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# **Systematic Review**

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# A systematic review of disease control strategies in beef herds, part 1: preweaned calf mortality

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#### **Abstract**

Calves sold at weaning are the main source of income for cow-calf operations, and their survival should be a priority. Given this, the effective use of management practices for pregnant dams and calves to prevent calf mortality is essential; however, decision-makers often do not have access to information about the effectiveness of many management practices. A systematic review was conducted to summarize the evidence of the effectiveness of biosecurity, vaccination, colostrum management, breeding and calving season management, and nutritional management practices for preventing preweaned beef calf mortality. The population of interest was preweaned beef calves from birth until at least 3 months of age. The outcome of interest was general preweaning calf mortality with stillbirths excluded. Eleven studies were deemed relevant. Ten were observational cross-sectional studies, and one was a randomized controlled trial (RCT). The practices that were statistically significantly associated with calf mortality were intervening with colostrum in case a calf had not nursed from its dam or was assisted at calving, timing and length of the calving season, and injecting selenium and vitamin E at birth. More well-executed RCTs and cohort studies are needed to provide evidence of effectiveness and help support implementation of recommended practices in herds.

# Introduction

On cow–calf operations, calves sold at weaning are producers' main revenue source (Chenoweth and Sanderson, 2005). Therefore, ensuring calf survival during the preweaning period is economically essential. In western Canada, 25% of herds had 2.8% and 5.3% calf mortality from 24 hours after birth until weaning in calves born from cows and heifers, respectively (Waldner et al., 2019). Calf mortality is associated with calf morbidity in herds, meaning that calves that get sick have higher odds of dying (Busato et al., 1997; Ganaba et al., 1995; Mõtus et al., 2018; United States Department of Agriculture Animal and Plant Health Inspection Service Veterinary Services National Animal Health Monitoring System, 2021). The two most important causes of morbidity before weaning are neonatal calf diarrhea (NCD) and bovine respiratory disease (BRD) (Murray et al., 2016; Pearson et al., 2019a; Waldner et al., 2013). Given this, evidence-informed health management is essential to ensure that the recommended practices are being used in herds to prevent disease and thus minimize mortality.

Direct disease control practices target disease by minimizing the contact between pathogens and hosts and enhancing antigen-specific immunity (Brandt *et al.*, 2008; Thrusfield and Christley, 2018), for example, vaccination and biosecurity (Chenoweth and Sanderson, 2005; Tizard, 2021). Indirect disease control practices manage factors that trigger disease. An example is reducing stress by using non-abrupt weaning methods (Griebel *et al.*, 2014; Hulbert and Moisá, 2016; Moggy *et al.*, 2017). Furthermore, various management practices are known to impact calf morbidity and mortality by mitigating or exacerbating the risk of these outcomes. For example, introducing more than 10 bulls was associated with an increased risk of BRD outbreaks (Wennekamp *et al.*, 2021), and theoretically, based on feedlot cattle, quarantining these animals could have decreased the risk (Santinello *et al.*, 2022).

There is a scarcity of evidence to guide health management recommendations for beef herds to prevent calf mortality. The effectiveness of practices has been mostly studied and reviewed for dairy calves (Dubrovsky *et al.*, 2019; Godden, 2008; Olson *et al.*, 1980; Robison *et al.*, 1988; Windeyer *et al.*, 2014) and feedlot cattle (O'Connor *et al.*, 2019). Differences in these production systems do not allow for direct extrapolation of results to beef cow–calf operations.

Therefore, there is a knowledge gap regarding the recommended practices to use in beef cow-calf herds, and the existing information has not been previously summarized. This leads to the overall question: What is the effectiveness of management practices to prevent beef calf mortality during the preweaning stage?

The objective was to assess and summarize the evidence regarding the effectiveness of disease control strategies in preventing calf mortality in beef cow–calf herds. A secondary objective was to assess the generalizability of this evidence to cow–calf operations in western Canada.

#### **Materials and methods**

This study was informed by O'Connor and Sargeant's articles on conducting systematic reviews in veterinary medicine (O'Connor et al., 2014; O'Connor and Sargeant, 2014; Sargeant et al., 2014a, 2014b; Sargeant and O'Connor, 2014). It is reported according to the guidelines for preferred reporting items for systematic reviews and meta-analyses (PRISMA 2020s) (Page et al., 2021).

#### **Protocol and registration**

Before the systematic review was conducted, a protocol was developed following the PRISMA-P guidelines (Moher *et al.*, 2015). It was published in the Digital Repository of the University of Calgary (https://prism.ucalgary.ca) and online with Systematic Reviews for Animals and Food (http://www.syreaf.org/) (Sanguinetti *et al.*, 2021). After this publication, minor amendments were made, mostly related to the risk of bias (ROB) assessment (Supplementary material 1).

# Eligibility criteria

The eligibility criteria were specified for the population (P), intervention (I), comparators (C), outcome (O), and study design (S) (O'Connor *et al.*, 2014).

# **Population**

The population of interest was preweaned beef calves. *Bos taurus* or *Bos indicus* and their hybrids were included. Studies that described postweaning beef calves, feedlot, stocker, veal, dual purpose, or dairy animals were excluded.

#### Interventions and comparators

The interventions of interest were biosecurity and biocontainment, vaccination, colostrum management, breeding and calving season management, and nutritional management practices. These practices could be applied to pregnant dams or preweaned beef calves. Studies were required to have a concurrent comparison group (e.g. placebo or alternate management practice).

# Outcome

The outcome of interest was general mortality, which included all calf deaths regardless of the cause. Studies were included if they explicitly removed stillbirths and assessed calf mortality for at least the three first months of life.

#### Study designs and report characteristics

Randomized and non-randomized controlled trials (RCTs and CTs) and observational studies reporting naturally occurring diseases were included. The studies were required to statistically assess the relationship between a management practice and calf mortality. The full text had to be written in English and published in a peer-reviewed journal or thesis.

#### Information sources

The electronic databases used for the literature search were CAB Abstracts, MEDLINE on the Ovid platform, Web of Science, and ProQuest Dissertations. The initial searches were carried out on the same day (20 May 2021) and updated (5 April 2023) to include recent publications (Supplementary material 2). Search results were imported into the software Covidence (Veritas Health Innovation, Melbourne, Australia), and the software removed duplicates. A reference list from other reviews was checked to ensure the search strategy was accurate (Chamorro and Palomares, 2020; Theurer *et al.*, 2015). Four additional studies were manually included (Gamsjäger *et al.*, 2023; Makoschey *et al.*, 2008, 2001; Schreiber *et al.*, 2000).

## Search strategy

The search strategy was performed in the databases using controlled vocabulary terms and keywords related to beef cattle, calves, and a list of diseases and pathogens of interest by a librarian with experience conducting systematic searches (H.G.). No language nor time restrictions were applied during the electronic database search.

## Screening and selection process

Studies were screened in two stages by two independent reviewers. Before starting each stage, the process was pre-tested to ensure both reviewers understood the screening criteria (detailed in Supplementary material 3). During the first stage, titles and abstracts were screened. Signalling questions were used to guide this process. During the second stage, full texts were screened. Reviewers could classify studies as to "include" or "exclude" from the review. Conflicts during both stages were resolved through discussion between reviewers. If necessary, a third reviewer was included (Dohoo *et al.*, 2009; Dubrovsky *et al.*, 2019; Sargeant and O'Connor, 2020).

#### Data collection process

Two independent reviewers extracted the data from studies included in this review using pre-tested tables in Microsoft Excel (Microsoft Corporation, Redmond, WA, USA). During this stage, studies were anonymized by using a numeric code (Table 1). Information was extracted at the study level (e.g., authors, year of publication, study design, mortality risk or rate) and the practice assessment (PA) level. Practice assessment refers to the statistical assessment between individual practice and the outcome of interest. Each PA was identified using an alphanumeric code in accordance with the numeric code given to each study (Table 2; Supplementary material 7). Significant statistical associations or effects were considered if  $P \leq 0.05$ . Statistically significant associations (A) or no statistically significant associations (NA) were

the terms used to describe the findings of PAs from observational studies. Statistically significant effects (E) or no statistically significant effects (NE) were the terms used to describe the findings of PAs from RCTs and CTs. Results from univariable analyses were preferred to those from multivariable ones if both were reported, given concerns about a lack of independence among practices. If the effects of a PA were isolated from multivariable models, other variables included in the model were noted. Results were preferably extracted from tables. However, given concerns regarding the precision and validity of these estimates, the focus was on the directionality of results (i.e., protective or harmful) rather than the effect estimate. Conflict among reviewers was resolved in the same way as described previously.

#### Risk of bias

The ROB assessment was done at the PA level. Practice assessments from RCTs and CTs were evaluated using the Rob2 tool (Sterne *et al.*, 2019), as described in the Cochrane Review Handbook for Systematic Reviews of Interventions (Higgins *et al.*, 2024). The ROBINS I tool was used to evaluate practice assessments from observational studies (Sterne *et al.*, 2016). A few signalling questions were modified to be applicable in veterinary medicine (Sargeant and O'Connor, 2014), and the details are shown in Supplementary materials 4 and 5.

#### Data synthesis

The evidence regarding general calf mortality was summarized using a narrative structure, while evidence regarding NCD and BRD-specific morbidity and mortality (Part 2) are reported elsewhere (Sanguinetti *et al.*, 2025). Firstly, a summary of findings table was compiled for all PAs. If the body of evidence for a specific practice included three or more PAs from at least three different studies, a GRADE approach was used to assess the certainty of the findings (Schünemann *et al.*, 2013) (Supplementary material 6). This assessment evaluated consistency among the direction of findings across studies (i.e., beneficial or harmful), comparability of practices and comparison groups, as well as if the geography and production conditions in which the studies were conducted were comparable to those of cow–calf operations in western Canada.

#### **Results**

The search strategy identified 4942 relevant studies of which 1480 duplicates were deleted. This left 3462 studies that underwent title and abstract screening, and 3247 were excluded during this stage. The remaining 215 studies were eligible for full-text screening, and 198 were subsequently excluded (Figure 1). In total, 25 studies were retained for Parts 1 and 2 of this systematic review.

Eleven studies were deemed relevant for the general mortality review (Part 1). These included one RCT and ten observational cross-sectional studies (Table 1). Eight took place in North America (USA and Canada), one in Europe (Estonia), one in Asia (Japan), and one in South America (Brazil). Seven out of eleven studies reported a specific case definition for mortality. The number of practices assessed in relation to mortality by each study ranged from 1 to 19, and the outcome of each practice assessment is detailed in Table 2 and Supplementary material 7.

# Practices with statistically significant effects or associations reported

#### Colostrum practices

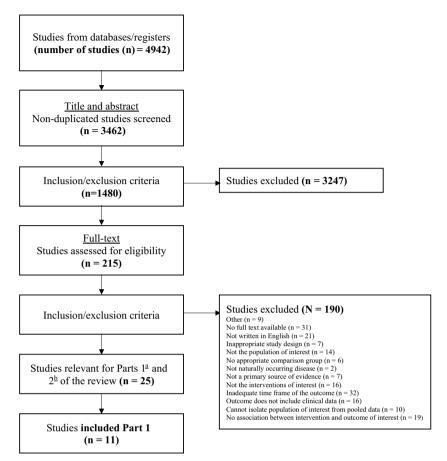
Three out of four PAs found that criteria used to intervene with a colostrum management strategy affected calf mortality (A: 4a, 4b, 4c; NA: 1e (Table 2)). Checking the fullness of the udder impacted the calf mortality risk from 1 to 7 days of age; herds that used this criterion had 0.7% lower mortality than those that did not (P = 0.01) (4c). Also, intervening with colostrum consumption for calves that required assistance at birth had a similar impact; herds that used this criterion had 0.8% less mortality than those that did not (P = 0.02) (4a). Herds that intervened with colostrum in the case that colostrum was abnormal had 1.9% higher mortality than those who did not (P = 0.001) (4b). Regardless of the criteria used to intervene, the findings concerning the timing to implement a colostrum management strategy (e.g., 4 hours, 12 hours after birth) (6a and 9a), the source of colostrum used to intervene (e.g., dairy) (1 f, 6b, and 6c), and the methods used to administer colostrum (e.g., using an esophagus tube) (1 g, 1 h, and 9a) did not show an impact on the odds nor rate of calf mortality (Supplementary material 7). In contrast, PA 11a reported that requiring intervention with colostrum consumption was associated with higher odds of mortality in calves (P < 0.0001, Table 2). The certainty of the evidence for colostrum practices could not be assessed, given the differences in the practices evaluated.

#### Timing of the calving season

Three out of four PAs reported a significant association between the timing of the year when calving took place and mortality (A: 2c, 4d, 5a; NA: 6e (Table 2)). These studies were all conducted in North America. Early calving herds had a 1.4 times higher incidence of mortality than those calving later (PA 2c). The mortality was 0.7% lower when the calving started in April (later) compared to January or February (earlier) (P = 0.02) (4d). Herds who calved earlier (January/February) had higher preweaning mortality (P = 0.02) for calves born to cows (1.9%) compared to later (March to May) calving herds (1.8%); however, this association was not detected for heifers (5a). The GRADE approach was used to assess the certainty of these findings, and it was determined that certainty was low (Table 3). Furthermore, two other studies assessed the proportion of calvings during each season as it related to calf-level outcomes and found similar results. For example, calf mortality was significantly lower in herds with a higher proportion of calvings in summer (June, July, and August) compared to those in autumn (September, October, and November), spring (March, April, and May), and winter (December, January, and February) (P < 0.001) (1a, 1b, 1c, and 1d). Also, calves born in winter and autumn had significantly higher odds of mortality than calves born in summer. There was no significant difference in mortality between summer and spring born calves (8a). However, comparisons between these two studies should be made cautiously, given that herdlevel mortality was reported in one study (1a, 1b, 1c, and 1d) and calf-level mortality in the other (8a). The PAs are reported in Table 2.

#### Length of the calving season

Two of four PAs that evaluated the length of the calving season found that it impacted calf mortality (A: 4e, 3b; NA: 1aa, 2b (Table 2)). The longer the calving season, the higher the mor-



**Figure 1.** PRISMA flowchart of a systematic review on the effect of management practices on preweaned calf mortality and morbidity in beef herds.

<sup>a</sup>General mortality, <sup>b</sup>Morbidity and mortality from NCD and BRD.

tality risk. The mortality from 7 days to weaning increased by 1.4% for every additional week of the calving season (P = 0.007) (4e). Similarly, another study reported a significant P-value (P = 0.002) (PA 3b), but no specific details were provided about its magnitude. The certainty of this body of evidence was determined to be low (Table 3).

# Nutritional management and mineral supplementation in calves

One out of four PAs assessing the use of minerals (e.g., selenium) and/or vitamins (e.g., vitamin E) found an association with calf mortality (A: 6f; NA: 1v, 1w, 4f (Table 2)). One study reported that herds that did not use vitamin E and selenium at birth had 10.3 higher odds of mortality than those who did use vitamin E and selenium (p = 0.003) (PA 6f). Feeding minerals (1v) or selenium supplements to calves (PA 1w) or giving mineral/vitamin injections (4f) had no associations with mortality.

# Practices with no statistically significant effects or associations reported

# Breeding and calving management

Breeding heifers before cows was not associated with the odds of calf mortality (2a; Supplementary material 7).

# Nutritional management and mineral supplementation

Using either "feeding houses" or feeding concentrates to calves did not influence the calf mortality rate (1t and 1u). Pre-calving

practices, including feeding silage or giving mineral injections to dams repeatedly, were also not associated with the calf mortality risk (2d and 10a). The type of pastures, described by the authors as cultural, seminatural, natural, cultural combined, seminatural, and natural pastures, used for the cow–calf pair did not impact the calf mortality rate (1z). The PAs are shown in Supplementary material 7.

# Biosecurity

Neither biocontainment nor biosecurity practices affected the calf mortality risk or rate (1i, 1j, 1r, 1s, 1x, 6d, and 6h). Biocontainment practices included disinfection of the navel cord of the newborn calf, using pastures not used for grazing in the previous year for cows and calves, grazing cows and calves separately from other animal groups, separating sick animals, removing calves from the calving facility to nursery pasture within 48 h of birth, and length of time separating calf and dam from other animals after calving. The only biosecurity practice assessed was the purchasing of foster calves, and this was not associated with mortality. Details are shown in Supplementary material 7.

#### Dam vaccination

The use of pre-calving vaccines against NCD pathogens were not associated with calf mortality (6g, 7b, 7c) (Supplementary material 7). The certainty of this body of evidence was determined to be low (Supplementary material 8).

Table 1. Characteristics of studies included in a systematic review on the effect of management practices on preweaned calf mortality in beef herds

Case definition	Number of deaths (unassisted deaths and euthanasia) in calves from ear tagging to 3 months/ sum of the individual animal-days of at-risk in the particular farm, based on the Animal Registers data.	Not defined	Not defined	Not defined	The frequency of dead calves in each age category comprised the number of dead calves in the age category (i.e., 1 to 7 days of age, 7 to 30 days of age, 30 days to weaning) divided by the total number of eligible live calves in that category (i.e., total number of live calves minus the number of stillborn calves and of calves that died in previous mortality age category) in each herd	A calf that died more than 1 h after birth and before the earlier of 3 months of age or June 30
Overall mortality risk or rate	Mean within-herd mortality rate up to 3 months of age: 0.37 per 100 calf-months (95% Confidence Interval (CI): 0.28 to 0.47), 69.9% of herds had no calf mortality	Mean calf mortality: 1.5%, median: 1.1% (range: 0.0–7.1)	5.4–5.6%	1 to 7 days of age mean herd-level incidence of mortality: 1.1% (95% CI: 0.9 to 1.3). 7 days of age to weaning mean herd-level incidence of mortality: 1.4% (95% CI: 1.2 to 1.7).	Mean herd-level incidence of mortality: 4.5%	
Comparator	Absence of a given practice, alternate management practices	Absence of a given practice, alternate management practices	Absence of a given practice, alternate management practices	Absence of a given practice, alternate management practice	Comparison group	Absence of a given practice, alternate management practices
Interventions assessed	Breeding and calving management, colostrum management, ment, nutritional management, mineral supplementation, vaccination, biosecurity	Breeding and calving management, nutri- tional management dams	Breeding and calving management, vaccination	Multiple	Breeding and calving management	Colostrum man- agement, mineral supplementation, breeding and calv- ing management, vaccination
Z	156 herds	58 responses (herds), 9846 calves	332 responses, 182 small herds, 150 large herds.	Neonatal Calf Diarrhea: 152 responses, Bovine Respiratory Disease: 142, Mortality: (1 to 7 days) 131 and (7 days to weaning) 133	97 respondents	601 calves
Study design	Cross-sectional	Cross-sectional	Cross-sectional	Cross-sectional	Cross-sectional	Cross-sectional
Country and year of the study	Estonia, 2014 –2016	United States, 1992	Canada, 1995	Canada, 2013	Canada, 2015 – 2016	Canada, 2002
Year published	Môtus et al., 2020	Clement <i>et al.</i> , 1993	Dutil <i>et al.</i> , 1999	Murray <i>et al.</i> , 2016	2019a	Waldner and Rosengren, 2009
First Author	Mõtus	Clement	Dutil	Murray	Pearson	Waldner
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Case definition	A calf that died more than 1 h after birth and before the earlier of 3 months of age or June 30. (The analysis removed stillbirths). The herd risk of calf mortality was the number of calf mortalities as a proportion of the total number of calves alive at 1 h after birth	Calves that were alive at birth but died within 120 days after birth	Calves that died until weaning (aprox 7 months of age) (stillbirths excluded)	Not defined	Non-mortality was confirmed if a weaning weight was recorded for an individual calf, mortality was confirmed when the date and suspected or confirmed cause of mortality was recorded for an individual calf, and mortality was recorded as unknown when neither a weaning weight nor a mortality event were recorded
Overall mortality risk or rate	Mortality risk between birth and earlier of 3 months of age or June 30: 3.6%	Mortality risk between 0 and 120 days of age: 3.6%	Mortality risk until weaning: 13.5%	Mortality risk in control group: 10.5%. Mortality risk in intervention group: 11.7%	Mortality risk: 3% (farm- level ranged between 0 – 15%)
Comparator	Absence of a given practice, alter- nate management practices	Comparison group	Absence of a given practice	Sterile physiological saline	Absence of a given practice
Interventions assessed	Dam vaccination, vaccination	Birth season	Colostrum management	Dam nutri- tion, mineral supplementation	Colostrum management
z	27,663 calves from 203 herds	40,462 calves born to 15,600 cows on 908 farms	73 male and 83 female calves	174 cow-calf pairs	389 calves
Study design	Cohort for gas (but risk factors were cross-sectional)	Cross-sectional	Cross-sectional	Randomized control trial	Cross-sectional
Country and year of the study	Canada, 2001	Japan, 2006–2010	Brazil, 2015–2016	USA	Canada
Year published	Waldner, 2008	Misaka <i>et al.</i> , 2022	Pires <i>et al.</i> , 2021	Stokes <i>et al.</i> , 2019	Gamsjäger et al., 2023
First Author	Waldner	Misaka	Pires	Stokes	Gamsjaeger
Study	۲	8	6	10	п

**Table 2.** Summary of findings table and ROB assessment for management practices with significant associations or effects detected within a systematic review on the effect of management practices on preweaned calf mortality in beef herds

Practice assessment	Details practice	Association/effect on mortality	Covariates in the final model	Overall ROB
Colostrum m	anagement			
4a	Routinely intervened with colostrum consumption for calves that were assisted at parturition (No (N)/Yes (Y))	1 to 7 days of age: No association 7 days of age to weaning: Association. Operations that routinely intervened with colostrum consumption for calves that were assisted at parturition had 0.8% lower mortality than those who did not $(P=0.02)$	7 days of age to weaning: Month that calving began, length of calving season (days), number of breeding age cows in herds, herd-level treatment risk of BRD.	HIGH
4b	Intervene if abnormal colostrum (N/Y)	1 to 7 days of age: Association. Operations that intervened when colostrum was abnormal had 1.9% higher mortality compared with other operations $(P=0.001)$	1 to 7 days of age: Verify if calf has sucked (observe fullness of udder), castrate by small elastrator band	HIGH
		7 days of age to weaning: No association		
4c	Verify if calf has sucked: observe fullness of udder (N/Y)	1 to 7 days of age: Association. Operations that verified calf suckled by observing fullness of udders had 0.7% lower mortality compared with those that did not $(P=0.01)$	1 to 7 days of age: Intervene if abnormal colostrum consumption, castrate by small elastrator band	HIGH
		7 days of age to weaning: No association		
1e	Checking calf colostrum consumption (N or sometimes/Y)	No association		SOME CONCERNS
11a	Colostrum intervention (Y/N)	Association univariable analysis: $P < 0.0001$ . Model 1: OR 6.1 (1.5 – 24.5) ( $P = 0.011$ )	Serum IgG concentration (fixed effect), farm (random effect)	HIGH
Breeding and	d calving management			
2c	Early (began calving on or before March 10) vs Late (began calving after March 10)	Association. Early calving herds had higher mortality risk than late calving ones. Adj. OR 1.4 (95%Cl 1 – 2)		HIGH
4d	Month that calving began (January/February, March, April, May/June)	1 to 7 days of age: No association 7 days of age to weaning: Association. Operations that started calving in April had 0.7% lower mortality compared to those in January or February ( $P=0.02$ )	7 days of age to weaning: Length of calving season, intervention with colostrum consumption if assisted calving, number of breeding age of cows in the herd, herd-level treatment risk of BRD	HIGH
5a	Month calving started (early = January or February; late = March, April, or May) for heifers or cows, respectively)	Association. Herds that started calving early (Jan/Feb) had higher mortality (1.9%) for calves born to cows compared to later calving herds (Mar/May) (1.8%) No association for heifers		LOW
6e	Calving month	No association		HIGH
1a	Proportion of calvings in winter	No association		LOW
1b	Proportion of calvings in spring	No association		LOW
1c	Proportion of calvings in summer	Association. The greater the proportion of calvings in summer was a protective factor for herd-mortality of calves.  Negative binomial: incidence rate ratio 0.96 $(P=<0.001)$	Herd size, use of consultancy service within last four years, day-time of checking calvings, frequency of adding bedding to calving pen/area, herd main breed, place of calving, type of production, region	LOW
1d	Proportion of calvings in autumn	No association		LOW

(Continued)

Table 2. (Continued.)

Practice assessment	Details practice	Association/effect on mortality	Covariates in the final model	Overall ROB
8a	Season of birth Winter (December to February), Spring (March to May), Summer (June to August), Autumn (September to November)	0 to 30 days of age: Association. Calves born in winter and autumn had significantly higher odds of mortality than the ones born in the reference season (summer) - Winter OR 1.42 (95%CI 1.15 – 1.75), Autumn OR 1.27 (95%CI 1.02 - 1.58). Calves born in spring had no difference with those from summer	0 to 30 years of age: Dam parity, calving status, gestation length (days), calf sex, birth type	HIGH
		31 to 60 days of age: No association		
		61 to 90 days of age: No association		
		91 to 120 days of age: No association		
4e	Length of calving season (days)	1 to 7 of age: No association. 7 days of age to weaning: Association. Higher mortality by 1.4% for every additional week of the calving season ( $p=0.007$ )	7 days of age to weaning: Month calving started, intervene with colostrum consumption if assisted calving, number of breeding age cows in herd, herd-level treatment risk of BRD	HIGH
3b	Length of calving season	Association. The longer the calving season, the higher the mortality ( $P = 0.002$ )		SOME CONCERN
1aa	Length of the average calving period (up to two months, two to three months, three to four months, longer than four months)	No association		LOW
2b	Length of the calving season	No association		HIGH
Nutritional n	nanagement calves			
6 f	Use of vitamin E/selenium at birth (N/Y)	Association. Higher mortality in herds that did not use the vitamin E/selenium at birth compared to those that did Adj. OR 10.3 (95%CI 2.2 $-$ 47) ( $P=0.003$ )	10 g/L decline in serum Immunoglobulin G	HIGH
1v	Feeding minerals to calves (N/Y or sometimes)	No association		SOME CONCERN
1w	Administering selenium supplements to calves (N/Y or sometimes)	No association		SOME CONCERN
4f	Administered vitamin and/or mineral injection	No association		HIGH

# Practices removed from the review

## Nutritional management and mineral supplementation

Feeding cows silage (2f) was excluded from the final narrative review, because it was not specified whether this was done precalving or post-calving.

# Vaccination

A non-inferiority trial comparing two different intranasal vaccines in calves was excluded from this review (Masset *et al.*, 2020). Both vaccines targeted Parainfluenza Virus Type 3 and Bovine Respiratory Syncytial Virus. Their differences included the strains used, tissue culture infectious doses, diluent, administration modalities, and dose of the vaccine. Vaccine A was not significantly inferior to Vaccine B (P=0.11) in preventing calf mortality. Nonetheless, non-inferiority does not provide direct evidence about vaccination as an effective strategy to prevent calf mortality.

Two other PAs were removed because of a lack of details regarding the production group that was vaccinated, disease targeted, type of vaccines used, or time of vaccination (1y and 7a).

#### Risk of bias assessment

Of the 42 PAs from observational cross-sectional studies and one PA from an RCT included, 22 had a 'high', 11 showed 'some concerns', and 10 had a 'low' ROB (Supplementary materials 9 and 10).

Twenty-three PAs were subject to selective reporting. For example, univariable analysis was not shown or only interventions with significant effects included in their final multivariable models were reported (4b and 6e). Twenty PAs did not select participants using systematic methods (e.g., used a convenience sample; 2b and 2c). Nineteen PAs did not sufficiently specify the intervention evaluated (e.g., no definition of the criteria used to define abnormal colostrum; 4b).

**Table 3.** Assessment of the certainty of the findings of management practices with significant effects or associations using the GRADE approach within a systematic review on the effect of management practices on preweaned calf mortality in beef herds

Practice category	Risk of Bias (ROB)	Directionality of results	Intervention, com- parison groups, and similarities with western Canada	Imprecision of results	Overall certainty
Timing of the calving season (umber of practice assessments (PAs), $n=4$ )	Critically high (Downgraded 2 levels) 3 PAs with high ROB and 1 low ROB	Consistent direction (No downgrading)  3 of 4 PAs indicated that herds that calved earlier had higher frequency of mortality	Consistency in comparison groups, intervention groups, and environmental conditions (No downgrading)	No estimate was calculated (Downgraded 1 level)	LOW
Length of the calving season $(n=4)$	Critically high (Downgraded 2 levels) 2 PAs with high ROB, 1 some concerns, and 1 low ROB	Semi-consistent direction (No downgrading) 2 of 4 PAs indicated that herds with longer calving seasons had higher frequency of mortality Possible explanation of why results were not consistent: differing risk of mortality (see Table 1)	Consistency in intervention groups, comparison groups, and comparable with western Canada (No downgrading)	No estimate was calculated (Downgraded 1 level)	LOW

#### **Discussion**

The evidence compiled for the criteria used to intervene with a colostrum management strategy, timing and length of the calving season, and vitamin and mineral supplementation in calves showed statistically significant associations with calf mortality.

Determining whether a calf needs colostrum intervention depending on whether they were assisted at calving or had not nursed from their dam has been shown to reduce calf mortality at the herd level (Murray et al., 2016). This aligns with the findings of an expert consensus study (Sanguinetti et al., 2024). Assisted calves are more likely to not consume colostrum by themselves within 4 hours after birth compared to unassisted ones (Homerosky et al., 2017). These calves also have less vigour than unassisted calves (Pearson et al., 2019b) and rely on colostrum intervention practices to increase their odds of survival (Besser and Gay, 1994). Intake of colostrum that contains maternal antibodies in a timely manner is essential because calves are born with a naïve adaptive immune system and lack their own circulating antibodies (Chase et al., 2008; Godden, 2008; Larson and Tyler, 2005; Windeyer and Gamsjäger, 2019). The maternal antibodies protect the newborn as their immune system matures, thus impacting health and survival (Waldner and Rosengren, 2009). Regardless, at the calf level, calves that received any colostrum practice including different methods and sources of colostrum, had higher odds of dying than those that did not (Gamsjäger et al., 2023). Therefore, according to the findings of this systematic review, the decision of whether a calf needs colostrum intervention based on not nursing by themselves or being assisted at calving is the only colostrum management practice that has been shown to have an effect on calf mortality at the herd-level. However, at the individual level, these calves still have a higher risk of dying compared to those that do not require a colostrum intervention practice to be used. It is important to differentiate between individual- and herd-level practices. While some practices that have an important effect on the odds of mortality in the individual, if the practice, such as colostrum invention, is relatively rare, it may have minimal impact on the herd-level mortality risk.

Winter calving was identified as a potential risk factor for increased calf mortality (Clement et al., 1993; Misaka et al., 2022; Mõtus et al., 2020; Murray et al., 2016; Pearson et al., 2019a). This was also described in another review (Uetake, 2013). Possible explanations involve the exposure of calves to cold temperatures and wind, which lower their metabolic rate and increase the time it takes to nurse from their dam (Uetake, 2013). At the intestinal level, this elapsed time affects the efficiency of absorbing colostrum immunoglobulins (Colazo and Kastelic, 2012; McGee and Earley, 2019; Weaver et al., 2000). Furthermore, cold stress reduces this process even more (Olson et al., 1980). Therefore, calves are more likely to have inadequate or failed transfer of passive immunity, thus increasing their risk of morbidity and mortality (Gamsjäger et al., 2023; Waldner and Rosengren, 2009; Windeyer et al., 2014). In winter calving herds, management practices used to protect newborn calves from climatic conditions may also be associated with an increased mortality risk. For example, calving in barns involves managing animals more intensively with a higher stocking density compared to animals calving on pasture (Ganaba et al., 1995; Pearson et al., 2019a; Radostits, 1991). A higher stocking density favours a high pathogen load in the barn and may increase the risk of transmission of pathogens between calves (Assié et al., 2009; Doeschl-Wilson et al., 2021). Consequently, disease incidence is affected, given its relationship with the transmission rates (Dohoo et al., 2009; Ogut et al., 2005). However, for some herds, for example, purebred or seedstock, calving later is not a viable option because calves need to be born as early as possible in the year to be competitive in animal shows and sales.

The length of the calving season was identified as a risk factor for calf mortality (Dutil *et al.*, 1999; Murray *et al.*, 2016). This may be explained by the calf acting as a pathogen amplifier during the calving season (Larson and Tyler, 2005). Within this review, studies that showed statistically significant associations had very different lengths of calving seasons (mean = 79 days; Murray *et al.*, 2016)

versus over four months long (Dutil et al., 1999). The findings of the first study align well with recommended management practices for herds, which state that the length should be from 60 to 80 days (Chenoweth and Sanderson, 2005; Colazo and Kastelic, 2012; WCCCS, 2017). Hypothetically, calves born at the beginning of the season are exposed to lower doses of environmental pathogens and are often asymptomatic if infected (Larson and Tyler, 2005). However, as the season progresses, the dose of environmental pathogens will increase, and consequently, later-born calves often develop clinical signs of disease (Larson and Tyler, 2005). Therefore, herds may reduce the risk of calf mortality by limiting the duration of the calving season. Alternatively, a short calving season may be a surrogate indicator of an unmeasured collection of good management practices that reduce calfhood mortality (i.e., herds with good reproductive management may also have good health management).

Injecting vitamin E and selenium (Se) at birth in calves also reduced calf mortality (Waldner and Rosengren, 2009). Similarly, the impact of injectable supplementation with selenium and vitamin E at birth has been reported to reduce the odds of treatment of NCD in dairy calves (Leslie et al., 2019). In contrast, an RCT assessing repeated mineral supplementation in pregnant dams included in this review did not detect a significant effect on calf mortality compared to a control group (Stokes et al., 2019) nor did another controlled trial done in western Canada assessing NCD in calves (Cohen et al., 1991). Within these dam studies, plasma concentrations of copper, manganese, Se, and zinc in calves at birth were not different between groups (Stokes et al., 2019), nor was Se in the second study (Cohen et al., 1991). However, different minerals were assessed in each of these PAs, so comparisons should be made cautiously. There are several possible explanations of why statistically significant associations were found when calves were supplemented but not dams. Several steps or factors may be involved for calves to benefit from the dam supplementation. These include the severity of the initial deficiency in the supplemented dams prior to supplementation and the type of the deficiency (Cohen et al., 1991), the age of dams (de Weyer Lm et al., 2010; Waldner et al., 2023), the timing of supplementation during gestation, characteristics of the products used (e.g., chelated or organic) (Ahola et al., 2004; Chenoweth and Sanderson, 2005; Marques et al., 2016), and the doses used to supplement (Awadeh et al., 1998). Furthermore, specific differences in placental or colostral absorption exist (Awadeh et al., 1998). For example, the absorption of Se starts in utero and is stored in the fetal liver (Gooneratne and Christensen, 1989), while vitamin E is exclusively obtained through colostrum after birth (Quigley and Drewry, 1998). In short, injecting calves is a more direct method of supplementation, avoiding these intermediate steps, and having a greater impact on calf mortality. Nevertheless, the evidence to support this practice in pregnant dams or calves within this systematic review is extremely scarce. Only one study reporting a statistically significant association is insufficient to support or discourage using this practice (Lash et al., 2021). Similarly, another review identified that the impact of trace mineral supplementation in dams and its impact on calfhood health needs more research (Van Emon et al., 2020). In western Canada, this is especially important given Se deficiency was frequently detected in the liver of beef calves that died after 3 days of age and that vitamin E deficiency was common in stillbirths (Waldner and Blakley, 2014), although this latter finding should be interpreted with caution as many of these calves probably did not consume colostrum (Quigley and Drewry, 1998). Overall, it is important to garner more information to better understand whether vitamin and mineral

supplementation programs meet the nutritional requirements of the cattle within a given herd and are effective in optimizing the production of calves.

Within the body of evidence discussed earlier, there is consistency in the directionality of findings for some practices assessed and not others (Clement et al., 1993; Dutil et al., 1999; Mõtus et al., 2020; Murray et al., 2016; Pearson et al., 2019a; Waldner, 2008; Waldner and Rosengren, 2009). Consistency among study results supports that an actual causal relationship may exist under field conditions (Dohoo et al., 2009). However, under certain circumstances, a cause-effect relationship may exist even when the change in the practice may not always be associated with a specific change in the direction of the outcome (Lash et al., 2021). For example, a practice's effect may vary with mortality risk (Dohoo et al., 2009). This could explain variation in the directionality of results attained between studies, as was observed among PAs examining the length of the calving season. For this practice, two of four PAs found a statistically significant association between the length of the calving season and mortality, and two did not. In studies that reported a statistically significant association (Dutil et al., 1999), mortality risk was > 5%. In contrast, when a statistically significant association was not observed, the mean mortality risk was estimated at 1.5% (Clement et al., 1993). For this hypothesis to be confirmed, several well-executed RCTs are needed to do a dose-response meta-analysis (Berlin et al., 1993).

Most of the practices assessed in this review were not reported to have a statistically significant impact on calf mortality (Clement *et al.*, 1993; Mõtus *et al.*, 2020; Pires *et al.*, 2021; Stokes *et al.*, 2019; Waldner, 2008; Waldner and Rosengren, 2009). The relationship between practices and calf mortality is not often direct, and mortality may occur only after several intermediary events, including morbidity and treatment of disease, which have a more direct relationship with management practice (Digitale *et al.*, 2022; Ganaba *et al.*, 1995). Similarly, unmeasured confounding variables may bias the reported association.

A limited number of calves dying may also limit the reliability of the findings by minimizing the sample size (Button *et al.*, 2013; United States Department of Agriculture Animal and Plan Health Inspection Service Veterinary Services National Animal Health Monitoring System, 2021). Within this systematic review, the mortality risk of studies varied from 1.5 to 13.5%, and none of them reported considering it for the sample size calculation. Given this, in future studies, when doing the sample size calculations, the mean mortality risk should be considered (Dohoo *et al.*, 2009; Wang and Cheng, 2020). This would help ensure that observational studies may provide more reliable results (Wang and Cheng, 2020). Therefore, this leads to the question of whether using these practices does not affect mortality or if a type II error is present (Akobeng, 2016; Dohoo *et al.*, 2009; Lash *et al.*, 2021).

The statistical analysis methods could have influenced the low number of practices that showed statistically significant associations. Eight out of nine cross-sectional studies used multivariable methods to analyze the data (Clement *et al.*, 1993; Dutil *et al.*, 1999; Misaka *et al.*, 2022; Mōtus *et al.*, 2020; Murray *et al.*, 2016; Pires *et al.*, 2021; Waldner, 2008; Waldner and Rosengren, 2009). Within these studies, variables selected to be retained in the models relied on p-values (Lash *et al.*, 2021). Yet, the biological plausibility of associations was not assessed using directed acyclic graphs (DAGs). Only one study reported the temporal criteria used to determine whether a practice was considered to potentially impact mortality (Waldner, 2008). One of the assumptions of multivariable models is the independence of variables

(Concato et al., 1993). Assuming practices used within herds are independent is questionable and most likely unreasonable, regardless of statistical attempts to detect collinearity among variables (Fox and Monette, 1992). For example, winter calving usually takes place in more confined areas with more intensive management, such as barns, to protect newborns from hostile temperatures and increase their odds of survival (Pearson et al., 2019a). None of the studies reported univariable analysis, so the unconditional associations between individual practices and mortality were unavailable. Therefore, although odds ratios and confidence intervals were extracted from the studies, the focus was on the directionality of the findings (e.g., beneficial or harmful to mortality risk). A meta-analysis could not be done because there was not enough reliable evidence to calculate effect estimates of any given practice.

The reliability of the findings within this systematic review is low, given that the largest bodies of evidence (i.e., timing and length of the calving season and dam vaccination against NCD pathogens) had low certainty of findings (Schünemann et al., 2013). The GRADE assessment incorporates the ROB in individual studies, directionality and imprecision of results, comparability between studies, and how comparable were production conditions in the studies relative to those in cow-calf operations in western Canada. Overall, individual PAs had a high ROB, and the certainty of the bodies of evidence was downgraded because many used a crosssectional study design. Cross-sectional studies are weak sources of evidence to infer causality given that outcomes and exposures are measured at the same time, and a temporal relationship between them cannot be demonstrated (Carlson and Morrison, 2009; Dohoo et al., 2009; Sargeant et al., 2014a). According to the levels of evidence approach, bodies of evidence from crosssectional studies are considered less reliable than those from RCTs (Canadian Task Force on the Periodic Health Examination, 1979; Sargeant et al., 2022). Because of this, under ideal circumstances, systematic reviews should include well-executed RCTs (Burns et al., 2011). However, assessing some practices using RCTs may be challenging, and well-executed cohort studies can also be a good source of evidence.

This review only included studies that explicitly removed still-births. Fifty percent of calf mortality occurs during the first 24 hours after birth (Pearson *et al.*, 2019a). Calves assisted at birth have an increased risk of dying during this period (Bond and Weinland, 1978; Ganaba *et al.*, 1995; Wittum *et al.*, 1994). Stillbirths were removed to ensure that the substantial effect of assisted calving did not statistically overshadow practices with smaller effects. However, not all calves born with assistance at calving die during the first 24 hours, and studies evaluating their survival during the preweaning stage were inevitably lost because of this exclusion criteria.

#### **Conclusions**

This review filled the knowledge gap concerning the evidence about disease control management practices to prevent calf mortality in preweaned beef calves. The timing and length of the calving season, criteria used to intervene with a colostrum management practice, and use of supplementation with vitamin E and selenium in calves were reported to have statistically significant protective associations with calf mortality. Conversely, most of the studies included were observational cross-sectional studies, and the certainty of the findings was low. Overall, the findings of this review reinforce the need to design well-executed RCTs

and cohort studies to estimate the effectiveness of practices, which should be combined with those of other systematic reviews to guide evidence-informed management.

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