

Title: Modifiable management practices to improve udder health in dairy cattle at dry-off: a protocol for a scoping review.

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Registration: This protocol is archived in the University of Guelph's institutional repository (The Atrium) available at: <https://atrium.lib.uoguelph.ca/xmlui/handle/10214/10046>, and registered online with Systematic Reviews for Animals and Food (SYREAF) available at: <http://www.syreaf.org>. The subsequent review will be reported using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR: <http://www.prisma-statement.org/Extensions/ScopingReviews>) guidelines (Tricco et al., 2018).

Amendments: Any amendments made to this protocol following its registration will be documented in the final manuscript as protocol deviations.

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INTRODUCTION

Rationale:

The dry period after lactation represents the time at which dairy cows are most at-risk for developing intramammary infections (IMI) (Halasa et al., 2009). IMI also increase the risk of clinical mastitis in the subsequent lactation, most commonly during the first 30 to 60 days in milk (Pantoja et al., 2009). A common approach to decrease the impact of IMI or clinical mastitis on milk quality and quantity in the subsequent lactation is the use of dry-off antibiotics. The National Dairy Study (2015) in Canada found 84% of herds used blanket dry-cow therapy (BDCT) and 11% used selective dry-cow therapy (SDCT) at dry-off (D.F. Kelton, unpublished data). Similar results were obtained from a survey of dairy farmers in Germany, which found 79% of farms performed BDCT and 31% performed SDCT (Bertulat et al., 2015). However, concern for the prudent use of antibiotics in agriculture creates the need to assess the efficacy of additional management practices that can be used to also protect cattle health during the dry period.

Regardless of the administration of antibiotic dry-cow therapy, almost all dairy cattle enter the dry period following some form of management changes (Zobel et al., 2015). The majority of the known body of literature regarding management practices that improve udder health around the

time of drying off exist on antibiotic dry-cow therapy and teat sealants (Berry & Hillerton, 2002; Dingwell et al., 2003; Bradley & Green, 2001). Two reviews, one systematic and the other narrative, discussed the importance of management strategies and their impact on udder health, but these articles only focused on method of milk cessation and bedding/housing of dry cows (Dufour et al., 2011; Dingwell et al., 2003). Another systematic review and meta-analysis only assessed the impact of adjusting dry period length on risk of clinical mastitis (van Knegsel et al., 2013). Thus, the objective of this scoping review remains to characterize all articles regarding modifiable management practices of dairy cattle during the dry period that are used to improve udder health. A few of the management practices known to have an effect on udder health in dairy cattle at the time of drying off include abrupt versus gradual cessation of milking, bedding materials, hygiene of the environment, standing behaviour following dry-cow therapy, timing of cows first foremilk, vaccinations, fly control, and nutrition (Green et al., 2007).

Understanding the efficacy of management practices that can be modified during the dry period of lactation is essential to help producers maintain good health within dairy herds and aids the prudent use of antibiotics in agriculture. A scoping review of available knowledge on the types of management practices that have been examined for efficacy allows the assessment of current evidence and identifies gaps in existing knowledge. If enough available knowledge exists on this topic, this scoping review will inform the need for a systematic literature review and meta-analysis into an area of dairy cattle management at dry-off.

Objectives: The objective of this protocol is to define the methods for a scoping review that will describe available literature on dairy management practices used during the dry period to aid in improving udder health, both during the dry period and into the following lactation. The specific review question to be addressed in this protocol, and the subsequent scoping review, is as follows: What modifiable management practices have been examined around dry-off to improve udder health in dairy cattle during the dry-period or the subsequent lactation?

Eligibility criteria:

- i. **Population:** Dairy cattle after their first or subsequent lactation.
- ii. **Intervention/Exposure:** Any modifiable management practices used by farmers/researchers at the time of dry-off that are implemented to improve udder health in dairy cattle. The eligible interventions will be classified as follows:
 - a. Antibiotics
 - b. Teat sealants
 - c. Vaccines (e.g. *E. coli* J5)
 - d. Homeopathic, herbal, vitamin/mineral supplementation, or probiotic products (e.g. vitamin E injections, selenium injections, Cinnatube intramammary product)
 - e. Housing (e.g. type, size, stocking rate, lying area, loafing area, cleaning out procedures, manure management, disinfection, ventilation, drainage, floor type)
 - f. Pasture (e.g. type, methods of rotation, stocking density, maintenance/disinfection of tracks and gateways)
 - g. Bedding (e.g. type, quantity used, methods of application, clean out, storage)
 - h. Nutrition (e.g. diet composition, feed access, cattle grouping, methods of provision, water hygiene)

- i. Dry-cow preparation (e.g. cow/teat preparation, abrupt cessation of milking, gradual cessation of milking)
- j. Other (e.g. fly control)
- iii. **Comparator:** At least one other of the above interventions, a non-treated control group or a placebo control group will be considered as a comparator group.
- iv. **Outcomes:** This scoping review will only include articles that mention an udder health outcome in the title and/or abstract. Articles which may measure these outcomes, but do not make mention of them in the abstract, are unlikely to have been designed appropriately to detect the outcome of most interest to us. Thus, the eligible outcomes are:
 - a. Clinical mastitis: author defined, herd/cow/quarter level will be accepted, at any period post-calving (author to define risk period).
 - b. Cure of existing IMI: author defined, herd/cow/quarter level will be accepted, IMI must be present at drying-off and cured in the milk sample taken at or shortly after calving.
 - c. Prevention of new IMI: author defined, herd/cow/quarter level will be accepted, IMI must not be present at drying-off but present in the milk sample taken at or shortly after calving.
 - d. Prevalence of IMI: author defined, herd/cow/quarter level will be accepted, at any point post-calving (author to define the sampling time).

In addition to the population, intervention/exposure, comparator and outcome elements defined above, other eligibility criteria that will be included are as follows:

Publication date: Articles must have been published within the last 30 years (1990-present). Due to major changes in the prevention of disease in dairy cattle within the last few decades, this eligibility criterion will ensure this scoping review captures and presents data that are relevant to current veterinarians and dairy producers (Leblanc et al., 2006).

Report characteristics: The study must be published in English and the publication can be both published and non-published if the article is ≥ 500 words and reports on primary data.

Study designs: Only analytic study designs (i.e. analytic observational studies, controlled trials and challenge trials) will be eligible for inclusion in this review.

METHODS

Information Sources: The search will include a range of biologically relevant databases to identify peer-reviewed literature. Table 1 represents the databases to be searched.

Table 1. Databases to be searched for relevant literature.

Database	Interface/URL
MEDLINE, MEDLINE In-Process and MEDLINE® Daily Epub Ahead of Print	Ovid SP
CAB Abstracts	CAB Interface
Science Citation Index	Web of Science
Scopus	
Agricola	Proquest

In addition, one reviewer will hand-search the table of contents of the following relevant conferences, provided the proceedings are ≥ 500 words:

- World Association for Buiatrics;
- National Mastitis Conference Proceedings.

Search strategy: The search strategy used for this review was developed using key concept terms and words. Population and outcome terms will be connected using Boolean operators ‘AND’, ‘OR’, or ‘NEAR’. Table 2 represents the search string that will be used for this review as applied in CABI database.

Table 2. Results of a search to identify articles reporting or examining modifiable management practices to improve udder health in dairy cattle at dry-off, published between 1990-present, conducted in CAB Abstracts (via CABI) on January 7, 2020.

#	Search Terms	Results
1	("cow") OR ("cows") OR ("cattle") OR (heifer*) OR ("dairy") OR ("milking") OR (bovine*) OR ("bovinae") OR (buiatric*) AND yr:[1990 TO 2020]	538 300
2	(ayrshire*) OR ("brown swiss") OR ("busa") OR ("busas") OR (canadienne*) OR (dexter*) OR ("dutch belted") OR ("estonian red*") OR (fleckvieh*) OR (friesian*) OR (girolando*) OR (guernsey*) OR (holstein*) OR (illawarra*) OR ("irish moiled*") OR (jersey*) OR ("meuse rhine issel*") OR (montebeliarde*) OR (normande*) OR ("norwegian red*") OR ("red poll") OR ("red polls") OR (shorthorn*) OR ("short horn*") AND yr:[1990 TO 2020]	61 277
3	1 OR 2	554 679
4	((("drying off") OR ("dry off") OR ("dried off") OR ("dry up") OR ("drying up") OR ("dried up") OR ("drying period") OR ("dry period") OR ("dry udder") OR ("dry teat*") OR ("pre-partum") OR ("prepartum") OR ("end" NEAR lactat*) OR (finish* NEAR lactat*) OR (stop* NEAR lactat*) OR (cess* NEAR lactat*) OR (ceas* NEAR lactat*) OR (nonlactat*) OR ("non-lactat*") OR (postlactat*) OR ("post-lactat*") OR (postmilk*) OR ("post-milk*") OR ("involution") OR ("steady state") AND yr:[1990 TO 2020])	41 877
5	3 AND 4	12 175
6	("dry cow") OR ("dry cows") AND yr:[1990 TO 2020]	1856
7	5 OR 6	13 092
8	((mastiti*) OR ((intramammar* NEAR infect*)) OR ((intramammar* NEAR inflamm*)) OR (("intra-mammar*" NEAR infect*)) OR (("intra-mammar*" NEAR inflamm*)) OR ("udder health*") OR ("somatic cell*") OR ("linear score*") OR ("bulk tank*") OR ("bulk-tank*") OR ("somatic-cell*") OR ("linear-score*")) AND yr:[1990 TO 2020]	33 547
9	7 AND 8	2697
10	((("dry cow" NEAR therap*)) OR (("dry cow" NEAR manag*)) OR ((("dry cow" NEAR intervention*)) OR (("dry cow" NEAR treat*)) OR ((("dry cow" NEAR strateg*)) OR (("dry cows" NEAR therap*)) OR	704

	((("dry cows" NEAR manag*)) OR (("dry cows" NEAR intervention*)) OR (("dry cows" NEAR treat*)) OR (("dry cows" NEAR strateg*)) AND yr:[1990 TO 2020]	
11	9 OR 10	2885

In order to validate the search strategy, 15 relevant journal articles were pre-selected by DFK and checked for inclusion in the search.

Table 3. Article title/author information for 15 relevant journal articles pre-selected by DFK to check for inclusion in the search in order to validate the search strategy.

	Author (Year)	Article Title	Country	Management Practice in T/AB	Outcome in T/AB
1	Arruda et al. (2013)	Randomized noninferiority clinical trial evaluating 3 commercial dry cow mastitis preparations: I. Quarter-level outcomes	USA	Antibiotics	IMI at calving / CM up to 100 DIM
2	Bradley & Green (2001)	An investigation of the impact of intramammary antibiotic dry cow therapy on clinical coliform mastitis	England	Antibiotics	CM up to 100 DIM
3	Cameron et al. (2015)	Evaluation of selective dry cow treatment following on-farm culture: milk yield and somatic cell count in the subsequent lactation	Canada	Antibiotics & Teat sealants	SCC in following lactation
4	Green et al. (2007)	Cow, farm, and management factors during the dry period that determine the rate of clinical mastitis after calving	United Kingdom	Antibiotics, Vaccines, Housing, Pasture, & Dry-cow preparation	CM within 30 DIM
5	Godden et al. (2003)	Effectiveness of an internal teat seal in the prevention of new intramammary infections during the dry and early-lactation periods in dairy cows when used with a dry cow intramammary antibiotic	USA	Antibiotics & Teat sealants	IMI during dry period / LS after calving / CM up to 60 DIM
6	Gott et al. (2016)	Intramammary infections and milk leakage following gradual or abrupt cessation of milking	USA	Dry-cow preparation	IMI at calving
7	Gott et al. (2017)	Effect of gradual or abrupt cessation of milking at dry off on	USA	Dry-cow preparation	Somatic cell score

		milk yield and somatic cell score in the subsequent lactation			up to 120 DIM
8	Newman et al. (2010)	Association of milk yield and infection status at dry-off with intramammary infections at subsequent calving	USA	Dry-cow preparation	IMI at calving
9	Odensten et al. (2007)	Effects of two different feeding strategies during dry-off on certain health aspects of dairy cows	Sweden	Nutrition	SCC during dry period
10	Odensten et al. (2007)	Metabolism and udder health at dry-off in cows of different breeds and production levels	Sweden	Dry-cow preparation	IMI after calving
11	Rajala-Schultz et al. (2005)	<i>Short Communication:</i> Association between milk yield at dry-off and probability of intramammary infections at calving	USA	Dry-cow preparation	IMI at calving
12	Rajala-Schultz et al. (2011)	Milk yield and somatic cell count during the following lactation after selective treatment of cows at dry-off	USA	Antibiotics	SCC during follow lactation
13	Schukken et al. (1993)	A randomized blind trial on dry cow antibiotic infusion in a low somatic cell count herd	Netherlands	Antibiotics	CM during dry period
14	Tucker et al. (2009)	Effect of milking frequency and feeding level before and after dry off on dairy cattle behavior and udder characteristics	New Zealand	Dry-cow preparation & Nutrition	IMI during dry period
15	Zobel et al. (2013)	Gradual cessation of milking reduces milk leakage and motivation to be milked in dairy cows at dry-off	Canada	Dry-cow preparation	Somatic cell score at calving

STUDY RECORDS

Data management: The results from the searches will be downloaded into a bibliographic software program (EndNote X7, Clarivate Analytics, Philadelphia) and de-duplicated. Any references that are not compatible for downloading into EndNote will be noted and saved in a Word or Excel file as appropriate. The de-duplicated references from the search will be loaded into an online reference management software (DistillerSR®, Ottawa, ON, Canada), and further de-duplicated using this software's internal de-duplication process. All study selection and characterization steps will also be conducted in DistillerSR® using forms specifically created for this project. All reviewers involved in the screening and data extraction process will have had previous training in epidemiologic principles and scoping review methods. Prior to both stages of

screening, a pilot test will be conducted to ensure reviewer compatibility and consistent data collection using the forms created in DistillerSR®.

Selection process: This review will entail two stages of screening. First, the titles and abstracts of each article identified by the search strategy will be assessed for eligibility. The pilot test for title and abstract screening will involve all reviewers screening 100 articles for eligibility, followed by a consensus meeting. Any disagreements will be thoroughly discussed to ensure all reviewers are consistent for the remaining articles. The remaining titles and abstracts will be independently assessed for relevance using the following primary screening questions by two independent reviewers:

- 1) “Does the title and/or abstract assess a dry-period management practice in dairy cattle?”
- 2) “Does the title and/or abstract describe a relevant udder health outcome?”
- 3) “Is the title and/or abstract available in English?”
- 4) “Does the title and/or abstract describe an analytic primary research study?”

All questions will include a response for YES, NO, and UNCLEAR. A reference will only be excluded if both reviewers give a final decision to exclude (i.e. both reviewers agree the response to any of the above questions is NO). Any conflicts will be resolved by consensus, and if agreement cannot be reached, a third member of the review team will be consulted.

The second stage of screening will involve assessing the full text of each article for eligibility by two independent reviewers. The full-text articles of the citations deemed eligible by the first stage of screening will be retrieved and uploaded into DistillerSR® with the naming convention: refID_title. If a full-text article cannot be retrieved online using available University of Guelph resources, articles will be requested via a University of Guelph librarian. All reviewers will conduct the pilot test involving 10 full-text articles to ensure reviewer consistency in applying questions. The following secondary screening questions will be used to assess the full text of each article by two reviewers working independently:

- 1) “Is the study available in English?”
- 2) “Is this an analytic primary research study?”
- 3) “Does this article describe dairy cattle after their first or subsequent lactation?”
- 4) “Was the management practice implemented at drying off?”
- 5) “Did the study measure a relevant udder health outcome?”

Answers to Questions 1 - 6 will be YES and NO. A reference will only be excluded if both reviewers answer NO to any screening question. Any conflicts will be resolved by consensus. If consensus cannot be reached, a third person on the review team will be consulted. Reasons for exclusions at this stage of screening will be documented. Included studies will further be asked two neutral questions, which will not be used for including/excluding the article, but they will be used to categorize study type and management strategy:

- 6) “What type of analytical study design was used in this article?” NEUTRAL
 - a. Observational study (cohort, case-control, cross-sectional)
 - b. Clinical trial (randomized or non-randomized)

- c. Challenge trial
- 7) “What categories of management strategy were evaluated in the article?” NEUTRAL
 - a. Antibiotics
 - b. Teat sealants
 - c. Vaccines
 - d. Homeopathic, herbal, vitamin/mineral supplement, or probiotic products
 - e. Housing
 - f. Pasture
 - g. Bedding
 - h. Nutrition
 - i. Dry-cow preparation
 - j. Other (specify)

Questions 6 and 7 are included in order to classify each article into appropriate study type and management strategy, but both questions will provide a NEUTRAL response and thus not contribute to inclusion/exclusion decision rules. Categories in Question 7 may be added to as needed depending on the information presented in relevant literature. Articles that will be characterized further must provide mention of at least one of the management strategies listed in Question 7 C-J, and articles that only mention antibiotics or teat sealants as the management practice will be enumerated but not further characterized.

Data extraction process: Two reviewers will extract data from eligible studies independently using a structured pre-tested form created in DistillerSR®. This form will be pilot tested using five references by all reviewers in order to ensure consistency in data extraction. Authors will not be contacted to request missing data or to clarify published results.

Data items:

The following information will be extracted:

- A) General study characteristics: year of publication, year study was conducted, and country where study was conducted (if not reported, use location of first author)
- B) Study approach (report actual study design regardless of the design reported by author)
 - a. Cross-sectional study
 - b. Cohort study
 - c. Case-control study
 - d. Randomized controlled trial
 - e. Non-randomized controlled trial
 - f. Challenge trial
 - g. Unclear (apply this option when the study design cannot be deciphered from the article)
- C) Study objectives and hypotheses (if reported by authors)
- D) Study population: farm type/herd type (i.e. research/university dairy, commercial dairy), breed.
- E) Intervention/Comparator/Exposure
 - a. Definition/type of management practice
 - b. Intervention application unit: farm, herd, cow, quarter
 - c. Implementation strategy of intervention
 - d. Implementation strategy of comparator (if applicable to study design)
- F) Outcome:

- a. Clinical mastitis:
 - i. Case definition
 - ii. Risk period
- b. Cure of existing IMI: (IMI present at drying off, but not present in milk samples taken at or shortly after calving)
 - i. Case definition, including method of outcome assessment (i.e. bacteriologic culture, somatic cell count, linear score, NAGase activity, milk electrical conductivity)
 - ii. Sampling period
- c. Prevention of new IMI: (IMI not present at drying-off, but present in milk samples taken at or shortly after calving)
 - i. Case definition, including method of outcome assessment (i.e. bacteriologic culture, somatic cell count, linear score, NAGase activity, milk electrical conductivity)
 - ii. Sampling period
- d. Prevalence of IMI:
 - i. Case definition
 - ii. Sampling period

Synthesis of Results: Tables will be used to provide descriptive analysis of study characteristics, target population, sample size, and the study approach. Descriptions and implementation practices of the management factors assessed in each article will be reported, along with any measures of cure, prevention, or prevalence of IMI or clinical mastitis. A combination of summary figures and tables will be used as needed to report study results. A histogram will be used to demonstrate the total number of eligible studies published by year.

RESULTS

Selection of sources of evidence: A flow diagram will be used to report on the study inclusion process. The total number of screened references at each data process will be documented, along with reasons for study exclusion as outlined by PRISMA (<http://www.prisma-statement.org/documents/PRISMA%202009%20flow%20diagram.pdf>). The full electronic search strategy for at least one database will be provided via a summary table such that the search could be replicated.

Characteristics of sources of evidence: Data tables will be used to record study statistics on eligible research articles that will include study characteristics (year of publication, year of conduct, country of conduct), study design and study population. A wide range of population and intervention categories will be eligible for inclusion, as long as the primary outcome of each article aims to assess the effect of dry-period management on clinical or subclinical mastitis across the dry-period or into the subsequent lactation. However, as this is a scoping review, the information that is found in relevant literature may be used to modify data characterization elements.

Results of individual sources of evidence: This scoping review aims to characterize the available evidence regarding modifiable management practices that are used at dry-off in dairy cattle to improve udder health during the dry period and in the subsequent lactation. We will report on each

management practice outlined in eligible studies, the type and definition of outcome assessed (categorized as clinical or subclinical mastitis), and the study methodology used.

DISCUSSION

Summary of evidence: In conducting a scoping review, we will present a summary of available primary research, published from 1990 to present, investigating modifiable management practices used at dry-off to improve udder health in dairy cattle. The results obtained from this review will help to identify gaps in the current body of evidence, which provides direction for future research into such practices that support the judicious use of antibiotics in the dairy industry and promote better udder health outcomes.

Limitations: Limitations at the study and review level will be discussed.

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