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Estimating the costs of interrelated reproductive disorders in dairy farms

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ABSTRACT

Several reproductive disorders can occur in dairy cows from peripartum until the start of pregnancy. Their occurrence can be interrelated, which complicates the estimation of subsequent economic impact. Estimation of the economic impact of reproductive disorders is essential for dairy farmers to make informed decisions. It enables them to prioritize the prevention of disorders with the highest economic impact. The aim of this study was to estimate the costs of dairy cow reproductive disorders, including dystocia, retained placenta, acute metritis, clinical endometritis, anovulation, cystic ovarian disease (COD), and sub-estrus, taking their complex interrelations into account. An existing individual cow-based, dynamic, and stochastic bio-economic simulation model of a 200-cow-herd with daily time steps was extended to include the interrelations of the 7 reproductive disorders studied. The parameterization of the probabilities of developing reproductive disorders was based on scientific literature and expert opinion. Nine scenarios were simulated and included (1) a default scenario, in which all reproductive disorders were included in the simulation model. The second to eighth scenarios were simulated with zero probability of each specific disorder, including (2) dystocia, (3) retained placenta, (4) acute metritis, (5) clinical endometritis, (6) anovulation, (7) COD, and (8) sub-estrus. In the ninth scenario, all disorders were absent. The annual net economic return (NER) of the herd was calculated for all the scenarios. Subsequently, the NER of the scenarios with zero probability of disorder (scenarios 2–9) were compared with the NER of the default scenario and its difference was considered the cost of each specific reproductive disorder (or of all 7 reproductive disorders combined). This study showed that taking all disorders into account resulted in a mean annual cost of €20,013/herd per year or €100/cow per year. At herd level, the highest mean annual cost was observed for acute metritis (€5,908/herd per year or €30/cow per year), whereas the lowest mean annual cost was observed for dystocia (€897/herd per year or €4/cow per year). In the context of cost per case, the highest cost was observed for acute metritis (€257/case), whereas the lowest cost was observed for COD (€58/case). Given the interrelationships between reproductive disorders, preventing one disorder reduces the occurrence of others, thereby lowering their overall economic impact.
Key words: reproductive disorder, interrelations, economics, simulation, dairy, fertility

INTRODUCTION

A range of reproductive disorders can occur in dairy cows. These include disorders, such as dystocia, retained placenta, acute metritis, and clinical endometritis, which can occur at different stages of lactation. Preceding reproductive disorders during early lactation can affect cyclicity and result in, for example, a delayed resumption of cyclicity and anestrus events, due to, for example, anovulation, cystic ovarian disease (**COD**), and sub-estrus. The incidence of each of these reproductive disorders is considerable. For instance, the incidence of clinical endometritis ranges between 10% and 36% (Leblanc et al., 2011; Plöntzke et al., 2011; Denis-Robichaud and Dubuc, 2015). Similarly, the incidence of anovulatory anestrus due to inactive ovaries varies between 5% and 38% (Rhodes et al., 2003; Walsh et al., 2007; Barański et al., 2018).

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The list of standard abbreviations for JDS is available at adsa.org/jds-abbreviations-25. Nonstandard abbreviations are available in the Notes.

Early postpartum reproductive disorders can significantly affect the cow's reproductive performance later in lactation. For instance, dystocia is associated with a reduced pregnancy rate (Quintela et al., 2004; Gaafar et al., 2011), an increased incidence of retained placenta, and more days open and a longer calving to first artificial insemination (**AI**) interval (Mahnani et al., 2021a). Postpartum uterine diseases are associated with a lower pregnancy rate and a higher risk of ovarian disorders (Opsomer and De Kruif, 2009; Molina-Coto and Lucy, 2018), and subsequently, preterm culling (Leblanc et al., 2011; Plöntzke et al., 2011; Molina-Coto and Lucy, 2018). Cows that experience anestrus and silent heats demonstrate longer intervals to first AI and calving to conception, lower pregnancy rates, and an increased intercalving period (e.g., Petersson et al., 2006; Santos et al., 2009; Ranasinghe et al., 2010). Reproductive disorders are often interrelated (Fourichon et al., 2000; Opsomer et al., 2000). For example, dystocia is associated with a higher occurrence of retained placenta and uterine diseases (Bruun et al., 2002; Mee, 2008; Kelly et al., 2020), whereas uterine diseases in turn can result in estrus problems (Opsomer and De Kruif, 2009; Molina-Coto and Lucy, 2018).

The economic impact of reproductive disorders is considerable. However, most studies carried out so far have focused on this within the context of individual disorders. For instance, the economic consequences of dystocia (Dematawena and Berger, 1997), acute metritis (Overton and Fetrow, 2008), retained placenta (Mahnani et al., 2021b), and COD (Kim et al., 2005) have been studied. Other studies have estimated the economics of poor fertility in general without studying any particular disease (Inchaisri et al., 2010; Shalloo et al., 2014; Kalantari and Cabrera, 2015). The economic impact of reproductive disorders has, thus, mostly been estimated without consideration of the interrelations between the various reproductive disorders.

This study aimed to estimate the costs of the most common dairy cow reproductive disorders including dystocia, postpartum puerperal disorders, and postpartum ovarian disorders, considering their complex interrelations into a stochastic bio-economic simulation model.

MATERIALS AND METHODS

Simulation Model in Brief

The basis for the bio-economic simulation model developed in this study was an individual cow-based dynamic Monte Carlo stochastic model, originally described by Edwardes et al. (2022) that simulates 200 cows in a typical Dutch dairy herd through daily time steps. This base model was recently extended to enable the simulation of the reproduction dynamics of a dairy herd (i.e., ovulation and estrous cycle, estrus detection, and successful pregnancy). A detailed description of the model simulation procedures regarding production (i.e., milk production, feed requirements, culling decisions) and reproduction dynamics can be found elsewhere (Edwardes et al., 2022; Wicaksono et al., 2024). In brief, the daily milk production of each cow is simulated based on the Wilmink lactation curve (Wilmink et al., 1987). The daily feed requirements of each cow are expressed in VEM (energy requirements in feed units; Remmelink et al., 2016; Van Es, 1978). The first ovulation event is 15 to 25 d after calving (Crowe et al., 2014), whereas subsequent estrus events occur every 19 to 26 d (Remnant et al., 2018); both are simulated by a uniform distribution (Wicaksono et al., 2024). An estrus detection rate of 60% is assumed. The probability of a successful pregnancy after insemination is dependent on the individual cow's characteristics including parity, number of AI, time of AI related to peak milk yield, season of AI, DIM at AI, milk yield at AI, and 4 interaction terms with DIM, based on a previous observational Dutch study (Inchaisri et al., 2011). Cows are bred a maximum of 6 times, and only when their daily milk yield is above 20 kg. Cows that do not meet these criteria are not bred anymore but are milked until their milk yield is below 15 kg, after which they are culled. These production levels may be lower than those typically used in more intensive dairy systems with higher production levels. Asides from culling for infertility, culling because of general (nonreproductive) reasons might be implemented. A mortality of 6.7% of all culled cows due to general culling is included (Rutten et al., 2014; Bisschop et al., 2023). A culled cow is replaced by a replacement heifer the following day. All relevant input parameter values on fertility are described in Table 1, and production inputs are described in Appendix Table A1.

To perform an economic evaluation of relevant reproductive disorders, the existing model was extended to simulate the occurrence of the disorders, their interdependency, and the effect of treatment, as described later. Anovulation, COD, and sub-estrus were already modeled previously (Wicaksono et al., 2024), but the model was expanded to also include other reproductive disorders (i.e., dystocia, retained placenta, acute metritis, and clinical endometritis), as well as their interrelations. The simulation model was developed in RStudio software Version 2022.12.0 Build 353 (Posit Software, 2023).

Defining Reproductive Disorders and Their Interrelations

The potential interrelations between 7 reproductive disorders, (1) dystocia, (2) retained placenta, (3) acute me-

Table 1. Input parameter values on cow fertility used in the bio-economic simulation model

Parameter	Description	Value	Source
First ovulation event	First ovulation after calving	Uniform (15–25)	Crowe et al., 2014
Length estrous cycle	Length of the estrous cycle	Uniform (19–26)	Remnant et al., 2018
Estrus detection			
Base probability	Base probability of estrus detection	0.6	Uniform-Agri, 2024; expert opinion
Risk factor: relative production level	Relative risk of estrus detection rate based on relative production level value of <0.9, 0.9–1.1, >1.1, adjusted for the milk lactation stage after the peak of milk yield (6 wk postpartum)	1.1, 1, 0.9	Inchaisri et al., 2010
Pregnancy			
Base probability	Base probability of successful pregnancy after insemination number 1 to ≥6	Cow-specific	Inchaisri et al., 2011
Risk factors	Relative risk of successful pregnancy		
	Parity: 1 and ≥2	1.2, 1	Santos et al., 2009
	Calving season: summer, autumn, winter, spring	1, 0.98, 1.13, 1.7	
	Presence of		
	Dystocia	0.89	Fourichon et al., 2000
	Retained placenta	0.81	
	Acute metritis	0.72	
	Anovulation	0.68	
	Cystic ovarian disease	0.88	
	Clinical endometritis (+corpus luteum)	0.61	Maquivar et al., 2015
	Clinical endometritis (−corpus luteum, cyclic)	0.77	Bogado Pascottini et al., 2017
Base probability hormone treatment	Probability of successful pregnancy based on previous hormonal treatments		
	Ovsynch, PRIDsynch	0.35	Santos et al., 2016
	Prostaglandin	0.414	McDougall et al., 2021
Pregnancy loss	Probability of pregnancy loss during gestation (d)		Albaaj et al., 2023
	>35 d until 45 d	0.13	
	>45 d until 60 d	0.07	
	>60 d until calving	0.02	

tritis, (4) clinical endometritis, (5) anovulation, (6) COD, and (7) sub-estrus, are presented in Figure 1. The first possible event after calving was dystocia, potentially followed by the postpartum puerperal disorders of retained placenta, acute metritis, and clinical endometritis. Cows with clinical endometritis could subsequently be noncyclic with (i.e., develop pyometra with a corpus luteum) or without (anovulatory) a corpus luteum, or cyclic. There was a possibility of getting an ovarian disorder (anovulation or COD) or estrus for cows without having clinical endometritis. The risk of having ovarian disorders or estrus was also included for cows without dystocia and postcalving puerperal disorders. The probability of estrus detection was assigned to cows that were in estrus. Based on the diagram developed, 49 possible cow reproductive statuses were identified, with each comprising combinations of one or more of the 7 reproductive disorders or estrus (Appendix Table A2).

To parameterize the simulation model, the conditional probabilities of occurrence of disorders were required. To estimate input values for these conditional probabilities, the overall incidences of reproduction disorders were first determined based on scientific literature and expert opinion. Next, following the potential interrelations of the disorders, the risks of developing each disorder given the previous event were estimated based on expert opinion. Finally, each conditional probability input, determined by a calibration process, was assigned to obtain the overall incidence of each disorder. Each conditional probability of developing a disorder is presented in Figure 1, and the incidence for each disorder and their conditional probabilities are described in Appendix Table A3).

Simulating Reproductive Disorders and Their Treatments

After defining the interrelations of the 7 reproductive disorders, their diagnosis, treatments, and associated costs are determined based on a discussion with a veterinary reproduction expert in the Netherlands, with the objective of simulating actual Dutch dairy practice as closely as possible.

Dystocia. Dystocia is defined as calving difficulty that results from a prolonged spontaneous calving or a prolonged, or severe, assisted extraction (Mee et al., 2011). At calving, the cow has a probability to get dystocia (P_{dyst}; Figure 1). The event of dystocia ($dyst$) is modeled by a Bernoulli (B) distribution: $dyst = B(1, P_{dyst})$. A 90-min calving assistance is assumed, for which 90% of dystocia cases are managed by a veterinarian, and 10% by the farmer.

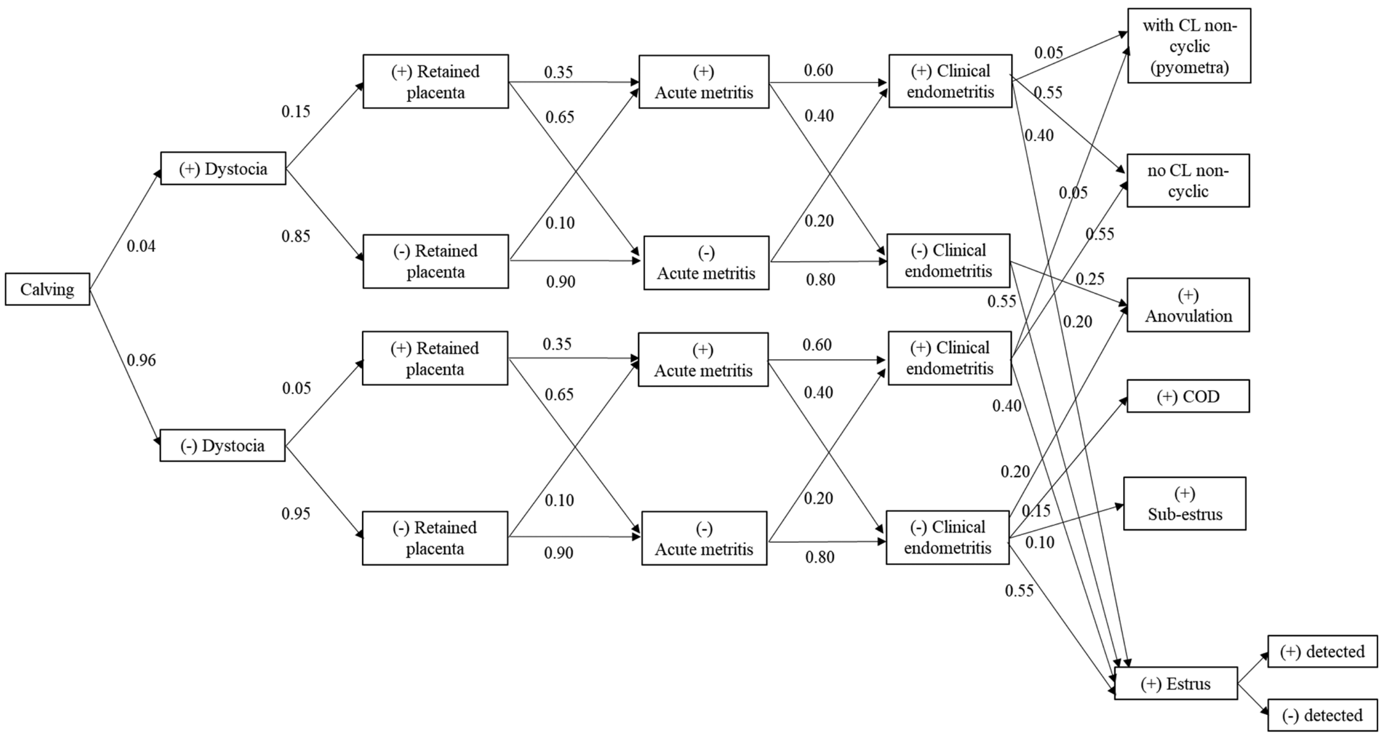

Figure 1. Flow diagram of the possible interrelations of reproductive disorders in the bio-economic simulation model. + and − indicate the presence and absence of disorder, respectively; CL = corpus luteum; COD = cystic ovarian disease. The number values beside the arrows are the conditional probabilities and are based on scientific literature and expert opinion (more detail in Appendix Table A3).

Retained Placenta. Retained placenta is defined as fetal membranes that are not delivered within 24 h postpartum (Sheldon et al., 2008). The probability of having retained placenta (P_{ret}) differs between a cow that has previously had dystocia (*dyst*) or not (*nondyst*; Figure 1). The event of retained placenta (*ret*) is modeled by 2 Bernoulli (*B*) distributions:

$$\text{IF } dyst\text{, then } ret = B\,(1, P_{ret\text{-}dsyt})\text{; IF } nondyst\text{,}$$
$$\text{then } ret = B\,(1, P_{ret\text{-}nondyst}).$$

A 10-min caring time for retained placentas as characterized by gently pulling the placenta is assumed, for which 5% of cases are managed by a veterinarian, and 95% by the farmer.

Acute Metritis. Acute metritis is defined as a systemic infection and inflammation of the uterine cavity and a deeper muscular layer of the uterus within the first 3 wk of calving, with the presence of a "reddish," odorous, fluid discharge (Sheldon et al., 2020). A cow can develop acute metritis either from retained placenta or a non-retained placenta event (Figure 1). The probability of having acute metritis (P_{met}) differs between cows that previously had a retained placenta (*ret*) or not (*nonret*) (Figure 1). The event of acute metritis (*met*) is modeled by 2 Bernoulli (*B*) distributions:

$$\text{IF } ret\text{, then } met = B\,(1, P_{met\text{-}ret})\text{; IF } nonret\text{,}$$
$$\text{then } met = B\,(1, P_{met\text{-}nonret}).$$

Treatment includes the intrauterine application of antibiotic (oxytetracycline, which was a one-time intrauterine oxytetracycline treatment via a capsule), nonsteroidal anti-inflammatory drugs (**NSAID**), and drenching. Therefore, a 30-min treatment time is assumed, for which 40% of cases are managed by a veterinarian, and 60% by the farmer. An oxytetracycline cure rate ($P_{cure\text{-}oxy}$) of 80% is assumed (Drillich et al., 2001; expert opinion; Table 2). The event of a cured metritis cow after oxytetracycline treatment ($cure_{met}$) is modeled by a Bernoulli (*B*) distribution: $cure_{met} = B\,(1, P_{cure\text{-}oxy})$.

Clinical Endometritis. Clinical endometritis is defined as a local infection and inflammation of the endometrium (superficial linings) of the uterus, with the presence of a purulent (or mucopurulent) uterine discharge detectable in the vagina; occurring >3 wk after calving (Sheldon et al., 2006; Opsomer and De Kruif, 2009). A cow can develop clinical endometritis following acute metritis or

Table 2. Economic input values used in the bio-economic simulation model

Parameter	Description or unit (or both)	Value	Source
Milk price	Average monthly price of milk with average fat and protein (€/kg) for the period 2021–2023	0.46	Wageningen Economic Research, 2023
Calf price	Average monthly price of 1- to 14-d-old male and female calves (€/calf) for the period 2021–2023	65	Wageningen Economic Research, 2023
Feed price	Average monthly price (€/kVEM[1]) for the period 2021–2023	0.35	Wageningen Livestock Research, 2023
Insemination price			
Conventional semen	€/insemination	20	Blanken et al., 2023
Treatment price			Expert opinion
GnRH	€/dose	6.5	
Prostaglandin	€/dose	6.5	
Progesterone	€/unit	20	
Oxytetracycline	€/dose	12	
Cefapirine	€/dose	12.5	
Nonsteroidal anti-inflammatory drugs (NSAID)	€/dose	17	
Dystocia treatment tools (with the treatment options such as oxytocin or cesarean section)	€/treatment (averaged cost from any treatment options)	20	
Treatment application duration	Accumulative time (min) per treatment per cow, including preparation and administration		Authors' expertise; expert opinion
Ovsynch		15	
PRIDsynch		15	
Prostaglandin		5	
GnRH		5	
Antibiotic		5	
Antibiotic cure rate	Cure rate after antibiotic treatment	0.8	Drillich et al., 2001; expert opinion
Farmer labor costs			
Hourly wage	€/h	23	Blanken et al., 2023
Insemination time	Farmer time for insemination (min/cow) including preparation and administration	10	Authors' expertise
Fetch time	Farmer time for fetching a cow for treatment (min/cow)	5	Authors' expertise
Veterinary service costs			
Hourly wage	€/h	140	Edwardes et al., 2022
Call-out fee	€/visit	40	Authors' expertise
	Emergency case on dystocia (€/visit)	60	
Diagnosing time	Veterinarian time for diagnosing pregnancy or reproductive disorders (min/cow)	5	
Calving cost	BW (kg) for milk replacement	42	Mohd Nor et al., 2012
	Milk replacement (kg)	4	
	Milk replacement price (€/kg)	2.25	Blanken et al., 2023
Culling cost	Rearing heifer price (€/animal), for every replacement heifer that enter the herd to replace a culled cow	2,342	Mohd Nor et al., 2015, reparametrized in 2019
	Carcass dressing percentage	60%	Rutten et al., 2014
	Averaged monthly third grade meat price (€/kg) for the period for the period 2021–2023	3.3	Wageningen Economic Research, 2023
	Carcass removal price (€/animal)	47	Rendac, 2023

[1]The feed requirements estimated as energy requirements in feed units for lactation (VEM; Van Es, 1978).

not (Figure 1). The probability of having clinical endometritis (P_{endo}) differs between cows that have previously had acute metritis (*met*) or not (*nonmet*) (Figure 1). The event of clinical endometritis (*endo*) is modeled by 2 Bernoulli (*B*) distributions:

$$\text{IF } met\text{, then } endo = B\,(1,\ P_{endo\text{-}met})\text{; IF } nonmet\text{, then } endo = B\,(1,\ P_{endo\text{-}nonmet}).$$

Subsequently, 3 types of clinical endometritis are modeled: (1) a noncyclic cow with a corpus luteum present (i.e., pyometra [*endo-CL*]), (2) a noncyclic cow with no corpus luteum present (*endo-nonCL*), or (3) a cyclic cow with endometritis (*endo-cyclic*). The probability of each type is incorporated and distributed over cows with a clinical endometritis event (Figure 1). Each clinical endometritis cow could acquire clinical endometritis of one of 3 types and is modeled by 3 Bernoulli (*B*) distributions:

IF endo, then: $endo\text{-}CL = B\ (1, P_{endo\text{-}CL})$; or $endo\text{-}nonCL = B\ (1, P_{endo\text{-}nonCL})$; or $endo\text{-}cyclic = B\ (1, P_{endo\text{-}cyclic})$.

A 5-min treatment time is assumed for cows with clinical endometritis, for which 80% of cases are managed by a veterinarian and 20% by the farmer. For an *endo-CL* cow, a prostaglandin injection is applied, followed by estrus detection when it exceeds the voluntary waiting period (**VWP**). For *endo-nonCL* cows, antibiotic (cefapirine) treatment is administered with a cure probability ($P_{cure\text{-}cefa}$) of 80% (Table 2). After treatment, cured cows acquire an *endo-cyclic* event, while the noncured cows would still have an *endo-nonCL* event. The event of a cured clinical endometritis after antibiotic treatment ($cure_{endo\text{-}nonCL}$) is modeled by a Bernoulli (*B*) distribution: $cure_{endo\text{-}nonCL} = B\ (1, P_{cure\text{-}cefa})$. No treatments are applied to *endo-cyclic* cows because these cows are cyclic and eligible for estrus detection after the VWP.

Ovarian Disorders. Asides from the puerperal disorders, 3 ovarian disorders were simulated: anovulation, COD, and sub-estrus. Anovulation is defined as true anestrus with inactive ovaries or less active ovaries with follicular growth and deviation, followed by either atresia or regression, which causes delay of cyclicity in the next estrous cycle (Peter et al., 2009). Cystic ovarian disease is defined as deviation, growth, and establishment of a follicular-cyst structure (>20–25 mm) that persists for >14 d, in the absence of a functional corpus luteum) that originates from a follicle that failed to ovulate (Peter et al., 2009; Parkinson, 2019). A sub-estrus cow is defined as a normal cycling cow that ovulates and develops a corpus luteum structure on the ovaries, but that experiences a suboptimal estrus expression or failure to detect estrus due to suboptimal estrus detection by the farmer (Peter et al., 2009; Parkinson, 2019). Normal cyclicity was assumed when a cow was showing and was detected for estrus, before the VWP of 65 DIM. Conversely, ovarian disorders were assumed when no estrus had not been detected at this point in the lactation.

Following the possible interrelations in Figure 1, cows without a clinical endometritis (*nonendo*) event have a probability to acquire one of 4 events: anovulation (P_{anov}), COD (P_{cod}), sub-estrus (P_{sub}), or cyclic (Figure 1), although sub-estrus could only occur if the cow had no previous events (*nondyst*, *nonret*, *nonmet*, and *nonendo*). The events of anovulation (*anov*), COD (*cod*), and estrus are modeled by 3 Bernoulli (*B*) distributions:

IF *nonendo*, then $anov = B\ (1, P_{anov})$; or $cod = B\ (1, P_{cod})$; or estrus $= B\ (1, [1 - (P_{anov} + P_{cod})]$.

If the cow previously did not have dystocia, retained placenta, acute metritis, and clinical endometritis; then 4 Bernoulli (*B*) distributions were simulated:

IF *nondyst* and *nonret* and *nonmet* and *nonendo*, then $anov = B\ (1, P_{anov})$; or $cod = B\ (1, P_{cod})$; or $sub = B\ (1, P_{sub})$; or estrus $= B\ (1, [1 - (P_{anov} + P_{cod} + P_{sub})]$.

Ovarian disorders are diagnosed during the fertility check by a veterinarian. For a cow diagnosed with anovulation, the PRIDsynch protocol is applied followed by timed artificial insemination (Santos et al., 2016; KNMvD, 2020; Hölper et al., 2023). Due to the time sequence, all hormone applications within the PRIDsynch protocol are done by the farmer after the prescription by the veterinarian. For a cow diagnosed with COD, a GnRH injection is administered by a veterinarian. If the cow is still not detected in estrus after 120 DIM, an Ovsynch protocol is applied followed by timed AI (Caraviello et al., 2006; KNMvD, 2020; Fricke and Wiltbank, 2022). This application is following the fertility guidelines in the Netherlands to represent the treatment conditions on Dutch dairy farms (KNMvD, 2020). All hormone applications within the Ovsynch protocol are carried out by the farmer. For a sub-estrus cow, a prostaglandin injection for estrus induction is applied by a veterinarian. The treatment durations for the hormone protocols and antibiotic treatment are described in Table 2. A schematic description of hormone protocols can be found in Appendix Figure A1. The occurrence of an ovarian disorder ended when the cow achieved a successful pregnancy through the application of a hormone protocol. Otherwise, the cow would be culled due to infertility.

Effect of Reproductive Disorders on Pregnancy Rate. The effect of each reproductive disorder on the possibility of cows becoming pregnant was included in the simulation model. The presence of reproductive disorders is a risk factor for pregnancy (based on the relative risk) and would reduce the probability for a successful pregnancy after insemination, following Inchaisri et al. (2010) and Wicaksono et al. (2024). The relative risks are listed in Table 1. When a cow has more than one disorder, the highest impact of a single disorder on pregnancy is assumed (i.e., the lowest relative risk value was selected). The event of pregnancy (*preg*) affected by 1 or more reproductive disorders is modeled by a Bernoulli (*B*) distribution:

$$preg = B\ (1, B_{preg} \times R_{dis}),$$

where B*preg* is the base risk of a successful pregnancy after insemination and R*dis* is the relative risk value of a certain reproductive disorder (or the lowest relative risk value in case of multiple reproductive disorders).

Economic Calculations

Economic outputs were calculated based on the result of the biological output provided by the model simulation. The economic calculations included the revenues from milk and calves and the costs of production (i.e., costs for feed, inseminations, calving, and culling) and reproductive disorders (i.e., costs for drugs, farm labor, veterinarian). Costs of production were explained previously (Edwardes et al., 2022; Wicaksono et al., 2024). In brief, the milk revenues were calculated based on the daily milk production and were adjusted in case of pregnancy (Bohmanova et al., 2009; Lainé et al., 2017). Feed cost was calculated based on the daily feed requirements per cow and expressed in VEM. One VEM equals 1.65 kcal of NEL; VEM was modeled as a function of daily fat- and protein-corrected milk (**FPCM**) produced (Van Es, 1978), where FPCM equals (0.337 + 0.116 × fat percentage + 0.06 × protein percentage) × daily milk yield. Maintenance requirements (**MR**) are 42.4 VEM per $kg^{0.75}$ of BW + 442 (Van Es, 1978). Therefore, the daily feed requirements were calculated by MR × FPCM. Parity 1, 2, and ≥3 cows respectively had a fat content (%) of 4.48, 4.5, and 4.51, and a protein content (%) of 3.55, 3.59, and 3.51 (Kok et al., 2017). Higher feed requirements for parity 1 and 2 cows, and 4 pregnancy stages were included to account for different feed requirements during pregnancy (Remmelink et al., 2016). Culling costs were calculated using a depreciation method that discounts the future value of older cows. The calculation also accounted for the loss of potential future returns from the culled cow and incorporated the cost of mortality (Edwardes et al., 2022). Cost of AI was calculated based on conventional semen and calving costs were calculated by incorporating the rearing costs for a 2-wk period for the surviving calves and the carcass removal for the dead calves (Wicaksono et al., 2024). All used economically related input parameter values are described in Table 2. The explanation of the economic calculations hereafter focuses on the costs related to the treatment of specific reproductive disorders. With these veterinary costs, call-out fees were assigned to dystocia, retained placenta, acute metritis, and clinical endometritis, but not for ovarian disorders as those were diagnosed during routine fertility checks.

Dystocia. Cost of dystocia was estimated per affected cow including the veterinarian call-out fee (C_{call}), the hourly rate of the veterinarian ($C_{hour\text{-}vet}$), the time spent for calving assistance (T_{treat}), the cost of dystocia treatment tools (C_{treat}), the time the farmer was present during treatment (T_{pres}), and the farm labor hourly rate ($C_{hour\text{-}farmer}$). The cost of dystocia (C_{dyst}) treatment was calculated as follows:

$$C_{dyst} = [C_{call} + (T_{treat} \times C_{hour\text{-}vet})] + C_{treat} + (T_{pres} \times C_{hour\text{-}farmer}).$$

Retained Placenta. Cost of retained placenta was estimated per affected cow including the veterinarian call-out fee (C_{call}), the hourly rate of the veterinarian ($C_{hour\text{-}vet}$), the time of treatment (T_{treat}), the time spent fetching the cow by the farmer (T_{fetch}), the time the farmer was present during treatment (T_{pres}), and the farm labor hourly rate ($C_{hour\text{-}farmer}$). The cost of retained placenta (C_{ret}) treatment was calculated as follows:

$$C_{ret} = [C_{call} + (T_{treat} \times C_{hour\text{-}vet})] + [(T_{fetch} + T_{pres}) \times C_{hour\text{-}farmer}].$$

Acute Metritis. Cost of acute metritis was estimated per affected cow including the veterinarian call-out fee (C_{call}), the hourly rate of the veterinarian ($C_{hour\text{-}vet}$), the time of treatment (T_{treat}), the cost of oxytetracycline (C_{oxy}) and NSAID (C_{nsaid}), the time spent fetching the cow by the farmer (T_{fetch}), the time the farmer was present during treatment (T_{pres}), and the farm labor hourly rate ($C_{hour\text{-}farmer}$). The cost of acute metritis (C_{met}) treatment was calculated as follows:

$$C_{ret} = [C_{call} + (T_{treat} \times C_{hour\text{-}vet})] + (C_{oxy} + C_{nsaid}) + [(T_{fetch} + T_{pres}) \times C_{hour\text{-}farmer}].$$

Clinical Endometritis. Cost of clinical endometritis was estimated per affected cow including the veterinarian call-out fee (C_{call}), the hourly rate of the veterinarian ($C_{hour\text{-}vet}$), the time of treatment (T_{treat}), the cost of prostaglandin (C_{pg}) for a noncyclic cow with CL (pyometra) or the cost of cefapirine (C_{cefa}) for a noncyclic cow with no CL present, the time spent fetching the cow by the farmer (T_{fetch}), the time the farmer was present during treatment (T_{pres}), and the farm labor hourly rate ($C_{hour\text{-}farmer}$). The cost of clinical endometritis (C_{endo}) treatment was calculated as follows:

$$\text{IF } \textit{endo-CL};\ C_{endo} = [C_{call} + (T_{\text{treat}} \times C_{hour\text{-}vet})] + C_{pg} + [(T_{fetch} + T_{pres}) \times C_{hour\text{-}farmer}];$$

$$\text{IF } \textit{endo-nonCL};\ C_{endo} = [C_{call} + (T_{treat} \times C_{hour\text{-}vet})] + C_{cefa} + [(T_{fetch} + T_{pres}) \times C_{hour\text{-}farmer}].$$

Anovulation. Cost of clinical endometritis was estimated per affected cow including the time for the diagnosis during the fertility check performed by the veterinarian (T_{diag}), the hourly rate of the veterinarian ($C_{hour\text{-}vet}$), the costs of PRIDsynch protocol application (C_{prid}), the time of PRIDsynch protocol application ($T_{treat\text{-}prid}$), the time spent fetching the cow by the farmer (T_{fetch}), the time the farmer was present during fertility check (T_{pres}), and the farm labor hourly rate ($C_{hour\text{-}farmer}$). The cost of anovulation (C_{anov}) treatment was calculated as follows:

$$C_{anov} = (T_{diag} \times C_{hour\text{-}vet}) + C_{prid} + [(T_{fetch} + T_{pres} + T_{treat\text{-}prid}) \times C_{hour\text{-}farmer})].$$

Cystic Ovarian Disease. Cost of COD was estimated per affected cow including the time for the diagnosis during the fertility check performed by the veterinarian (T_{diag}), the hourly rate of the veterinarian ($C_{hour\text{-}vet}$), the time of a GnRH treatment by veterinarian ($T_{treat\text{-}gnrh}$), the costs of a GnRH application (C_{gnrh}), the time spent fetching the cow by the farmer (T_{fetch}), the time the farmer was present during the fertility check (T_{pres}), and the farm labor hourly rate ($C_{hour\text{-}farmer}$). The cost of COD (C_{cod}) treatment was calculated as follows:

$$C_{cod} = [(T_{diag} + T_{treat\text{-}gnrh}) \times C_{hour\text{-}vet}] + C_{gnrh} + [(T_{fetch} + T_{pres}) \times C_{hour\text{-}farmer}].$$

If the cow was still not detected in estrus after 120 DIM (*nodetect-120d*), additional costs were added, including the cost of an Ovsynch protocol application ($C_{ovsynch}$), the time of an Ovsynch protocol application ($T_{treat\text{-}ovsynch}$), the time spent fetching the cow by the farmer (T_{fetch}), and the farm labor hourly rate ($C_{hour\text{-}farmer}$). The cost of COD (C_{cod}) treatment was calculated as follows:

$$\text{IF } nodetect\text{-}120d;\ C_{cod} = (T_{diag} \times C_{hour\text{-}vet}) + C_{ovsynch} + [(T_{fetch} + T_{treat\text{-}ovsynch}) \times C_{hour\text{-}farmer})].$$

Sub-estrus. Cost of sub-estrus was estimated per affected cow including the time for the diagnosis during the fertility check performed by the veterinarian (T_{diag}), the hourly rate of the veterinarian ($C_{hour\text{-}vet}$), the time of treatment (T_{treat}), the cost of a prostaglandin application (C_{pg}), the time spent fetching the cow by the farmer (T_{fetch}), the time the farmer was present during fertility check (T_{pres}), and the farm labor hourly rate ($C_{hour\text{-}farmer}$). The cost of sub-estrus (C_{sub}) treatment was calculated as follows:

$$C_{sub} = [(T_{diag} + T_{treat}) \times C_{hour\text{-}vet}] + C_{pg} + [(T_{fetch} + T_{pres}) \times C_{hour\text{-}farmer}].$$

Net Economic Return. The economic outputs were calculated for all 200 cows in the herd through daily time steps over one year-time (365 d) and were summed to obtain an annual estimate of the net partial economic result. The annual net economic return (**NER**) was determined as follows:

$$NER_n = \sum_{i=1}^{200}\sum_{t=1}^{365} R_{i,t,n}^{(total)} - \sum_{i=t}^{200}\sum_{t=1}^{365} C_{i,t,n}^{(total)},$$

where NER_n is the annual net economic return for iteration *n* (a repetition during the simulation process), $R_{i,t,n}^{(total)}$ is the total annual revenues for cow *i* in time step *t* comprising milk yield revenues and calf revenues, and $C_{i,t,n}^{(total)}$ is the annual total costs comprising cost of feed, insemination, calving, culling, reproductive disorder treatment, veterinary services, and farm labor. The mean NER was obtained by considering the revenues on milk yield and calves sold and all the cost elements. Economic outputs were expressed by the mean and the 5th and 95th percentiles.

Model Simulation and Sensitivity Analysis

Model Scenarios. To calculate the cost of reproductive disorders, 9 scenarios were simulated and the NER of each scenario was estimated. The scenarios included a (1) default scenario in which the probabilities of all reproductive disorders were included in the simulation model. This scenario represents an average Dutch dairy farm with regular reproductive disorder prevention measures, resulting in overall average incidence rates. Then, to determine the net cost of each single reproductive disorder, the second to eighth scenarios included a zero probability for each specific disorder to occur, including (2) dystocia (**no-dyst** scenario), (3) retained placenta (**no-ret** scenario), (4) acute metritis (**no-met** scenario), (5) clinical endometritis (**no-endo** scenario), (6) anovulation (**no-anov** scenario), (7) COD (**no-cod** scenario), and (8) sub-estrus (**no-sub** scenario).

During the model runs, reproductive disorders were excluded one at a time while keeping the settings of the other disorders similar to the default scenario. In the ninth scenario, all disorders were absent (**no-dis** scenario). The NER of the scenarios with zero probability of disorder (or of all reproductive disorders combined; scenario 9) were compared with the NER of the default scenario, and the difference was considered the cost of each specific reproductive disorder (or of all reproductive disorders combined; scenario 9 in the herd).

To address the uncertainty of input parameters, several what-if scenarios were conducted. Uncertainty related to the incidence of disorders was evaluated. Subsequently, the conditional probabilities were adjusted, either for all reproductive disorders combined (scenario 1) or for each individual reproductive disorder (scenarios 2–8). These adjustments involved increasing or decreasing the probabilities by 20%. Additionally, uncertainty regarding the impact of disorders on pregnancy rates was evaluated, leading to the simulation of 2 alternative scenarios. In the default scenario, the highest impact of a single disorder on pregnancy was assumed (i.e., the lowest relative risk value was selected). The first alternative scenario assumed the lowest impact of a single disorder on pregnancy (i.e., the highest relative risk value was selected). The second alternative scenario assumed the accumulative impact of combined disorders on the pregnancy rate by multiplying the relative risks to obtain the final relative risk value. These 2 alternative models were performed on the default scenario only.

Model Calibration and Validation. Input parameter values were calibrated to ensure accuracy of model input, as input parameter values were obtained from a variety of scientific literature and expert opinion. Calibrated inputs were then internally and externally validated. Internal validation processes consisted of adjusting several input parameter values (e.g., setting disorder probability to 0 or 1), a tracing and tracking process on an individual cow's outputs during each time step, and testing the process with debugging modes on model simulation. External validation was conducted through several discussions with dairy reproduction experts and veterinary practitioners and by comparing model outputs to the scientific literature.

Model Convergence. Model convergence was evaluated by running the simulation model until the variance of the model outputs (i.e., incidence rates, estrus detection rate, number of cows culled, amount of milk produced) stabilized. The process showed that the simulation model converged at 500 iterations. Thus, 500 iterations were consequently run in each scenario. The distribution of cow parity was stabilized at the end of year 7, which ensured a 7-year burn-in period (Wicaksono et al., 2024). The model scenario was therefore implemented in year 8 and model output was consequently derived in year 9.

Sensitivity Analysis. A sensitivity analysis was performed for the default scenario to evaluate the sensitivity of input parameter values on the NER in the model simulation. The NER of each adjusted input parameter was compared with the NER of the default scenario. Adjusted input parameters included prices (milk, hormones, farm labor, and veterinary services) and the estrus detection rate, and only one input parameter was changed in this sensitivity analysis. Prices were adjusted by increasing and decreasing the value by 20%. The estrus detection rate was adjusted to 30% to represent a poor visual estrus detection rate by the farmer (Inchaisri et al., 2010), and to 80% to represent an estrus detection rate using sensors (Rutten et al., 2014).

RESULTS

Reproductive Performance and Disorder Incidence

The mean annual reproductive performance and disorder incidences are shown in Table 3. The mean annual calving interval was 414 d for the default scenario where all reproductive disorders were present, whereas the shortest calving interval was 410 d for the scenarios when metritis, clinical endometritis, COD, and sub-estrus were absent (no-met, no-endo, no-cod, and no-sub scenarios). The scenario with no reproductive disorders at all (no-dis scenario) resulted in an average calving interval of 397 d. Similar trends were observed for the calving to first AI interval and the calving to pregnancy interval. The numbers of hormone protocol applications and antibiotic treatments were on average 134 and 30 applications/herd per year for the default scenario, respectively. Concerning the scenarios where single disorders were absent, the lowest average number of hormone applications was observed when anovulation was absent (no-anov scenario; 96 applications/herd per year), whereas the lowest average number of antibiotic applications was observed when acute metritis was absent (no-met scenario; 15 applications/herd per year). Hormone protocols and antibiotic treatments for reproductive disorders were not applied when all disorders were absent (no-dis scenario). The default scenario resulted in an average of 123 calves born/herd per year and an average milk yield from lactating cows in herd of 8,490 kg/cow per year. When all reproductive disorders were absent (no-dis scenario), 135 calves/herd per year were born and the average milk yield was 8,551 kg/cow per year. When acute metritis was absent, the highest average number of calves born per year was observed (no-met scenario; 129 calves/herd per year), whereas when clinical endometritis was absent, the highest average milk yield was observed (no-endo scenario; 8,505 kg/cow per year).

The default scenario resulted in a mean annual incidence of 4.5% for dystocia, 5.3% for retained placenta, 11.4% for acute metritis, 19.5% for clinical endometritis, 15.2% for anovulation, 9.3% for COD, and 11.5% for sub-estrus. When individual reproductive disorders were absent, slight differences in the incidences were observed. The incidence of acute metritis decreased to 8.5% when retained placenta was absent (no-ret scenario). Cystic ovarian disease incidence decreased to 8.3% in the absence of acute metritis (no-met scenario). Sub-estrus incidence decreased to 7.7% and 9.7% when

Table 3. Average (and 5th and 95th percentiles) annual reproductive performance and disorder incidences for different reproductive disorder scenarios in a 200-cow dairy herd

		Reproductive disorder scenario							
Parameter	Default[1]	no-dyst[2]	no-ret[3]	no-met[4]	no-endo[5]	no-anov[6]	no-cod[7]	no-sub[8]	no-dis[9]
Reproductive performance									
Calving interval (d)	414 (350; 511)	413 (350; 510)	413 (350; 510)	410 (350; 506)	410 (350; 507)	411 (350; 504)	410 (350; 508)	410 (350; 550)	397 (349; 483)
Calving to first AI (d)	97 (68; 145)	97 (68; 145)	97 (68; 145)	95 (68; 143)	95 (68; 142)	98 (68; 148)	95 (68; 141)	95 (68; 140)	90 (68; 134)
Calving to pregnancy (d)	158 (99; 253)	157 (99; 253)	158 (99; 153)	156 (99; 251)	156 (99; 250)	156 (99; 248)	155 (99; 251)	155 (99; 248)	147 (99; 232)
Number of AI to pregnancy	1.9 (1.0; 5.0)	1.9 (1.0; 5.0)	1.9 (1.0; 5.0)	1.9 (1.0; 5.0)	1.9 (1.0; 4.0)	1.9 (1.0; 4.0)	1.9 (1.0; 5.0)	1.9 (1.0; 5.0)	1.8 (1.0; 4.0)
Number of culled cows	72 (61; 83)	71 (61; 83)	71 (60; 83)	68 (58; 81)	71 (60; 83)	71 (59; 83)	72 (61; 84)	72 (61; 84)	66 (55; 78)
Number of hormone protocol applications	134 (105; 166)	134 (101; 169)	139 (107; 174)	117 (87; 150)	125 (93; 157)	96 (69; 126)	98 (72; 125)	98 (75; 134)	0.0 (0.0; 0.0)
Number of antibiotic applications	30 (22; 38)	30 (22; 38)	26 (18; 34)	15 (9; 21)	16 (9; 23)	30 (22; 39)	30 (21; 38)	30 (21; 38)	0.0 (0.0; 0.0)
Total number of calves born	123 (113; 134)	124 (113; 134)	125 (113; 136)	129 (118; 140)	125 (113; 135)	125 (113; 137)	124 (113; 135)	124 (113; 135)	135 (125; 146)
Net milk yield (kg)	1,698,036 (1,666,993; 1,727,005)	1,696,697 (1,666,588; 1,724,384)	1,699,035 (1,668,261; 1,728,304)	1,700,955 (1,671,918; 1,728,766)	1,701,024 (1,670,494; 1,728,426)	1,700,431 (1,671,878; 1,728,723)	1,700,059 (1,672,017; 1,728,982)	1,700,059 (1,672,431; 1,729,307)	1,710,199 (1,681,998; 1,736,775)
Disorder incidence (%)									
Dystocia	4.5 (1.8; 7.5)	0.0 (0.0; 0.0)	4.5 (1.8; 7.3)	4.5 (1.7; 7.8)	4.5 (1.7; 7.4)	4.6 (1.8; 7.3)	4.4 (1.7; 6.6)	4.5 (1.7; 7.4)	0.0 (0.0; 0.0)
Retained placenta	5.3 (2.7; 8.2)	4.9 (1.8; 7.4)	0.0 (0.0; 0.0)	5.5 (2.5; 8.6)	5.5 (2.7; 8.1)	5.6 (2.7; 8.7)	5.4 (2.6; 8.1)	5.4 (2.6; 8.1)	0.0 (0.0; 0.0)
Acute metritis	11.4 (6.2; 16.4)	11,3 (6.3; 16.4)	8.5 (4.4; 13.2)	0.0 (0.0; 0.0)	11.4 (6.2; 17.3)	11.5 (7.0; 16.7)	11.5 (6.2; 17.7)	11.4 (6.2; 17.0)	0.0 (0.0; 0.0)
Clinical endometritis	19.5 (15.0; 23.1)	19.3 (14.3; 23.1)	19.1 (14.1; 23.5)	19.6 (15.2; 24.2)	0.0 (0.0; 0.0)	19.0 (15.0; 23.3)	19.1 (15.0; 23.7)	18.8 (14.1; 22.2)	0.0 (0.0; 0.0)
Anovulation	15.2 (10.8; 19.8)	14.9 (9.9; 19.1)	15.9 (10.9; 20.7)	14.7 (9.4; 19.1)	15.4 (10.8; 20.1)	0.0 (0.0; 0.0)	15.4 (10.8; 19.9)	15.6 (11.7; 20.7)	0.0 (0.0; 0.0)
Cystic ovarian disease	9.3 (6.3; 14.3)	9.3 (4.8; 13.5)	9.5 (4.8; 12.7)	8.3 (4.7; 13.2)	8.9 (5.4; 13.6)	11.7 (6.8; 16.2)	0.0 (0.0; 0.0)	9.2 (5.4; 14.5)	0.0 (0.0; 0.0)
Sub-estrus	11.5 (6.7; 15.7)	12.1 (6.7; 15.9)	12.0 (7.8; 16.4)	7.7 (3.7; 10.5)	9.7 (4.5; 13.5)	12.0 (6.7; 16.5)	11.9 (7.1; 16.1)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)

[1]All reproductive disorders were included.
[2]Dystocia was not included.
[3]Retained placenta was not included.
[4]Acute metritis was not included.
[5]Clinical endometritis was not included.
[6]Anovulation was not included.
[7]Cystic ovarian disease was not included.
[8]Sub-estrus was not included.
[9]All reproductive disorders were not included.

Table 4. Average (and 5th and 95th percentiles) annual economic (€) simulation results for different reproductive disorder scenarios in a 200-cow dairy herd

Parameter	Default[1]	Reproductive disorder scenario							
		no-dyst[2]	no-ret[3]	no-met[4]	no-endo[5]	no-anov[6]	no-cod[7]	no-sub[8]	no-dis[9]
Revenue									
Milk revenues	781,096 (766,816; 794,422)	780,480 (766,630; 793,216)	781,556 (767,400; 795,019)	782,439 (769,082; 795,232)	782,471 (768,427; 795,076)	782,198 (781,871; 795,212)	782,027 (769,128; 795,331)	782,465 (769,318; 795,481)	786,691 (773,719; 798,916)
Calf revenues	7,535 (6,825; 8,255)	7,529 (6,756; 8,320)	7,624 (6,890; 8,385)	7,828 (7,085; 8,645)	7,601 (6,890; 8,320)	7,605 (6,890; 8,385)	7,552 (6,825; 8320)	7,541 (6,760; 8,320)	8,226 (7,540; 8,970)
Cost									
Feed cost	245,966 (244,645; 247,248)	245,913 (244,646; 247,227)	246,055 (244,728; 247,338)	246,277 (245,091; 247,537)	246,137 (244,692; 247,458)	246,092 (244,756; 247,447)	246,051 (244,637; 247,450)	246,091 (244,741; 247,337)	246,894 (245,521; 248,171)
Calving cost	18,100 (16,462; 19,752)	18,078 (16,320; 19,833)	18,282 (16,614; 20,112)	18,820 (17,125; 20,614)	18,236 (16,521; 19,968)	18,249 (16,556; 20,081)	18,113 (16,396; 19,815)	18,103 (16,346; 19,727)	19,756 (18,135; 21,549)
Culling cost	45,648 (37,600; 53,722)	45,760 (38,119; 53,466)	44,584 (36,996; 53,225)	41,711 (33,587; 49,493)	45,125 (37,103; 53,715)	44,776 (36,583; 53,538)	46,154 (38,420; 54,247)	45,872 (37,664; 54,508)	38,968 (30,951; 46,977)
Hormone cost	2,871 (2,014; 3,813)	2,844 (2,020; 3,687)	3,009 (2,150; 3,979)	2,553 (1,792; 3,437)	2,774 (1,979; 3,771)	791 (546; 1,067)	2,555 (1,675; 3,408)	2,684 (1,854; 3,676)	0.0 (0.0; 0.0)
Antibiotic cost	374 (279; 476)	375 (269; 487)	323 (220; 419)	190 (112; 263)	195 (108; 276)	381 (269; 501)	378 (268; 490)	375 (268; 489)	0.0 (0.0; 0.0)
Farmer labor cost	2,621 (2,369; 2,887)	2,446 (2,226; 2,679)	2,568 (2,330; 2,825)	2,414 (2,173; 2,663)	2,477 (2,222; 2,735)	2,317 (2,105; 2,528)	2,468 (2,237; 2,713)	2,505 (2,253; 2,758)	1,471 (1,345; 1,598)
Veterinary service cost	9,871 (8,741; 11,066)	8,589 (7,731; 9,380)	9,794 (8,636; 11,104)	9,079 (8,028, 10,408)	8,785 (7,624; 9,958)	9,680 (8,487; 11,016)	9,577 (8,431; 10,852)	8,840 (7,702; 10,062)	4,978 (4,790; 5;143)
Total cost	333,475 (327,006; 340,129)	331,992 (325,412; 339,453)	332,680 (325,821; 340,211)	329,202 (322,256; 336,390)	331,582 (324,474; 338,311)	330,001 (322,736; 337,529)	333,330 (326,295; 340,933)	332,499 (325,291; 340,307)	319,757 (312,855; 327,100)
Net economic returns (NER)	455,146 (441,441; 467,433)	456,043 (442,427; 469,243)	456,499 (444,375; 470,170)	461,054 (448,122; 473,830)	458,511 (443,447; 472,072)	459,465 (446,268; 472,281)	456,250 (442,543; 468,846)	457,531 (444,347; 471,693)	475,159 (460,837; 488,672)
Cost of disorder per herd (Δ NER)		897	1,353	5,908	3,365	4,319	1,104	2,385	20,013
Cost of disorder per cow[10]		4	7	30	17	22	6	12	100
Cost of disorder per case[11]		100	123	257	146	144	58	104	

[1]All reproductive disorders were included.
[2]Dystocia was not included.
[3]Retained placenta was not included.
[4]Acute metritis was not included.
[5]Clinical endometritis was not included.
[6]Anovulation was not included.
[7]Cystic ovarian disease was not included.
[8]Sub-estrus was not included.
[9]All reproductive disorders were not included.
[10]The cost of disorder per herd was divided by the 200 cows in the simulated herd.
[11]The cost of disorder per herd was divided by the number of cows experiencing disorder (disorder incidence multiplied by 200 cows).

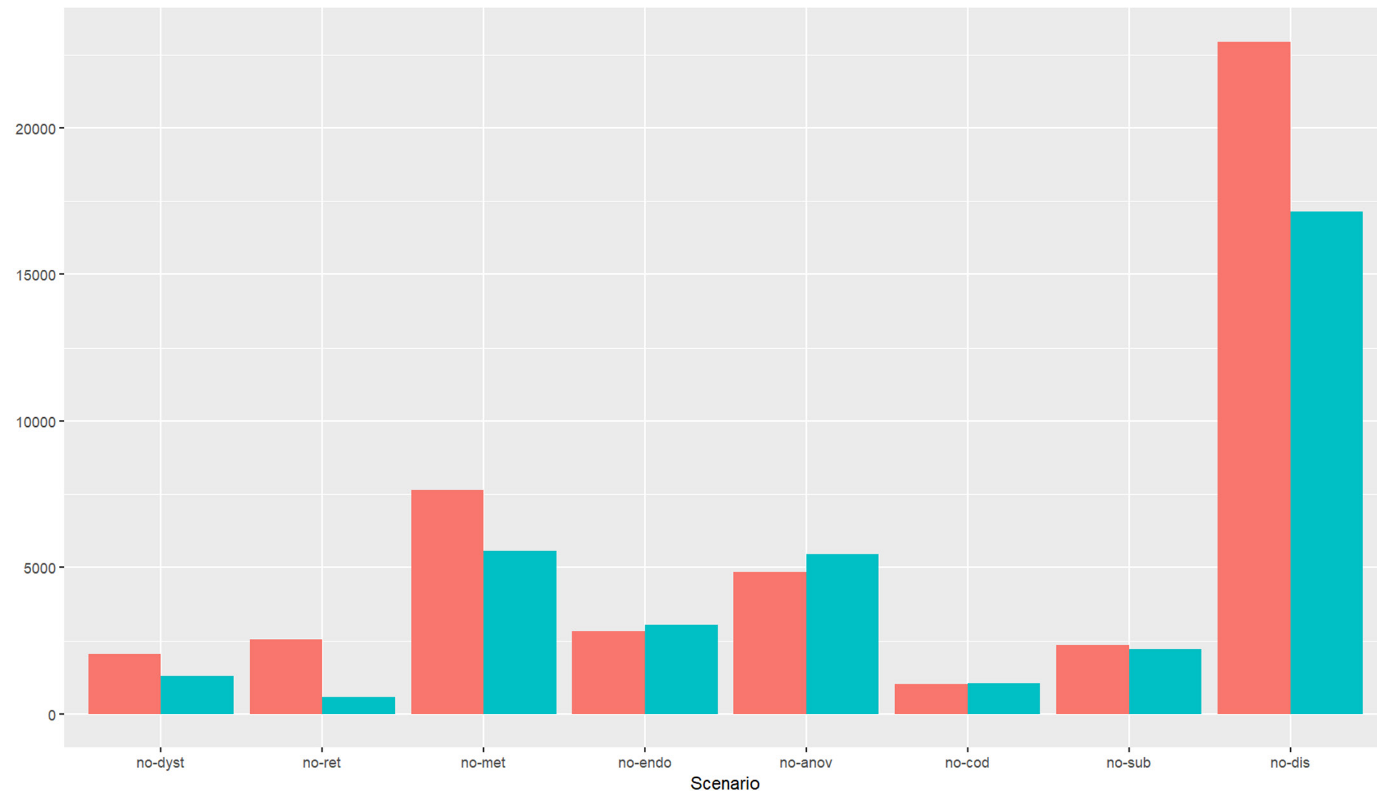

Figure 2. Cost of 7 reproductive disorders and their combined effect when disorder incidence rates were increased (red) and decreased (blue) by 20% for scenarios where one or all disorders were absent from the model. no-dyst = dystocia was absent; no-ret = retained placenta was absent; no-met = acute metritis was absent; no-endo = clinical endometritis was absent; no-anov = anovulation was absent; no-cod = cystic ovarian disease was absent; no-sub = sub-estrus was absent; no-dis = all disorders were absent.

acute metritis and clinical endometritis were absent (no-met and no-endo scenarios).

Economic Effect and Cost of Reproductive Disorders

Table 4 presents the mean total annual economic effects of different reproductive disorder scenarios. The default scenario resulted in €781,096/herd per year and €7,535/herd per year for the milk and calf revenues, respectively. Among the scenarios where individual disorders were absent, slight differences of the mean total revenues were observed. For instance, higher milk revenue of €1,375/herd per year was observed when clinical endometritis was absent (no-endo scenario). Slight differences in the mean total costs were observed among the scenarios when individual disorders were absent. The default scenario resulted in the highest mean total costs of €333,475/herd per year, whereas the scenario when all disorders were absent resulted in the lowest mean total costs, which was €13,718/herd per year lower than the default scenario.

The highest mean annual NER among the scenarios when individual disorders were absent was observed when acute metritis was absent (€461,054/herd per year). The default scenario gave the lowest NER of €455,146/herd per year, whereas the highest NER of €475,159/herd per year was observed when all disorders were absent (no-dis scenario). The mean annual cost of all disorders combined was €20,013/herd per year, or €100/cow per year. At herd level, the highest mean annual cost was observed for acute metritis (€5,908/herd per year or €30/cow per year), whereas the lowest mean annual cost was observed for dystocia (€897/herd per year or €4/cow per year). In the context of cost per case, the highest cost was observed for acute metritis (€257/case), whereas the lowest cost was observed for COD (€58/case).

What-If Scenarios and Sensitivity Analysis

The results of the what-if scenarios related to the incidence of disorders are shown in Figure 2. Among individual disorders, the highest mean annual cost was observed for acute metritis when disorder incidence was increased by 20% (€7,643/herd per year), whereas the lowest mean annual costs were observed for retained placenta when disorder incidences were decreased by

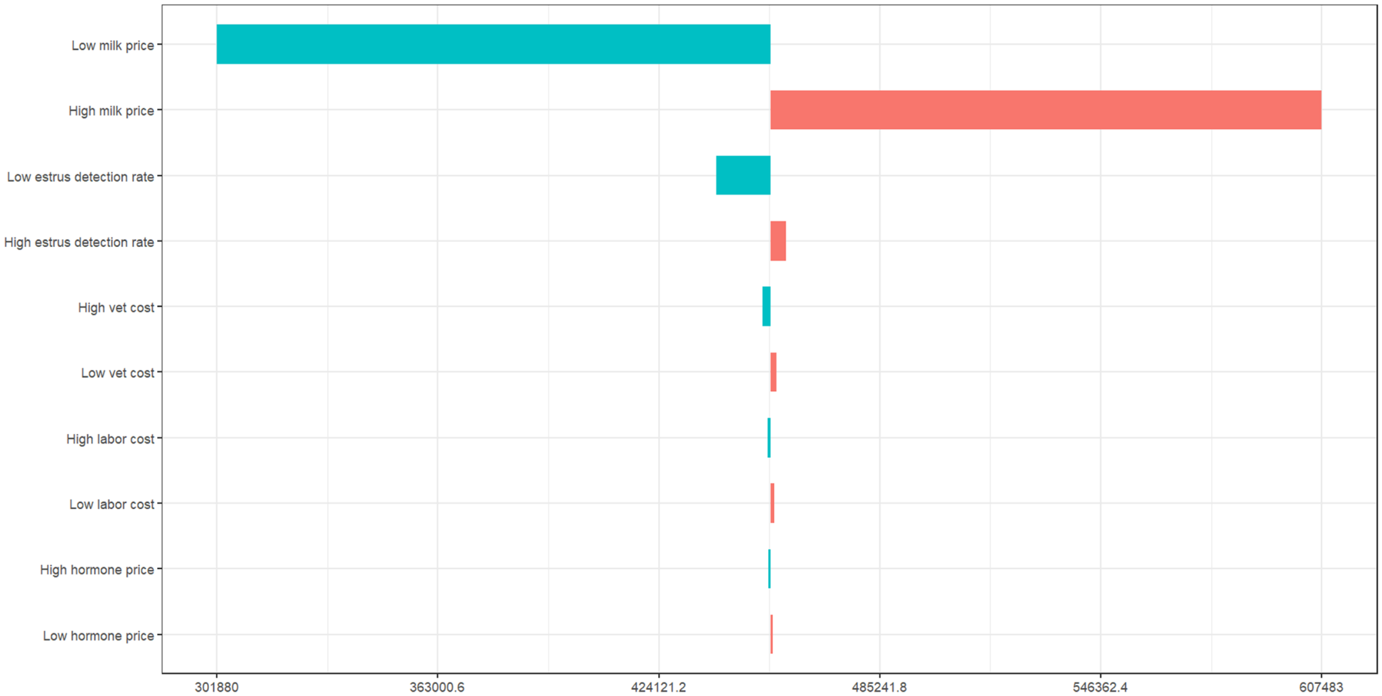

Figure 3. Sensitivity of the net economic return (NER; €) for different input parameter values in an alternative scenario compared with the NER of the default scenario. vet = veterinary.

20% (€570/herd per year). With 20% decreased disorder incidences, the lowest mean annual cost changed from dystocia in the default scenario (Table 4) to retained placenta. Most of the reproductive disorder costs were higher when disorder incidences were increased by 20% compared with when they were decreased by 20%, except for clinical endometritis, anovulation, and COD. The mean annual cost for all disorders was €22,940/herd per year when disorder incidences were increased by 20% and was €17,151/herd per year when disorder incidences were decreased by 20%.

The NER of the 2 alternative scenarios of the impact of disorders on pregnancy rates were slightly different from the default scenario. When the lowest impact of a single disorder on pregnancy rate was assumed (i.e., the highest relative risk value was selected), the NER was €110/herd per year higher compared with the default scenario. Meanwhile, when the accumulative impact of combined disorders to the pregnancy rate was assumed (i.e., multiplication of the relative risks), a €471/herd per year lower NER was observed.

The sensitivity analysis showed that the NER result of the default scenario was very sensitive to milk price changes (Figure 3). Increasing the milk price by 20% gave a €152,337/herd per year higher NER, whereas decreasing the milk price by 20% gave a €153,266/herd per year lower NER. The second most influential parameter was the estrus detection rate, with a €15,198/herd per year lower NER for a 30% estrus detection rate and a €4,157/herd per year higher NER for an 80% estrus detection rate, compared with the default scenario. The model was less sensitive to changes in veterinary costs, farm labor costs, and hormone prices (Figure 3).

DISCUSSION

To the best of our knowledge, this study presents a novel, bio-economic simulation model that incorporates the interrelations between the 7 most common reproductive disorders in dairy cows. The model includes conditional probabilities of each disorder occurring in relation to others, and highlights the complexity involved in simulating these interrelationships. The approach taken enables a precise evaluation of the economic impact of reproductive disorders. The simulation model performed logically, as the absence of one reproductive disorder resulted in a reduced incidence of subsequent disorders (Table 3). In addition, the technical output of the default scenario was comparable to Dutch averages. For example, the simulated average calving interval was 414 d, closely aligning with the Dutch national average of 408 d (CRV, 2023).

This study showed that the mean annual economic impact due to all 7 reproductive disorders was, on average, €100/cow per year. This economic impact was mostly influenced by the costs of culling, veterinary services and treatments, and milk yield losses. The cost for feed, calving, and farm labor did not influence much. The economic impact was comparable with another existing study, in which the economic losses from all reproduction-related disorders was $114/cow per year (Rasmussen et al., 2024). That study, however, estimated global losses associated with 12 common dairy cow diseases, and incorporated adjustments for comorbidities between diseases by using estimated odds ratios. Distinctly, we calculated the costs of 7 specified dairy cow reproductive disorders by identifying all possible pathways for disorder development and then integrating the probabilities associated with each pathway (Figure 1). The economic impact observed from the current study also corroborated by another existing Dutch simulation study, which stated that the economic losses of poor fertility, in general, were between €34 and €231/cow per year (Inchaisri et al., 2010). The result from the current study fell within this previously estimated range. Unlike the earlier study, however, the current study used more recent Dutch data, including updated prices for milk, feed, and heifers (Kulkarni et al., 2024). The variation between the 5th and 95th percentiles for the average annual economic impact in this simulation model was found to be relatively small. This is likely due to the large dairy herd size simulated, which comprised 200 cows. The small variation in output indicated that the model is stable and produces consistent results under similar input conditions.

Among individual disorders at the herd level, acute metritis had the highest economic impact of €5,908/herd per year, or approximately €30/cow per year. In the absence of acute metritis, treatment costs (i.e., costs for hormones, antibiotic and veterinary service) and culling costs decreased while milk revenues increased. These results were in agreement with another recent study, in which metritis gave the highest annual economic impact ($43/cow per year) among observed reproductive disorders (Rasmussen et al., 2024). Similarly, the economic impact of acute metritis was strongly influenced by the costs of treatment and culling in the study of Pérez-Báez et al. (2021). In that study, a metritis case cost on average $511 (median was $398) with a range from $240 to $884/case (Pérez-Báez et al., 2021). The considerable economic impact of acute metritis generates a need to prevent its occurrence on dairy farms. The prevention of acute metritis involves preventing pathogenic bacterial infection of the genital tract by avoiding trauma and ensuring a clean and gentle intervention during parturition (Galvão, 2012; Sheldon et al., 2020). To achieve this, dairy farmers should prioritize the cleanliness of calving areas and calving assistance to reduce the risk of genital tract infections during calving. Besides, other prevention strategies could be implemented such as maximizing DMI at prepartum period, preventing metabolic disorders like hypocalcemia and hyperketonemia, and preventing mineral and vitamin deficiencies (Galvão, 2013; Sheldon et al., 2020).

Dystocia gave the lowest economic impact among individual disorders at herd level with approximately €4/cow per year. This result was in the same range as the estimated costs for dystocia of €3.6/cow per year (Rasmussen et al., 2024) and $10/cow per year (Dematawena and Berger, 1997) in other studies. From this result, dystocia is not a reproductive disorder with high economic impact for dairy farmers. As well as the evidence that dystocia has the lowest economic impact at herd level, its incidence is also relatively low. This is likely due to genetic selection of sires and heifers (Lopez-Villalobos et al., 2020). The lowest economic impact per case was observed for COD (€58/case), while its incidence is relatively high, making its cumulative economic impact at the herd level an important consideration for dairy farmers. Directly preventing COD can be challenging, as it is a difficult reproductive disorder to control; its occurrence is associated with increasing parity (Kim et al., 2005; Nelson et al., 2010) and the presence of a negative energy balance in the postpartum period (Vanholder et al., 2006; Peter et al., 2009). The incidence of COD could be minimized by preventing diseases that are related to the occurrence of COD, such as acute metritis (Peter, 2004; Opsomer and De Kruif, 2009) and clinical mastitis (Cattaneo et al., 2014).

From the sensitivity analysis, it was obvious that the annual NER in the default scenario was sensitive to the milk price and the estrus detection rate. As discussed in other economic simulation studies in dairy cows, milk price influences economic outputs (e.g., Han et al., 2024; Kulkarni et al., 2024) as milk revenue is heavily dependent on milk yield and milk price. A low estrus detection rate also results in a smaller net economic output, as shown by other dairy cow simulation studies (e.g., Giordano et al., 2012; Rutten et al., 2014; Ferchiou et al., 2021). Consequently, dairy farmers may consider increasing estrus detection rates to increase their NER. One strategy to achieve this is by enhancing estrus detection through the use of sensors (Crowe et al., 2018).

To simulate the interrelations between reproductive disorders, it is crucial to have accurate input parameters regarding the probabilities and incidences of these disorders. To the best of our knowledge, no studies have determined the probabilities of the combined reproductive disorders in one study. Furthermore, available information on the incidence of reproductive disorders in Dutch dairy farms is scarce and outdated. These findings highlight the need for future epidemiological studies on reproductive disorders within this context. However, observational studies to collect herd-level data on reproductive disease incidence would be resource-intensive and costly. In the context of Dutch dairy farms, alternative strategies could be considered. First, disease recordings from veterinarians during routine veterinary checks, could be used. This recording system provides records of each diagnosed case of dairy cow diseases, including reproductive disorders. Second, data can be collected through sensors for estrus detection that can indicate the number of cows not detected in estrus, potentially identifying cases of ovarian disorders. Subsequently, it is important to note that the underlying cause of cows with an undetected estrus would still need to be followed by a veterinary diagnosis.

To address uncertainties in this simulation study, input parameters for reproductive disorder incidences and probabilities were gathered using expert opinion. This can substantially enhance the quality and relevance of the study, particularly in situations where empirical data are limited or absent (Burgman et al., 2011; Drescher and Edwards, 2019). Expert opinion has been similarly used in bio-economic simulation studies to fill gaps in available data, though further calibration of input parameters is often necessary to improve accuracy (e.g., Ferchiou et al., 2021; Edwardes et al., 2022). However, using expert opinion also has limitations, particularly due to psychological biases and the inherent subjectivity involved (Burgman et al., 2011; Martin et al., 2012). Despite these challenges, this approach proved valuable in parameterizing disorder incidences for our simulation study. The experts consulted were dairy reproduction researchers from the North-West European region, who provided insights in current Dutch dairy farm conditions.

This study has limitations as it focuses primarily on common reproductive disorders that occur peripartum until the start of a new pregnancy. Other reproductive disorders, such as stillbirth and twinning, which are related to an increased risk for dystocia, retained placenta, and metritis (Opsomer and De Kruif, 2009; Mahnani et al., 2018), were not taken into account. Incorporating other disorders in the model could introduce more complex interrelations and pose even more challenges in parameterizing the interrelated conditional probabilities. The assumption of using the highest impact of a single disorder on pregnancy may have resulted in a slight underestimation of the disorder's cost because only the lowest relative risk value from one disorder was considered in its effect on pregnancy. It must be noted, however, that using alternative assumptions resulted in only slight differences in comparison with the default scenario.

This study estimated a considerable impact of reproductive disorders on costs for a farmer; thereby, prevention to avoid economic loss is required. Dairy farmers have several preventive options available. In typical Dutch dairy farm management, veterinary herd health programs are offered, including fertility checks for dairy cows. However, not all Dutch dairy farmers participate in these programs, often due to concerns about cost and time commitment (Derks et al., 2012). Increasing participation in veterinary herd health programs, with more frequent veterinary visits, could allow for early detection of disorders. A prompt diagnosis would enable immediate treatment to quickly resolve the reproductive disorders and avoid further economic losses. Another preventive measure is to improve cow nutrition management, particularly by ensuring adequate DMI during early lactation. This application helps to prevent a severe negative energy balance, which is associated with ovarian disorders (van Knegsel, 2007; Moore and DeVries, 2020), and prevent ketosis, which is associated with uterine diseases (Galvão, 2013). Additionally, maintaining hygienic conditions in the calving area and during calving assistance, and reducing stress levels are effective strategies for preventing uterine diseases in dairy cows (Sheldon et al., 2020).

This study simulated the production system of a dairy farm under Dutch conditions, where thresholds for management decisions regarding the discontinuation of breeding and culling may be substantially different compared with other systems, such as those in the United States, Canada, Mexico, and other countries with a more intensive dairy herd management. As a result, the application of reproductive disorder prevention strategies may differ across dairy systems that operate with a higher intensity and higher milk production.

Given the use of reproductive hormones in Dutch dairy farming (van der Laan et al., 2021; Wicaksono et al., 2023), implementing systematic hormone-based reproductive programs presents a viable option. In dairy farms with a year-round calving pattern, more systematic use of hormones could be applied to individual cows with a particular DIM for a timed AI (Wicaksono et al., 2024).

CONCLUSIONS

This simulation study provides insight into the complex interrelations between dairy cow reproduction disorders, and subsequently estimates the economic losses of each individual reproduction disorder, as well as the disorders in combination. The study has shown that taking all reproductive disorders into account resulted in a mean annual cost of €100/cow per year. This economic impact was mostly attributable to milk production losses, culling, veterinary services, and treatments, whereas feed, calving, and farm labor were less impactful. At herd level, the highest mean annual cost was observed for acute metritis (€30/cow per year), whereas the lowest mean annual cost was observed for dystocia (€4/cow per year). Given the interrelationships among reproductive disorders, preventing one disorder reduces the occurrence of others, thereby lowering their overall economic impact and improving both the health status and economic situation of the farm.

NOTES

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Nonstandard abbreviations used: AI = artificial insemination; CL = corpus luteum; COD = cystic ovarian disease; FPCM = fat- and protein-corrected milk; MR = maintenance requirements; NER = net economic return; no-anov = anovulation was absent; no-cod = cystic ovarian disease was absent; no-dis = all disorders were absent; no-dyst = dystocia was absent; no-endo = clinical endometritis was absent; no-met = acute metritis was absent; no-ret = retained placenta was absent; no-sub = sub-estrus was absent; NSAID = nonsteroidal anti-inflammatory drug; PRID = progesterone-releasing intravaginal device; PRID Delta = progesterone; FTAI = fixed timed artificial insemination; RP = retained placenta; VWP = voluntary waiting period.

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APPENDIX

Table A1. Input parameter values on cow production used in the bio-economic simulation model

Parameter	Description	Value	Source
Parity distribution	Probability of a cow being in parity 1 to ≥5	0.29, 0.25, 0.19, 0.13, 0.15	CRV, 2023
Maximum parity	Assumed maximum reachable parity	10	Authors' expertise
Dry period length	Prepartum dry period length (d)	56	Inchaisri et al., 2010
Voluntary waiting period	Voluntary waiting period for first insemination after calving (d)	65	Authors' expertise
Daily weight gain	Average daily weight gain (kg/d) until the end of second lactation	0.13	Kok et al., 2017
Daily milk production	Factors responsible for shape of Wilmink lactation curve[1]		Kok et al., 2017
α			
Parity 1		31.6	
Parity 2		40.6	
Parity 3		44.1	
b			
Parity 1		−0.0447	
Parity 2		−0.0708	
Parity 3		−0.0835	
c		−16.1	
k		0.06	
Daily energy requirement (VEM[2])			
Growth	Daily growth energy requirements in parity 1 and 2	660, 330	Van Es, 1978
Prepartum	Daily energy requirements during stage of pregnancy from 4 mo to last month before calving	450, 850, 1,500, 2,700	Remmelink et al., 2016
Milk loss	Milk loss due to pregnancy	$\sum_{i=30}^{n=240} - 0.06 \cdot e^{0.135 \cdot \left(\frac{i}{7}\right)}$	Bohmanova et al., 2009; Lainé et al., 2017; Wicaksono et al., 2024
Culling			
General culling	Probability is distributed over each daily time step		Calibrated input to get an overall annual culling rate of 30% (Mohd Nor et al., 2014)
	Parity 1	2.74e−5	
	Parity 2	2.74e−5	
	Parity 3	8.22e−5	
	Parity 4	1.10e−3	
	Parity ≥5	2.74e−3	
Mortality	Probability of mortality of all culled cows due to general culling	0.067	Rutten et al., 2014
Infertility culling	Decision to stop inseminating a cow:		
	Maximum number of inseminations	6	Authors' expertise
	Maximum number of inseminations after pregnancy loss	3	
	Milk yield threshold (kg)	<20	
	Daily milk yield threshold (kg) to cull cows	15	Edwardes et al., 2022

[1]*α*, *b*, *c*, and *k* are factors responsible for the shape of the curve to obtain the expected daily milk yield for a cow in a particular parity (Wilmink, 1987; Edwardes et al., 2022).

[2]The feed requirements are estimated as energy requirements in feed units for lactation (VEM; Van Es, 1978).

Table A2. Forty-nine possible reproductive disorder statuses included in the bio-economic simulation model[1]

					Not estrus					
Reproductive status	Dyst	RP	Metr	Endo	Endo noncyclic and CL	Endo noncyclic and non-CL	Anov	COD	Sub	Estrus
1	+	+	+	+	+	−	−	−	−	−
2	+	+	+	+	−	+	−	−	−	−
3	+	+	+	+	−	−	−	−	−	+
4	+	+	+	−	−	−	+	−	−	−
5	+	+	+	−	−	−	−	+	−	−
6	+	+	+	−	−	−	−	−	−	+
7	+	+	−	+	+	−	−	−	−	−
8	+	+	−	+	−	+	−	−	−	−
9	+	+	−	+	−	−	−	−	−	+
10	+	+	−	−	−	−	+	−	−	−
11	+	+	−	−	−	−	−	+	−	−
12	+	+	−	−	−	−	−	−	−	+
13	+	−	+	+	+	−	−	−	−	−
14	+	−	+	+	−	+	−	−	−	−
15	+	−	+	+	−	−	−	−	−	+
16	+	−	+	−	−	−	+	−	−	−
17	+	−	+	−	−	−	−	+	−	−
18	+	−	+	−	−	−	−	−	−	+
19	+	−	−	+	+	−	−	−	−	−
20	+	−	−	+	−	+	−	−	−	−
21	+	−	−	+	−	−	−	−	−	+
22	+	−	−	−	−	−	+	−	−	−
23	+	−	−	−	−	−	−	+	−	−
24	+	−	−	−	−	−	−	−	−	+
25	−	+	+	+	+	−	−	−	−	−
26	−	+	+	+	−	+	−	−	−	−
27	−	+	+	+	−	−	−	−	−	+
28	−	+	+	−	−	−	+	−	−	−
29	−	+	+	−	−	−	−	+	−	−
30	−	+	+	−	−	−	−	−	−	+
31	−	+	−	+	+	−	−	−	−	−
32	−	+	−	+	−	+	−	−	−	−
33	−	+	−	+	−	−	−	−	−	+
34	−	+	−	−	−	−	+	−	−	−
35	−	+	−	−	−	−	−	+	−	−
36	−	+	−	−	−	−	−	−	−	+
37	−	−	+	+	+	−	−	−	−	−
38	−	−	+	+	−	+	−	−	−	−
39	−	−	+	+	−	−	−	−	−	+
40	−	−	+	−	−	−	+	−	−	−
41	−	−	+	−	−	−	−	+	−	−
42	−	−	+	−	−	−	−	−	−	+
43	−	−	−	+	+	−	−	−	−	−
44	−	−	−	+	−	+	−	−	−	−
45	−	−	−	+	−	−	−	−	−	+
46	−	−	−	−	−	−	+	−	−	−
47	−	−	−	−	−	−	−	+	−	−
48	−	−	−	−	−	−	−	−	+	−
49	−	−	−	−	−	−	−	−	−	+

[1]Dyst = dystocia; RP = retained placenta; Metr = acute metritis; Endo = clinical endometritis; CL = corpus luteum; Anov = anovulation; COD = cystic ovarian disease; Sub = sub-estrus.

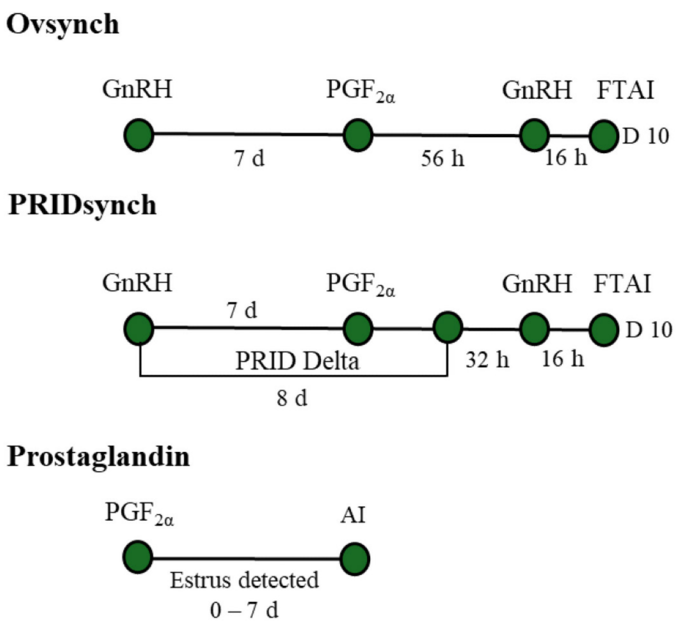

Figure A1. Schematic description of each hormone protocol. PRID Delta = progesterone; FTAI = fixed timed artificial insemination.

Table A3. Disorder incidences and the conditional probabilities of a cow obtaining reproductive disorders status in the bio-economic simulation model

Parameter	Description	Value	Source
Dystocia probability	Incidence rate of dystocia	0.04	Mee et al., 2011; de Amicis et al., 2012; expert opinion
Retained placenta (RP) probability	Incidence rate of RP	0.05	Sheldon et al., 2008; authors' expertise; calibrated input
From (+) dystocia	Probability of a cow obtaining RP after having dystocia	0.15	
From (−) dystocia	Probability of a cow obtaining RP after not having dystocia	0.05	
Acute metritis probability	Incidence rate of acute metritis	0.1	Opsomer and De Kruif, 2009; Sheldon et al., 2020; expert opinion
From (+) RP	Probability of a cow obtaining acute metritis after having RP	0.35	Authors' expertise; calibrated input
From (−) RP	Probability of a cow obtaining acute metritis after not having RP	0.1	
Clinical endometritis probability	Incidence rate of clinical endometritis	0.2	Opsomer and De Kruif, 2009; Sheldon et al., 2020; expert opinion
From (+) acute metritis	Probability of a cow obtaining clinical endometritis after having acute metritis	0.6	Authors' expertise; calibrated input
From (−) acute metritis	Probability of a cow obtaining clinical endometritis after not having acute metritis	0.2	
Distributed probability	Distributed probability of 3 types of clinical endometritis		Expert opinion
	Noncyclic with corpus luteum (pyometra)	0.05	
	Noncyclic with no corpus luteum	0.55	
	Cyclic	0.4	
Ovarian disorder probability	Incidence rate of		
	Anovulation	0.15	Peter et al., 2009; expert opinion
	Cystic ovarian disease	0.1	Peter et al., 2009; Gernand et al., 2012; expert opinion
	Sub-estrus	0.1	Gernand et al., 2012; expert opinion