had high negative predictive values for the presence of major pathogen IMI, which may account for their success in the field (Rowe et al., 2021c).

It is becoming evident that various selection methods can be effective: SDCT protocols based on either SCC or pathogen detection can identify cows that would benefit from antimicrobial DCT to varying degrees. Apart from test characteristics, the choice of a particular selection method for SDCT may also include factors such as cost and ease of implementation for the producer and farm workers. In summary, despite no perfect selection method, various methods can be effectively employed in a SDCT protocol.

Other Diagnostic Tests

Other diagnostics that promote decision-making for IMI identification, such as CMT (Poutrel and Rainard, 1981; Bhutto et al., 2012; Swinkels et al., 2021), MLD (Denis-Robichaud et al., 2019), electrical conductivity (Manning et al., 2019), lactate dehydrogenase (Rowe et al., 2020b), and *N*-acetyl-β-D-glucosaminidase (Hassan et al., 1999), have been evaluated for use in SDCT protocols. Although these diagnostics have been evaluated for their ability to identify IMI, their success depends on diagnostic thresholds and subjective interpretations (Poutrel and Rainard, 1981; Godden et al., 2017).

Few published studies have evaluated the effectiveness of selection criteria based on these tests when used in SDCT protocols in comparison with BDCT or with another method for selection of cows or quarters for SDCT (Poutrel and Rainard, 1981; Denis-Robichaud et al., 2019; Swinkels et al., 2021). Instead, the major focus has been addition of these diagnostics to either bacteriological diagnosis or SCC threshold methods to increase sensitivity/specificity or to specifically detect infected quarter(s) once a cow has been diagnosed with an IMI (Rindsig et al., 1978; Cameron et al., 2014; Gonçalves et al., 2017).

In a small study (n = 83 cows) electrical conductivity was deemed not to be an accurate measure of IMI identification for SDCT (Manning et al., 2019), whereas Rowe et al. (2020b) stated that lactate dehydrogenase had poor agreement with IMI status at drying-off. When a CMT-based SDCT protocol was used, approxi-

mately 80% of major pathogen IMI and only 23% of minor pathogen IMI were identified, whereas 13% of uninfected quarters were false positives (Poutrel and Rainard, 1981). More recently, both cow- and quarter-level CMT-based SDCT maintained udder health [CM incidence, major pathogen cure rates, milk yield in the first 100 DIM, and decreasing AMU 31 to 55% (Swinkels et al., 2021)], with internal TSL use in all quarters of all cows. Based on these study findings, CMT could potentially be used to guide SDCT treatment decisions in high SCC cows, and antimicrobial DCT in low-SCC cows does not appear to improve udder health, regardless of CMT results (Swinkels et al., 2021). However, as these findings have not been replicated, further evidence is needed.

In a recent MLD-based SDCT study, CM incidence rate, moderate and severe CM incidence rate, SCC, milk production, and odds of AMU for CM in the first 100 DIM did not differ compared with BDCT (Denis-Robichaud et al., 2019). However, with a modest sample size (n = 328 cows), the evidence to support using an MLD-based selection method was limited. Although *N*-acetyl-β-D-glucosaminidase has been suggested as an effective diagnostic tool to detect IMI, Hassan et al. (1999) deemed high activity of *N*-acetyl-β-D-glucosaminidase was not an accurate IMI identification method, as only 29.7% of quarters with high activity had a mastitis pathogen detected by culture, compared with 14.5% in the normal activity group.

Although the use of CMT and MLD-based SDCT protocols is promising, until more research describing the accuracy and utility of these cow-side diagnostic methods is available, pathogen detection or DHIA SCC threshold-based selection methods provide more reliable information than currently available described diagnostics.

TEAT SEALANTS

To prevent new IMI in the dry period, it is important to reduce the likelihood of udder pathogens entering the teat canal and proliferating in the udder. Up to 50% of teats remain open 10 d after drying-off (Williamson et al., 1995), and 23% are open for up to 6 wk into the dry period (Dingwell et al., 2004), considerably increasing the risk of pathogens entering the teat canal. Teat sealants were developed to offer protection against new IMI by adding a physical barrier with more reliability than relying solely on keratin plug formation (Krömker et al., 2014; Biggs, 2017). Further, most IMI during the dry period are caused by environmental bacteria (Crispie et al., 2004; Dingwell et al., 2004; Green et al., 2005), and TSL may provide greater IMI protection compared with an IMM antimicrobial DCT alone for environmental bacteria (Huxley et al., 2002). This method provides a good opportunity for reducing prophylactic AMU by providing another means of preventing IMI, although TSL use does not replace other measures to prevent dry period IMI.

Both internal and external TSL are available. External TSL are an external coating on the teat end typically applied using a dipping cup. However, they can be difficult to apply correctly, are ineffective long term, and require frequent reapplication (Crispie et al., 2004; McDougall et al., 2009; Biggs et al., 2016). In contrast, internal TSL consist of supposedly inert substances infused into the teat canal and teat cistern, ideally forming a physical barrier that remains in the distal teat cistern during the dry period but are stripped out at the first milking after calving (Meaney, 1976; Bhutto et al., 2011). An internal TSL plug was confirmed at first milking in 83% (ranging from 45 to 100% by herd) of treated quarters (Kabera et al., 2018). Based on positive research findings, the NMC (2006) has recommended TSL application as part of dry cow management.

Internal TSL use without concurrent AMU in cows identified as noninfected at drying-off has been successful, with no difference compared with BDCT for CM incidence in the dry period (Huxley et al., 2002) and during the first 120 DIM (Cameron et al., 2014; Rowe et al., 2020a), for risk of new IMI during the dry period (Bradley et al., 2010; Cameron et al., 2014) and at calving (Patel et al., 2017), and for SCC and milk production in the subsequent lactation (Cameron et al., 2015). Internal TSL reduces new dry period IMI risk by 52% compared with no treatment and by 23% compared with IMM antimicrobials in cows entering the dry period without an IMI (Dufour et al., 2019). External TSL was evaluated in 2 SDCT studies, and it was also successful compared with BDCT, with no differences for SCC (Denis-Robichaud et al., 2019), linear score, new IMI risk (Vasquez et al., 2018), milk production, culling, or CM incidence (Vasquez et al., 2018; Denis-Robichaud et al., 2019).

If administered with IMM antimicrobials, TSL may increase IMI protection (Godden et al., 2003; Bradley et al., 2011) and was associated with decreased SCC compared with IMM antimicrobials alone (Golder et al., 2016). Specifically, concurrent administration of TSL and IMM antimicrobials [with antibacterial activity, especially against gram-positive bacteria (e.g., cloxacillin)], may improve protection against gram-negative bacteria later in the dry period (Bradley et al., 2011). However, other studies (Woolford et al., 1998; Huxley et al., 2002; Cook et al., 2005) suggested no increased

IMI protection with combined internal TSL and IMM antimicrobials in low-SCC cows. In studies conducted with low-SCC cows, no difference in IMI protection was found between internal TSL only and cows treated with a combination of internal TSL and IMM antimicrobial (Cameron et al., 2014; Patel et al., 2017; Kabera et al., 2020).

In a meta-analysis (1974–2020), if internal TSL was administered to untreated, healthy quarters or cows at drying-off, no difference was observed between BDCT and SDCT regarding the risk of IMI incidence during the dry period and at calving and regarding early-lactation CM risk, milk yield, and SCC (Kabera et al., 2021). However, without an internal TSL, new IMI dry period risk and harboring an IMI at calving was higher with SDCT versus BDCT (Kabera et al., 2021).

Furthermore, mechanisms of action of internal TSL may also include antimicrobial activity, in addition to physical blocking of the teat canal (Notcovich et al., 2020). Specifically, bismuth subnitrate, a component of TSL, is associated with reduced bacterial growth of major mastitis-causing pathogens, with the extent of inhibition varying among bacterial species (Notcovich et al., 2020). In addition, a small German study (n = 50 cows) detected no difference in IMI protection of a bismuth subnitrate-free TSL between experimentally treated and control (untreated) cows (Kiesner et al., 2015). The impacts of this potential growth inhibition on udder health and SDCT need to be studied.

Low-SCC cows (<200,000 cells/mL for the entire preceding lactation) receiving only internal TSL had higher mean daily milk production but slightly higher lactational SCC (34,001 cells/mL with IMM antimicrobials versus 41,523 cells/mL for no IMM antimicrobials) compared with concurrent antimicrobial and internal TSL use in the subsequent lactation (McParland et al., 2019). However, no other studies detected a positive effect of TSL use on milk production.

Despite numerous studies documenting overall internal TSL benefits both in healthy quarters untreated with antimicrobials (Winder et al., 2019b: Kabera et al., 2021) and in combination with IMM antimicrobials (Godden et al., 2003; Bradley et al., 2011; Golder et al., 2016), some research suggests the possibility of negative TSL and IMM antimicrobial interactions. Internal TSL use in combination with IMM antimicrobials limited antimicrobial penetration to teat canal lining and potentially impaired the effectiveness of eliminating chronic bacterial infections within this udder niche (Derakhshani et al., 2018). Furthermore, IMM oil-based antimicrobials have been theorized to undermine internal TSL retention through affecting the viscosity of TSL [Bradley et al., 2010; specific combination of Cepravin Dry Cow (Intervet Schering-Plough Animal Health) and OrbeSeal (Pfizer Animal Health)], where TSL presence at calving improved when used alone compared with being used in combination with IMM antimicrobial (Kabera et al., 2018). Although the specifics of TSL and IMM antimicrobial interactions are unclear, it is evident that TSL should at a minimum be administered in non-antimicrobial-treated quarters as part of an SDCT protocol (Cameron et al., 2015; Winder et al., 2019b; Kabera et al., 2021).

IMPACTS OF SDCT

Udder Health

If SDCT programs are successful, IMI dynamics (i.e., new IMI, bacteriological cures) during the dry period will be similar to BDCT, resulting in equivalent IMI prevalence at calving. If this equivalence is achieved, udder health and performance in the subsequent lactation should be equivalent to BDCT. The majority of recent clinical trials concluded that SDCT can be implemented in commercial dairy herds without negative consequences for udder health (Bradley et al., 2010; Cameron et al., 2014, 2015; Vasquez et al., 2018; Rowe et al., 2020a; Rowe et al., 2020c; Kabera et al., 2020; Swinkels et al., 2021). This conclusion was supported by recent meta-analyses that determined udder health was similar for BDCT and SDCT, provided that SDCT protocols used on-farm culture systems (Minnesota Easy 4Cast plate or Petrifilm) or SCC-based selection and internal TSL were administered to untreated healthy quarters or cows (Winder et al., 2019b; Kabera et al., 2021).

When considering studies presenting negative impacts of SDCT (Table 2), explanations can often be derived through careful assessment of study methods. Scherpenzeel et al. (2014) used SCC thresholds of <150,000 and <250,000 cells/mL for primiparous and multiparous cattle, respectively, and reported increases in SCC at calving and 14 DIM and higher CM incidence after introducing SDCT in low-SCC cows. In addition, Rajala-Schultz et al. (2011) reported that low-SCC cows treated with antimicrobials had 16% lower SCC (approximately 35,000 cells/mL) than untreated low-SCC cows in the subsequent lactation. However, herd selection was not described, and TSL was not administered in either study (Rajala-Schultz et al., 2011; Scherpenzeel et al., 2014). Further, Scherpenzeel et al. (2014) employed a split-udder design in which exclusion of TSL acted as a risk factor for development of IMI in other quarters (Barkema et al., 1997; Robert et al., 2006b; Paixão et al., 2017). Zecconi et al. (2020)

reported a slight increase in new IMI after calving with SDCT; however, one factor may be that only 3 of 5 included herds used TSL, although results from all herds were combined, potentially overestimating negative effects of SDCT when TSL are applied.

Vasquez et al. (2018) reported bacteriologic cure remained slightly higher for cows entering the dry period with an IMI and receiving IMM antimicrobials, whereas Huxley et al. (2002) reported no significant differences between SDCT and BDCT for CM incidence, CM severity, or bacteriological cure of existing IMI. The only difference noted was that quarters receiving TSL acquired fewer major pathogen IMI (Huxley et al., 2002). On a larger scale, the BDCT ban in the Netherlands resulted in significant DCT AMU reduction (36%) without major negative udder health impacts (Santman-Berends et al., 2021). However, a small but significant increase occurred in high test-day SCC (>150,000 cells/mL for primiparous cows, >250,000 cells/mL for multiparous cows; +0.41%) and a new high test-day SCC (either at first test after calving, or a high SCC report after low SCC at previous test day during lactation; +0.06%) (Santman-Berends et al., 2021). The only notable health impact was an increase in the probability of belonging to a herd with >25% of multiparous cows with a new high SCC test when lactation started (odds ratio = 1.23) (Santman-Berends et al., 2021). Results may have been affected by concurrent national dairy industry changes (e.g., increasing herd sizes with removal of chronic high-SCC cows). Furthermore, the impact of TSL use is unknown, as this study included higher level national surveillance data but excluded individual farm drying-off practices (Santman-Berends et al., 2021). However, Vanhoudt et al. (2018) stated that from 2013 to 2015, TSL sales in the Netherlands increased by 73%. Regardless, these higher-level surveillance data provided further evidence that most herds can enact SDCT without negative udder health consequences.

To summarize, in consideration of cow udder health, SDCT is a viable option for producers, with consistent reports of no negative impact on SCC after calving (Cameron et al., 2015; Kabera et al., 2020; Rowe et al., 2020a), IMI elimination, new IMI risk (Cameron et al., 2014; Patel et al., 2017; Vasquez et al., 2018; Kabera et al., 2020; Rowe et al., 2020c), and presence of IMI at calving (Rajala-Schultz et al., 2011; Cameron et al., 2014; Patel et al., 2017; Rowe et al., 2020c). With appropriate consideration of selection criteria and other mastitis control procedures (i.e., TSL, good overall hygiene) to reduce IMI, SDCT can be implemented without negative consequences for udder health.

Milk Production

As IMI reduce milk production (Deluyker et al., 1993; Hadrich et al., 2018), increases in SCC or CM incidence through failure to identify infected cows or quarters in an SDCT program could adversely affect milk production and farm profitability. High SCC and CM could occur due to the persistence of unidentified IMI not treated at drying-off or the development of new IMI or CM during the dry period. Although selection criteria and specific udder health impacts differed among studies on SDCT outcomes (Table 2), based on available literature, many reported no difference between BDCT and SDCT with respect to milk production in the subsequent lactation (Cameron et al., 2015; Vasquez et al., 2018; Kabera et al., 2020; Rowe et al., 2020a). However, most studies reporting no effect on milk production included either internal TSL (Cameron et al., 2015; Kabera et al., 2020; Rowe et al., 2020a) or external TSL (Vasquez et al., 2018; Denis-Robichaud et al., 2019) in their SDCT protocols, although Rajala-Schultz et al. (2011) excluded TSL use and did not report negative milk production impacts.

Interestingly, in an Irish study, low-SCC cows (<200,000 cells/mL throughout lactation) that received only internal TSL had increased mean daily milk yield (0.67 kg) over the entire lactation, compared with low-SCC cows receiving both internal TSL and IMM antimicrobials (McParland et al., 2019). However, no other studies indicated similar findings for milk production. Various studies demonstrated variable effects of TSL versus combination treatments with TSL and IMM antimicrobials on milk production, and authors speculated that pathogen profiles may influence effects of SDCT versus BDCT including TSL on milk production (McParland et al., 2019).

Based on available literature, with selection criteria sensitive enough to identify most infected cows at drying-off and TSL administration to prevent new IMI, negative milk production consequences can be avoided. However, further research is needed to better define relationships among SDCT, TSL, and milk production.

Economics

Producer DCT decision-making is likely influenced by financial costs and benefits as well as udder health impacts (Friedman et al., 2007; Scherpenzeel et al., 2016b; Poizat et al., 2017). Huijps and Hogeveen (2007) suggested that CM after calving, culling probability, dry period IMI rate, antimicrobial costs, production losses, and hourly labor rates had the greatest impacts

on DCT costs. However, a major limitation with some economic comparisons of SDCT and BDCT is that the studies included SDCT-associated increases of CM incidence (Huijps and Hogeveen, 2007; Scherpenzeel et al., 2016a), SCC (McNab and Meek, 1991; Scherpenzeel et al., 2016a; Lhermie et al., 2018), or decreased milk production in the subsequent lactation (McNab and Meek, 1991). Such assumptions were based on earlier literature assuming negative health impacts associated with SDCT implementation that are no longer relevant, as recent literature suggests no difference between CM incidence or milk production for SDCT and BDCT (McParland et al., 2019; Kabera et al., 2020; Rowe et al., 2020a). It should also be noted that TSL is not always included in the economic model (Huijps and Hogeveen, 2007; Scherpenzeel et al., 2016a; Scherpenzeel et al., 2018a), although its importance for preventing new IMI during the dry period has been established (Dufour et al., 2019; Winder et al., 2019b; Kabera et al., 2021). Therefore, structural limitations are introduced through model development that inherently put SDCT herds at an economic disadvantage when assumptions are made regarding health and production parameters that do not reflect current literature. Furthermore, economic evaluations are country or region specific, due to variations in costs or milk prices, as the latter differ between countries with or without a supply-managed system (Huijps and Hogeveen, 2007) and whether low-SCC incentives are offered, as well as other regional differences.

Most DCT economic evaluations are limited to evaluation of AMU at drying-off compared with no DCT (McNab and Meek, 1991; Berry et al., 1997; Yalcin and Stott, 2000) or blanket TSL use instead of IMM antimicrobials (Berry et al., 2004; Lhermie et al., 2018). Economic comparisons of BDCT and SDCT are presented in Table 4. Although it is not possible to directly compare included studies because of differences in modeling techniques, assumptions, year of study, and currency, efforts have been made to provide a common currency (USD) and year to highlight model differences (Table 4).

Although some results appeared to support SDCT (Table 4), models were developed with the assumption that drying-off IMI status would be known, and therefore, testing costs were not included, assuming producers already had SCC or culture data (e.g., Halasa et al., 2010). In addition, the consequences of misdiagnosing cows were ignored (Berry et al., 2004; Huijps and Hogeveen, 2007). Further, the economic model presented by Halasa et al. (2010) had meta-analyses inform the new IMI rate included in the model (with or without TSL) in cows treated with IMM antimicrobials, but only a single study (Huxley et al., 2002) was used to calculate new IMI rates for cows receiving only TSL (Halasa et al., 2010). Subsequently, the new IMI rate for cows receiving only TSL was higher in the model than IMM antimicrobials alone, or in combination with TSL (Halasa et al., 2010). However, in the original paper of Huxley et al. (2002), the authors stated that compared with quarters receiving only IMM antimicrobials, quarters with only TSL developed fewer new IMI, with no difference in IMI severity, number of infected quarters, or CM cases. Therefore, these data appeared to be misrepresented in the model. Overall, owing to model assumptions, existing economic models comparing BDCT and SDCT should be interpreted with care as many factors influence economic costs and benefits of SDCT versus BDCT protocols.

Some studies included assumptions based on current literature in their model (Patel et al., 2017; Rowe et al., 2021b), assuming no inherent udder health disadvantages for SDCT cows were present. In the study by Patel et al. (2017), assumptions were made regarding incubator costs attributed to each cow, as authors assumed a large herd size (800 cows), that producers would also use the culture system for lactational IMI identification (in addition to SDCT), and its cost would be amortized over 5 yr. Therefore, actual culturing costs per cow may be higher for SDCT. Regardless, a successful AMU reduction of 48% was possible with additional economic benefits (Patel et al., 2017), and no negative udder health impacts were observed.

Meanwhile, Rowe et al. (2021b) stated that SDCT was more economically beneficial than BDCT, and they also specified that SCC-based SDCT was more economically beneficial than culture-guided SDCT (mean costs savings per cow of 7.85 USD versus 2.14 USD, respectively). However, DHIA SCC testing was assumed to be an already occurring cost, and therefore, no additional testing costs were included. Furthermore, economic impacts varied considerably among herd economic conditions. In a sensitivity analysis, the authors identified that the economic advantages of SDCT would be substantially reduced in situations in which its implementation increased clinical and subclinical mastitis after calving (Rowe et al., 2021b). Although economic benefits of SDCT were higher in herds with lower CM incidence and BMSCC, all herd types can have reduced AMU at drying-off without economic losses (Scherpenzeel et al., 2018a).

Overall, economic impacts of SDCT likely differ among herds and management systems owing to varying pathogen profiles, selection criteria, costs for antimicrobial treatments, and the level of AMU reduction achieved (Huijps and Hogeveen, 2007; Cameron et al., 2014; Scherpenzeel et al., 2018a). Therefore, it would be useful to have general agreement on

Table 4. Summary of reported economic comparisons of blanket dry cow therapy (BDCT) and selective dry cow therapy (SDCT), sorted by reference[1]

Reference	Method	Assumptions[2]	Drying-off AMU	Costs (USD/cow)[3]
Hogeveen (2005)	- Stochastic Monte Carlo model	- SDCT had higher IMI rate at drying-off, reduced cure rate, new IMI in dry period, IMI at calving and mastitis after calving - No TSL use or labor costs - Selection methods not described (assumed to have SCC reports and CM history) - Assumed sensitivity (95%) and specificity (60%)	48.9%	No DCT: 81.18 BDCT: 43.18 SDCT: 57.00
Huijps and Hogeveen (2007)	- Stochastic Monte Carlo model - Pathogen-specific IMI (*Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Streptococcus uberis*, *Staphylococcus aureus*, and *Escherichia coli*)	- Unclear assumptions for SDCT selection and sensitivity/specificity - No TSL use - SDCT had higher IMI rate at calving, CM rate, and increased production losses - CM occurring during dry period and not cured was not included - Labor costs included	35%	No DCT: 7.36–76.79 (mean 23.71) BDCT: 19.13–47.97 (mean 28.12) SDCT: 8.76–53.01 (mean 24.74)
Halasa et al. (2010)	- Stochastic bio-economic model, milk quota applied, with pathogen-specific IMI (*Strep. dysgalactiae*, *Strep. uberis*, *Staph. aureus*, and *E. coli*) (1) BDCT; (2) BDCT and TSL; (3) SDCT (at least 1 SCC >200,000 cells/mL last 3 tests before drying-off, or CM case during lactation), unselected cows had TSL only; (4) SDCT and all TSL	- Milk production recording assumed to happen every 4 wk - Sensitivity 96%, specificity 100% - PPV = 100%, NPV = 98% - No testing costs, assumed as standard management practices (SCC and CM records) - Labor costs included	29%	BDCT: 146.66 BDCT (with TSL): 152.97 SDCT (AMU or TSL): 154.04 SDCT (with TSL): 157.24
Scherpenzeel et al. (2016a)	- Deterministic model based on field data (Scherpenzeel et al., 2014) to predict outcomes for 7 SDCT scenarios - Based on last SCC (cells/mL) before drying-off, with primiparous (P) and multiparous (M) treated separately for some scenarios (1) BDCT; (2) 50,000 overall; (3) 100,000 overall; (4) 150,000 overall; (5) 150,000 (P), 50,000 (M); (6) 150,000 (P), 100,000 (M); (7) 150,000 (P), 200,000 (M); and (8) 150,000 (P), 250,000 cells/mL (M)	- Model informed by Scherpenzeel et al. (2014),[4] where SDCT cows had a significant increase in SCC at calving and CM risk - No TSL use - Labor costs included - SCC testing costs not included	(1) 3.15[5] (2) 2.48 (3) 1.94 (4) 1.56 (5) 2.09 (6) 1.83 (7) 1.37 (8) 1.27	BDCT (1): 63.93 SDCT (2): 62.36 SDCT (3): 65.44 SDCT (4): 66.33 SDCT (5): 61.69 SDCT (6): 65.84 SDCT (7): 66.52 SDCT (8): 67.87
Patel et al. (2017)	- Partial budget analysis informed by group study results culture-guided SDCT at quarter level	- Assumed large herd (800 cows) - Culture system used for lactational CM and paid over 5 yr - 2 IMM antimicrobial tubes/cow for SDCT group compared with 4 in BDCT group, no TSL costs included (applied to both groups) - Sensitivity 82.4%, specificity 73.2%, NPV 88.6%, PPV 62.2% - Labor costs included	48% reduction	SDCT: 3.09 (net return)
Scherpenzeel et al. (2018a)	- Linear programming model - 9 cow groups considered with 4 SCC classes of primiparous (P) (0–50,000; 51,000–100,000; 101,000–150,000; and >150,000 cells/mL), and 5 classes of multiparous (M) (0–50,000; 51,000–100,000; 101,000–150,000; 151,000–250,000; and >250,000 cells/mL) - BMSCC (cells/mL) ranged from low (<150,000), average (≥150,000, but <250,000), and high (≥250,000, but <400,000)	- Model informed by previous study (Scherpenzeel et al., 2014), where SDCT cows had a significant increase in SCC at calving and CM risk and literature data for high-SCC cows dried off with AMU (Barkema et al., 1998) - No TSL use - Labor costs included - SCC testing costs not included	100% 50% 75% 85%	BDCT in low (57.89), average (60.70), and high (65.51) BMSCC SDCT: 57.75 (low bulk tank SCC) SDCT: 60.70 (average bulk tank SCC) SDCT: 65.51 (high bulk tank SCC)

Continued

Table 4 (Continued). Summary of reported economic comparisons of blanket dry cow therapy (BDCT) and selective dry cow therapy (SDCT), sorted by reference[1]

Reference	Method	Assumptions[2]	Drying-off AMU	Costs (USD/cow)[3]
Rowe et al. (2021b)	- Partial budget model using Monte Carlo simulation (first 30 DIM considered) - BMSCC (90,000–230,000 cells/mL); herd size (850–5,700) - Culture-guided (quarter-level) treating only culture positive (Minnesota Easy 4Cast plate) - Algorithm-guided SDCT (cow-level) if cow had an SCC test >200,000 cells/mL or 2+ CM cases in current lactation	- Based on data from 1,275 cows (7 herds) across the US randomized to BDCT, culture-guided SDCT, or algorithm-guided SDCT (Rowe et al., 2020a,c) - No differences in dry period IMI dynamics and after-calving udder health - Internal TSL in all cows (no costs included) - No SCC testing costs, assumed as standard management practice	55% reduction (mode of distribution) (quarter-level, both SDCT methods)	Culture-guided SDCT—cost savings of 2.14 (−2.31 to 7.23 for 5th and 95th percentiles) compared with BDCT (75.5% of iterations ≥0.00 USD) Algorithm-guided SDCT: cost savings of 7.85 (3.39–12.90 USD) compared with BDCT (100% of iterations ≥0.00 USD)
Hommels et al. (2021)	- Logistic regression models developed using DHIA data and individual dairy herds in California to predict SCM (set 1) and CM incidence risk (set 2) in next lactation for 96 last test-day SCC categories - Linear programming used to optimize DCT costs in 3 simulated herds (set 1) of 1,000 cows with various BMSCC levels (low: 121,009–164,710 cells/mL; medium: 188,782–222,688 cells/mL; and high: 257,941–373,702 cells/mL)	- Set 1, assumed to use BDCT with internal TSL - Set 2, all 6 dairy herds used BDCT with internal TSL (assumed TSL used when antimicrobials were not) - Assumed risk ratio based on Scherpenzeel et al. (2018a; higher SCM/CM incidence when only TSL used versus AMU and TSL) - Internal TSL in all cows (no costs included) - No extra labor, culling, AMU, or SCM milk quality loss - Assumed 80% of discarded milk substituted for milk replacer - No SCC testing costs included	P/M 22/89% 30/88% 38/89%	Low BMSCC—SDCT: 37.3, BDCT: 38.0, no DCT: 42.9 TCMD Medium BMSCC—SDCT: 38.1, BDCT: 38.8, no DCT: 43.7 TCMD High BMSCC—SDCT: 39.3, BDCT: 39.9, no DCT: 45.2 TCMD

[1]AMU = antimicrobial use; BMSCC = bulk milk SCC; CM = clinical mastitis; DCT = dry cow therapy; NPV = negative predictive value; P/M = primiparous/multiparous; PPV = positive predictive value; SCM = subclinical mastitis; TCMD = total costs of mastitis around the dry period; TSL = teat sealant.

[2]Not all model assumptions included in table, only those relevant to interpretation of model differences.

[3]Published results were converted from EUR to USD/cow when required using mean conversion rate for publishing year (https://www.macrotrends.net/2548/euro-dollar-exchange-rate-historical-chart), and all studies with publishing years before 2021 were calculated with inflation rates to standardize them, from August of the year of publication to August 2021 (https://www.bls.gov/data/inflation_calculator.htm).

[4]For full list of bulk tank and CM incidence combinations, see Scherpenzeel et al. (2018a); Tables 2 and 3.

[5]Drying-off AMU values are expressed as animal daily dose.

economic model development and coefficient inclusion, such as routine mastitis management strategies (e.g., pre- and postmilking teat disinfection, culling of recurrent high-SCC cows, bedding management), as well as the ability to adapt economic analysis to farm-specific scenarios, to enable producers to predict expected costs or benefits (Huijps and Hogeveen, 2007). Therefore, economic models need to consider costs associated with evaluating current mastitis management practices on these farms, implementation of new management practices as required, and then application of SDCT. Models must also be updated with data supported by literature and be contextually specific, while minimizing structural limitations introduced through model development.

A partial budgeting tool that can be adapted to a variety of herd contexts for individual producers to compare economic impacts of various DCT approaches is available at https://dairyknow.umn.edu/research/udder-health/selective-dry-cow-therapy-cost-calculator/. Further economic evaluations specific to different industry contexts are needed to fully inform producers and provide tools to increase SDCT uptake.

Additional Considerations

Various factors affect drying-off decision-making and dry cow management, including social determinants of AMU, product availability, and the physical environment of the cows, all of which have changed over time (Biggs et al., 2016). Further, IMM administration is not completely risk-free and provides an opportunity for injection of bacteria into the teat canal (Leelahapongsathon et al., 2016). Therefore, hygienic drying-off practices and other management decisions are also important for overall dry cow well-being and for limiting IMI risks. Other factors influencing drying-off decisions for individual cows include, but are not limited to, parity, teat-end condition, milk production level at drying-off (abrupt cessation of milking versus gradual reduction), nutrition, body condition score, dry cow and calving area hygiene, culling of chronically infected cows, DIM at drying-off, and dry period duration (Barkema et al., 1999; Dingwell et al., 2003; Dingwell et al., 2004; Green et al., 2007; Henderson et al., 2016; Rajala-Schultz et al., 2018; Nitz et al., 2021), as well as limiting lactational IMI to reduce drying-off IMI prevalence. Although these other management practices, alongside lactational IMI prevention, are important in overall dry cow management, an in-depth discussion of them is outside the scope of this review.

ANTIMICROBIAL RESISTANCE

As AMR is a major public health concern, AMU reduction in livestock is an important area of focus (World Health Organization, 2015; Wall et al., 2016; World Bank, 2017). Selection pressure imposed by AMU in dairy cows could result in emergence, maintenance, and horizontal transfer of AMR genes (Oliver et al., 2011). Although most AMU on dairy farms is related to udder health (Oliver and Murinda, 2012; Saini et al., 2012a; Stevens et al., 2016; Ruegg, 2017) and BDCT has been propagated for decades, prevalence of AMR among udder pathogens of dairy cows in developed dairy nations is relatively low (Call et al., 2008; Bengtsson et al., 2009; Cameron et al., 2016).

Regardless, increased AMR levels would adversely affect animal health and welfare, as well as dairy farm profitability and sustainability, and is of public health concern. As reductions in livestock-related AMU are expected to decrease or at least stabilize AMR associated with production systems (Tang et al., 2017; Nóbrega et al., 2021), SDCT represents an important area for consideration to reduce AMU in the dairy industry.

The impacts of widespread SDCT adoption and reduced AMU on AMR development and spread is not fully understood, as studies considering direct relationships between antimicrobial DCT and AMR are limited. However, associations between DCT AMU and AMR on dairy farms have been observed. Specifically, penicillin and ampicillin resistance of *Staph. aureus* were associated with penicillin-novobiocin AMU for DCT, and ampicillin-intermediate or ampicillin-resistant *Escherichia coli* were associated with DCT AMU of cloxacillin, penicillin-novobiocin combination, cephapirin (Saini et al., 2012b, 2013), cefquinome, and framycetin (Schubert et al., 2021). Cephalosporin DCT administration was associated with reduced susceptibility of fecal coliforms to cephalothin and streptomycin (Mollenkopf et al., 2010). Conversely, IMM administration of antimicrobials was not associated with increased AMR prevalence among NAS species (Nóbrega et al., 2018; Stevens et al., 2018). Although organic dairy herds had lower antimicrobial MIC among NAS species and streptococci isolated from milk, compared with herds using antimicrobial DCT, differences in MIC levels were below clinical breakpoints, meaning that differences in bacteriological cure rates would not necessarily be observed (McDougall et al., 2021a).

Broader farm impacts of DCT AMU should also be considered. Antimicrobial residues may be present in colostrum fed to newborn calves, although levels are expected to be low (European Food Safety Agency Panel

on Biological Hazards et al., 2017). The European Food Safety Agency Panel on Biological Hazards concluded that the risk of fecal shedding of AMR bacteria in newborn calves fed colostrum will not increase when dams receive antimicrobial DCT if the time between drying-off and calving is longer than the antimicrobial withdrawal period.

A recent small (n = 2 farms) observational study showed lower fecal shedding of AMR bacteria in calves on farms employing SDCT (Tetens et al., 2019). Specifically, compared with SDCT, BDCT was associated with a considerably higher concentration of extended spectrum beta-lactamase-producing *E. coli* in feces of 3-d-old calves (Tetens et al., 2019). As no calf was treated with β-lactams or aminoglycosides or was fed waste milk before testing, authors stated these differences were most likely associated with DCT methods. The external validity of this study must be questioned because the sample size was very small and presumed selection effects of DCT antimicrobials decreased within the next 3 wk (Tetens et al., 2019). Although these results should be interpreted with care, broader farm impacts of DCT AMU reduction should be investigated. Specifically, the One Health approach of AMU and AMR incorporates human, animal, and environmental considerations because antimicrobial and bacterial interactions are complex and are not limited to one health sector or species (McCubbin et al., 2021). The importance of One Health considerations in AMR is supported by AMU reductions in livestock production leading to a reduction in human occupation-associated AMR infections in the associated production system (Tang et al., 2017).

It is currently unknown whether widespread SDCT adoption will directly reduce AMR prevalence in mastitis pathogens, or in part, mitigate AMR development. Potential AMU reduction through widespread SDCT adoption could influence selection pressure on the microbiome. Overall, attempts to reduce AMU on dairy farms could confer benefits to producers and animal health and improve consumer perception of animal agriculture, in addition to potential reductions in AMR. In conclusion, further research to inform best practices for mitigation of AMR development in mastitis pathogens, or more broadly in the dairy industry, is needed.

ANTIMICROBIAL USE MOTIVATIONS

Even with described literature supporting SDCT adoption, it can be difficult to convince some producers and veterinarians of its importance and facilitate sustained behavior change. It is, therefore, essential to consider various drivers and barriers to SDCT adoption to significantly increase uptake. For example, regulations and fines for "overuse" can be introduced, but unintended consequences must be considered, such as the prevention of illegal AMU requiring constant enforcement, and animal welfare concerns (Speksnijder and Wagenaar, 2018). Furthermore, a negative producer attitude toward regulations is associated with increased AMU (Kramer et al., 2017) and veterinary consultation for antimicrobial decision-making and treatment for antimicrobials routinely in the producer's possession may be limited (Kramer et al., 2017; Rees et al., 2021). Another important consideration is the public perception of AMU in the dairy industry and the external pressure that this places on the industry. For example, 91% of public respondents from the United States claimed dairy industry AMU represents a threat to human health, whereas 72% stated they would pay more for milk from cows raised without antimicrobials (Wemette et al., 2021).

Some research has been conducted to improve understanding of motivations of producers (Lam et al., 2011; Jones et al., 2015; Scherpenzeel et al., 2016b) and veterinarians (Postma et al., 2016; Higgins et al., 2017a; Scherpenzeel et al., 2018b) with respect to decreasing on-farm AMU (Speksnijder and Wagenaar, 2018; Farrell et al., 2021).

Producers

Although cattle health and welfare influence on-farm AMU (Valeeva et al., 2007; Jansen et al., 2010; Scherpenzeel et al., 2016b), other factors influencing AMU in general and dry cow AMU include producer attitudes, behavior, and perceptions (Valeeva et al., 2007; Lam et al., 2011; Poizat et al., 2017); previous experience (Scherpenzeel et al., 2016b); economic considerations (Friedman et al., 2007; Scherpenzeel et al., 2016b; Poizat et al., 2017), including lack of time (Friedman et al., 2007; Farrell et al., 2021) and resources (Poizat et al., 2017); atmospheric climate; farm biosecurity (Postma et al., 2016); societal pressure (Jones et al., 2015; Lam et al., 2017; Poizat et al., 2017); risk aversion (Speksnijder and Wagenaar, 2018; Rees et al., 2021); difficulty of implementing management changes; and a moral duty to treat a sick animal (Scherpenzeel et al., 2016b; Poizat et al., 2017; Rees et al., 2021). Concern for financial consequences and uncertainty regarding mastitis recovery without AMU were among the most important factors for producers choosing BDCT over SDCT (Scherpenzeel et al., 2016b).

The existence of prudent AMU guidelines and the awareness about them vary around the globe, with producer AMR knowledge and awareness being greater in high-income countries (Farrell et al., 2021). Skepticism has been identified regarding the degree to which agri-

cultural AMU contributes to AMR, especially regarding human health impacts (McDougall et al., 2017; Morris et al., 2016; Etienne et al., 2017), where awareness of the relationship between AMR in humans and agriculture was low (Farrell et al., 2021). In South Carolina, 86% of producers interviewed were not concerned that livestock antimicrobial overuse could cause AMR infections in farm workers (Friedman et al., 2007). Minimal concerns regarding consequences of AMU may contribute to a lack of desire to reduce AMU (Speksnijder and Wagenaar, 2018). In contrast, in the United Kingdom, 70% of producers thought reducing AMU was a good idea (Jones et al., 2015).

Selective DCT education, training, and campaigns are important in generating changes in producer attitude and behaviors regarding mastitis management (Lam et al., 2013; Farrell et al., 2021). However, successful communication of farm management improvement opportunities must acknowledge various producer attitudes, capabilities, opportunities, and learning styles (Lam et al., 2011). Producers motivated to improve udder health are more likely to be affected by a "central route" of information, including providing instruction cards, treatment plans, checklists, and software presenting a rational argument for change (Jansen et al., 2010). Furthermore, previous research showed that producers without initial behavioral change motivation were more likely to be influenced by a "peripheral route" utilizing a subconscious or indirect method without reasoning or rational arguments that focused on a single message (e.g., wearing gloves while milking) (Jansen et al., 2010). These methods should therefore be combined to optimize effectiveness of AMU reduction campaigns (Jansen et al., 2010).

Crucial components of successful communication include employing a proactive approach, personalizing messages, providing producers with practice-based examples, and using a social environment (Lam et al., 2011). The integration of science and producers' knowledge and experience increased recommendation credibility and practicality, leading to measurable and lasting changes in AMU (van Dijk et al., 2017).

Veterinarians

As BDCT was endorsed by veterinarians in many countries until recently (Scherpenzeel et al., 2016b), and some continue their adamant support (Poizat et al., 2017), it is important to consider the perspective of veterinarians, especially as they substantially influence producers regarding AMU (Friedman et al., 2007; Lam et al., 2011; Jones et al., 2015; Speksnijder and Wagenaar, 2018; Farrell et al., 2021). Literature regarding attitudes and perceptions of veterinarians toward AMU and AMR generally indicated agreement on the importance of reducing AMU in livestock production, despite some differences.

In the Netherlands, views regarding SDCT differed among veterinarians (Scherpenzeel et al., 2018b). National policy was introduced in 2013 that determined that only SDCT could be used; whereas, many veterinarians agreed with this in research conducted shortly after policy implementation, others felt they were endorsing a decision not aligned with their own belief of dry period risks (Scherpenzeel et al., 2018b). Antimicrobial prescribing behavior of livestock veterinarians is dependent on multiple factors, including obligations to ease animal suffering, financial dependency on clients, risk avoidance, advisory skill limitations, producer economic limitations, lack of producer compliance, public health safety, and beliefs regarding degree of veterinary AMU contributions to AMR (Speksnijder et al., 2015a). Veterinarians consider economic drivers to be strongly correlated with producer compliance with veterinary recommendations (Speksnijder et al., 2015b; Postma et al., 2016).

Higgins et al. (2017a) reported most UK veterinarians interviewed (n = 20) preferred SDCT as it aligned with prudent AMU strategies. Regarding veterinary SDCT perspectives, 3 themes were identified: (1) prioritizing prudent AMU and attempting to maintain producer engagement; (2) veterinary experience and ability to influence producer decisions; and (3) veterinary perceptions about SDCT risks and implementation difficulties, which varied greatly. With increasing experience in the field, veterinarians were less likely to consider veterinary contributions to AMR as a concern (Speksnijder et al., 2015b), whereas junior veterinarians were less likely to take a primary prescribing role or make suggestions contradicting senior colleagues (Speksnijder et al., 2015b), despite an expressed desire to assume more prescribing responsibility (Higgins et al., 2017a). As senior veterinarians have greater influence on producer AMU, they should facilitate the transition from BDCT to SDCT, where prudent to implement, and increase producer trust of their junior colleagues to further optimize AMU decisions (Higgins et al., 2017a). Furthermore, initiatives to mitigate negative veterinary perceptions of SDCT risks and improve producer perceptions of the veterinary community as a "united front" of SDCT support will likely promote industry changes (Speksnijder et al., 2015b; Higgins et al., 2017a).

Changing veterinary perceptions and access to new information did not always follow a logical progression (Higgins et al., 2017b). Although new data supporting TSL use were accepted by most veterinarians, research conclusions close to their own beliefs were more readily

accepted. Consequently, new data on SDCT and TSL may contribute to feelings of uncertainty and decreased confidence in decision-making (Higgins et al., 2017b). Advocating SDCT instead of BDCT, the long-standing industry norm, is a considerable change from an udder health perspective; it may therefore take substantial evidence to convince some veterinarians to change their beliefs regarding SDCT.

Some UK producers and veterinarians felt their personal stewardship efforts were undermined by the actions of others, including other agricultural sectors, with specific blame on the human medical community (Golding et al., 2019). Previous research suggests increasing One Health stewardship efforts that are focused on individual knowledge and motivations may increase personal responsibility and reduce blame placed on others (Fynbo and Jensen, 2018; Johnson et al., 2018; Farrell et al., 2021) in pursuit of a common goal (Golding et al., 2019). The relationship between producers and veterinarians can either be a barrier or a facilitator of antimicrobial stewardship, depending on the dynamic, with enabling producer-veterinary partnerships fostering shared responsibility and improved stewardship efforts (Farrell et al., 2021). Promoting desired behavior change requires end users (i.e., producers and farm workers) to perceive that their actions regarding AMR are effective and important (Fishbein and Cappella, 2006; Speksnijder and Wagenaar, 2018).

FURTHER STEPS TO IMPLEMENT SDCT

With increasing scrutiny of prophylactic AMU and calls to decrease agricultural AMU worldwide, adoption of SDCT can be expected to increase. Specifically, an industry paradigm shift is required to transition from indiscriminate antimicrobial DCT to justified AMU based on IMI presence or risk (Biggs et al., 2016). As this shift occurs, it is worth considering how to facilitate sustained behavior change using a holistic approach. It is important to integrate priorities of all relevant stakeholders in development of any public health initiative that will be both impactful and practical (Rajala-Schultz et al., 2021). Providing benchmarks of antimicrobial prescribing to veterinarians and producers compared with their peers may allow them to contextualize their antimicrobial prescribing and use, allowing for more open conversations regarding AMU practices (Speksnijder and Wagenaar, 2018). Overall, national SDCT guideline development that considers country-specific industry differences, along with supportive veterinarians and effective communications, would provide producers with tools to successfully implement SDCT with limited negative consequences on udder health and productivity. This should be coupled with ongoing evaluation of AMU and impacts on AMR in the dairy industry.

CONCLUSIONS

Although described selection protocols and results differed, common themes emerged that present a positive argument in favor of SDCT. Producers should be provided with SDCT protocol options that reflect their access to data as the basis of antimicrobial treatment decision-making, as well as their motivation to choose one method over another. Further, sufficient evidence supports that TSL should be included as an integral part of an SDCT protocol (Winder et al., 2019b; Kabera et al., 2021). If SDCT recommendations are practical and based on producer situations, uptake will likely increase. Furthermore, ongoing producer and veterinary education is essential to increase antimicrobial stewardship in the dairy industry (Farrell et al., 2021) and increased personal responsibility in AMR mitigation is required to promote the required behavior change (Fishbein and Cappella, 2006). In addition, proper evaluation mechanisms should be in place to evaluate impacts of introduced SDCT protocols. In summary, SDCT protocols can be enacted in countries with developed dairy industries without negative udder health and production impacts and will substantially reduce DCT-associated AMU, potentially reducing the impact on AMR.

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