INPLASY

Effects of vitamin A, vitamin E, and selenium supplementation on uterine health and reproductive outcomes in female cattle: a systematic review and meta-analysis protocol

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ADMINISTRATIVE INFORMATION

Support - No specific funding.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202690025

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 September 2026 and was last updated on 5 September 2026.

INTRODUCTION

Review question / Objective In female cattle, what are the effects of supplementation with vitamin A, vitamin E, and/or selenium, administered alone or in eligible combinations, compared with no specific supplementation, placebo, conventional treatment, or alternative supplementation strategies, on uterine health and reproductive outcomes?

Rationale Vitamin A, vitamin E, and selenium participate in biological processes relevant to bovine reproductive health. Vitamin E and selenium have complementary antioxidant and immune functions that may influence placental separation, postpartum uterine health, and reproductive function, whereas vitamin A contributes to epithelial integrity, ovarian function, and maintenance of the reproductive tract. However, intervention studies have reported heterogeneous findings. Differences in baseline nutritional status, supplement formulation, dose, chemical source, route and timing of administration, physiological stage, co-interventions, and outcome definitions may contribute to this variability. A systematic synthesis is therefore warranted to integrate comparative intervention studies, assess their risk of bias, characterize the direction and consistency of the evidence, explore potential sources of heterogeneity, and determine which outcomes are sufficiently comparable for quantitative synthesis.

Condition being studied Uterine health and reproductive performance in female cattle, including postpartum uterine disorders, resumption of ovarian activity and estrus, ovarian and endocrine function, conception, pregnancy and pregnancy loss, and reproductive intervals.

METHODS

Search strategy PubMed/MEDLINE: ("Vitamin A"[Mesh] OR "Vitamin E"[Mesh] OR "Selenium"[Mesh] OR retinol[Title/Abstract] OR tocopherol[Title/Abstract] OR selenium[Title/Abstract]) AND ("Cattle"[Mesh] OR cattle[Title/Abstract] OR bovine[Title/Abstract] OR cow[Title/

Abstract] OR dairy[Title/Abstract] OR beef[Title/Abstract]) AND ("Reproduction"[Mesh] OR "Fertility"[Mesh] OR fertility[Title/Abstract] OR pregnancy[Title/Abstract] OR conception[Title/Abstract] OR reproductive[Title/Abstract])
Web of Science: TS=(("vitamin A" OR "vitamin E" OR selenium OR retinol* OR tocopherol*) AND (cattle OR bovin* OR cow* OR dairy OR beef) AND (reproduct* OR fertil* OR pregnan* OR concept*))
Scopus: TITLE-ABS-KEY(("vitamin A" OR "vitamin E" OR selenium OR retinol* OR tocopherol*) AND (cattle OR bovin* OR cow* OR dairy OR beef) AND (reproduct* OR fertil* OR pregnan* OR concept*))

The electronic database search was completed on July 30, 2026. The search was supplemented by backward reference searching of included primary studies and other relevant publications, which was completed on August 30, 2026. No language restrictions were imposed.

Participant or population Female cattle, including cows and heifers of Bos taurus, Bos indicus, or their crossbreds, used for dairy, beef, or dual-purpose production. Animals could be evaluated at different physiological or reproductive stages, including late gestation, the transition period, postpartum, the estrous cycle, breeding, or reproductive synchronization.

Intervention Supplementation with vitamin A, vitamin E, and/or selenium, administered alone or in eligible combinations by dietary, oral, intramuscular, subcutaneous, or other parenteral routes. Different doses, chemical sources, frequencies, and timings of administration were eligible. Multinutrient formulations were included only when the effect attributable to vitamin A, vitamin E, and/or selenium could be reasonably distinguished from that of the other components.

Comparator No specific supplementation, placebo, conventional treatment or management, or an alternative supplementation strategy differing in dose, chemical source, frequency, route, or timing of administration.

Study designs to be included Randomized controlled trials and experimental or quasi-experimental intervention studies with a concurrent comparator group were eligible. Observational studies without an intervention, in vitro or ex vivo studies, and studies without a concurrent comparator were excluded.

Eligibility criteria Primary comparative studies were eligible when they included female cattle (cows or heifers; Bos taurus, Bos indicus, or crossbreds), evaluated supplementation with vitamin A, vitamin E, and/or selenium, included an eligible concurrent comparator, and reported at least one reproductive or uterine-health outcome. Randomized controlled trials and experimental or quasi-experimental intervention studies with concurrent controls were eligible. Studies were excluded if they were observational without intervention, in vitro or ex vivo investigations, studies in non-bovine species, secondary publications, reviews, meta-analyses, conference abstracts, non-peer-reviewed theses, studies without an eligible comparator, studies without eligible reproductive or uterine-health outcomes, or multinutrient interventions in which the specific contribution of vitamin A, vitamin E, or selenium could not reasonably be distinguished. Multiple publications derived from the same experimental population were treated as a single independent study to avoid double counting of animals, comparisons, and outcomes.

Information sources PubMed/MEDLINE, Web of Science, and Scopus were searched electronically. The database search was supplemented by backward reference searching of included primary studies and other relevant publications. Reports identified by reference searching were assessed using the same eligibility criteria as database-derived records. Records were managed and screened using Rayyan. No language restrictions were imposed.

Main outcome(s) The main outcome domain was uterine health and postpartum events, including retained fetal membranes (RFM), placental expulsion, metritis, endometritis, and uterine involution. RFM was the outcome suitable for quantitative synthesis. The definition and postpartum diagnostic threshold used by each primary study were accepted. For RFM, effects were expressed as risk ratios (RRs) with 95% confidence intervals when exact events and denominators were available. No single primary outcome had been prospectively designated.

Additional outcome(s) Additional outcomes were grouped into four domains: (1) resumption of ovarian activity and expression of estrus; (2) ovarian and endocrine function, including follicular dynamics, corpus luteum characteristics, progesterone, and estradiol; (3) conception, pregnancy, and pregnancy loss; and (4) reproductive intervals and services per conception. Outcomes were retained in the units and at the assessment times reported by the primary studies.

Data management Electronic records were imported into Rayyan for deduplication and screening. Two reviewers independently assessed titles and abstracts and subsequently evaluated potentially eligible full-text reports. Studies identified through backward reference searching were assessed directly at the full-text stage. Disagreements were resolved by consensus and, when necessary, by consultation with a third reviewer. Two reviewers independently extracted data using a structured form covering population and study design, intervention and comparator, dose, formulation, route and timing of administration, sample size, outcomes, group-level results, dispersion measures, measures of association, and reported P values when available. Multiple reports from the same experimental population were linked to avoid double counting. Missing data were not imputed. Quantitative analyses were conducted using Review Manager (RevMan), version 11.3.1.

Quality assessment / Risk of bias analysis Randomized trials were assessed using the Cochrane Risk of Bias 2 tool (RoB 2), whereas non-randomized and quasi-experimental intervention studies were assessed using ROBINS-I. Classification was based on the actual allocation procedure described in each publication, with conservative judgments when reporting was incomplete. Risk-of-bias judgments could differ across outcomes. Disagreements were resolved by consensus. Risk of bias informed interpretation of robustness and confidence but was not used as an automatic exclusion criterion. Formal GRADE assessment was not performed. Instead, evidence within each reproductive domain was narratively classified as consistent, suggestive, inconsistent, or insufficient considering risk of bias, consistency, precision, applicability, completeness of information, and plausible alternative explanations.

Strategy of data synthesis Most outcomes were synthesized narratively because of clinical and methodological heterogeneity, following the principles of Synthesis Without Meta-analysis (SWiM). Results were organized into five reproductive domains and interpreted considering direction of effect, consistency, precision, risk of bias, comparability, applicability, and completeness of information. Statistical significance alone was not used to determine effect direction or importance.

Retained fetal membranes were quantitatively synthesized when exact and verifiable numbers of events and denominators were available for an eligible supplemented group and a concurrent control. Counts were not reconstructed from rounded percentages when exact events could not be established unequivocally. In multi-arm studies with a shared control, eligible intervention groups were combined when necessary to avoid double counting of the comparator. Independent experiments reported within the same publication were retained as separate comparisons. Risk ratios and 95% confidence intervals were pooled using an inverse-variance random-effects model. Between-study variance (τ^2) was estimated using restricted maximum likelihood (REML), with Wald-type confidence intervals. A continuity correction of 0.5 was applied when one study arm contained zero events. Heterogeneity was assessed using Cochran's Q, τ^2, and I^2. Formal funnel-plot asymmetry tests were not performed because of the limited number of independent publications and the contribution of multiple experiments by one publication.

Subgroup analysis No formal statistical subgroup analyses were performed because the number of quantitatively comparable studies was limited. Potential sources of heterogeneity were explored narratively according to baseline nutritional status, supplement source and dose, route and timing of administration, physiological category, study design, sample size, risk of bias, reporting quality, and completeness of data. These comparisons were considered exploratory and were not interpreted as confirmatory tests of subgroup interactions.

Sensitivity analysis Robustness of the retained fetal membranes meta-analysis was evaluated through leave-one-out analysis and a sensitivity analysis restricted to studies assessed with RoB 2. The same effect measure, random-effects model, REML estimator, Wald-type confidence intervals, and continuity correction used in the primary meta-analysis were retained.

Language restriction No language restrictions were imposed.

Country(ies) involved Mexico.

Other relevant information This protocol is being registered retrospectively. Prospective registration was not incorporated into the review workflow at project initiation. At the time of INPLASY submission, the electronic database search, backward reference searching, study selection, data extraction, risk-of-bias assessment, qualitative synthesis, meta-analysis, and sensitivity analyses had already been completed, but the systematic review had not been published. This

registration is intended to provide a transparent, citable, and permanently accessible record of the methods actually used. The information reported in this registration reflects the procedures applied in the completed review and has not been modified on the basis of the observed results. Researchers from Universidad Autónoma de Baja California Sur and Universidad Autónoma de Baja California, Mexico, participated in the review.

Keywords bovine fertility; cattle reproduction; uterine health; retained fetal membranes; vitamin A; vitamin E; selenium; micronutrient supplementation.

Dissemination plans The systematic review and meta-analysis will be submitted for publication in a peer-reviewed journal in animal science, veterinary medicine, or animal reproduction. Supplementary materials will report the complete search strategies, study characteristics, risk-of-bias assessments, individual outcome data, and other supporting information. The INPLASY registration number and DOI will be reported in the final manuscript to provide a permanent link to the registered methodological record.

Contributions of each author

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