J. Dairy Sci. 107:11016–11035
https://doi.org/10.3168/jds.2023-24109

The economic effect of cow-based reproductive management programs with a systematic use of reproductive hormones

A. Wicaksono,[1,2]* F. Edwardes,[1] W. Steeneveld,[3] B. H. P. van den Borne,[1,4] P. Pinho,[5] F. Randi,[5] and H. Hogeveen[1]

[1]Business Economics Group, Department of Social Sciences, Wageningen University and Research, 6706 KN Wageningen, the Netherlands
[2]Veterinary Public Health and Epidemiology Division, School of Veterinary Medicine and Biomedical Sciences, IPB University, Kampus IPB Dramaga, 16680 Bogor, Indonesia
[3]Faculty of Veterinary Medicine, Department of Population Health Sciences, Section Farm Animal Health, Utrecht University, 3584 CL Utrecht, the Netherlands
[4]Quantitative Veterinary Epidemiology Group, Department of Animal Sciences, Wageningen University and Research, 6708 PB Wageningen, the Netherlands
[5]CEVA Santé Animale, 33500 Libourne, France

ABSTRACT

Hormone-based reproductive management programs can be beneficial to improve dairy cow's reproductive performance. This study aimed to compare the economic impact of reproductive management programs using systematic hormonal treatments to individual cows with a specific DIM range, with a reproductive management program using cow-specific hormonal treatment based on a veterinary diagnosis of ovarian dysfunction during a fertility check. An existing individual cow-based, dynamic, and stochastic bio-economic simulation model, mimicking the production dynamics of a 200 cow-herd in daily time steps, was extended with ovarian dysfunction and fertility inputs. Four hormone-based reproductive management programs were modeled. In the default reproductive management program, reflecting the current reproductive management of Dutch herds, lactating dairy cows are inseminated based on detection of estrus and noncyclic dairy cows are treated with hormones based on a veterinary diagnosis of ovarian dysfunction during a fertility check. Hormone treatments prescribed by the veterinarian for anestrus, cystic, and subestrus cows were an 8-d progesterone-releasing intravaginal device (PRID)-synch protocol (PRIDsynch), an Ovsynch protocol, and a $PGF_{2\alpha}$ treatment, respectively. The 3 other reproductive management programs reflected systematic hormonal treatments to cows at specific DIM and included (1) a Double-Ovsynch protocol for times AI (TAI) with nonpregnant cows submitted to a resynchronization protocol (FTAI), (2) a Double-Ovsynch protocol for TAI with nonpregnant cows detected in estrus or submitted to a resynchronization protocol (FTAI+ED), and (3) detection of estrus with cows not detected submitted to a PRIDsynch protocol (ED+TAI). All nonpregnant cows were submitted to a resynchronization protocol based on the absence (PRIDsynch) or presence (Ovsynch protocol) of a corpus luteum. The annual mean net economic return (NER) was calculated for all reproductive management programs. Compared with the default reproductive management program, the highest NER was observed for the FTAI+ED reproductive management program with €23,764 higher net revenues, followed by the FTAI and the ED+TAI reproductive management programs with €19,550 and €14,314 higher net revenues, respectively. Overall, systematic hormone-based reproductive management programs gave higher costs due to more hormones administered and higher calving and feed costs due to more pregnant cows. Nevertheless, the additional revenues of milk and calves in the systematic hormone-based reproductive management programs outweighed the total cost. For instance, the FTAI+ED reproductive management program gave €8,953 higher total cost per year compared with the default but with €32,654 higher revenues. In summary, reproductive management programs where hormones were systematically used gave economic advantages over the current default reproductive management program in which hormones are administered to individual cows based on a veterinary diagnosis of ovarian dysfunction during a fertility check.
Key words: economics, simulation, reproductive hormones, fertility, dairy

INTRODUCTION

Reproductive performance of dairy cows is associated with the economic performance of a dairy farm. For in-

Received August 22, 2023.
Accepted July 22, 2024.
*Corresponding author: ardilasunu.wicaksono@wur.nl or ardilasunu@apps.ipb.ac.id

The list of standard abbreviations for JDS is available at adsa.org/jds-abbreviations-24. Nonstandard abbreviations are available in the Notes.

stance, shorter days open (Meadows et al., 2005; Galvão et al., 2013), a shorter calving interval (Inchaisri et al., 2010), a higher 21-d pregnancy rate and a better service rate (Giordano et al., 2011, 2012; Ricci et al., 2020) were associated with a higher profitability of dairy farms. The profitability due to improved reproductive performance is mainly associated with higher milk revenues (Meadows et al., 2005; Inchaisri et al., 2010). Implementing a good reproductive management program, however, also requires additional costs (e.g., costs for reproductive hormones). Therefore, all factors related to reproductive performance in dairy farms need to be considered for deciding on a reproductive management program.

Several hormonal synchronization strategies with timed AI (**TAI**) exist to improve dairy cow's reproductive performance. The Ovsynch protocol has been commonly used in synchronization programs for TAI worldwide (Caraviello et al., 2006; Fricke and Wiltbank, 2022), this protocol consists of GnRH and $PGF_{2\alpha}$-based treatments to synchronize ovulation of lactating dairy cows for TAI 10 d after the first GnRH treatment (Pursley et al., 1995). Modifications of the Ovsynch protocol exist and encompass additional hormone injections (i.e., Double-Ovsynch protocol) or supplements such as progesterone to optimize its efficacy (i.e., progesterone-releasing intravaginal device [**PRID**]-synch protocol; Santos et al., 2016; Stevenson and Britt, 2017; Hölper et al., 2023). The PRIDsynch protocol gave higher pregnancies per AI of dairy cows compared with Ovsynch protocol (Hölper et al., 2023). Moreover, the implementation of the Double-Ovsynch protocol increased submission rate and pregnancy per AI of dairy cows compared with other synchronization protocols (Souza et al., 2008; Herlihy et al., 2012; Santos et al., 2017).

Reproductive management programs using hormonal synchronization protocols are applied in different approaches worldwide. A group-based approach implements a routine use of hormone protocols to a group of cows to synchronize their ovulation facilitating the reproductive management of dairy farms (Herlihy et al., 2011; Colazo and Mapletoft, 2014; Stevenson, 2016). Such an approach is especially applied in larger dairy herds to synchronize the estrous cycle of group of cows or in production systems with seasonal calving (Fricke and Wiltbank, 2022). Another approach is an individual cow-based systematic approach, in which hormones are administered to individual cows with a specific DIM range for a TAI. This way, a cow can achieve a shorter calving to first AI interval and a higher submission rate (Fricke et al., 2014; Rial et al., 2022). A less systematic cow-based approach also exists, and includes the decision to use hormones to individual cows based on a veterinary diagnosis of ovarian dysfunction during a fertility check (KNMvD, 2020; van der Laan et al., 2021). Such diagnosis-based reproductive management programs are applied in multiple European countries (with smaller herd sizes and a year-round calving pattern), such as in the Netherlands (van der Laan et al., 2021; Wicaksono et al., 2023).

Previously, economic simulation studies have compared several hormone-based reproductive management programs (Galvão et al., 2013; Ricci et al., 2020; Li et al., 2023). Those studies showed that in synchronization programs, the more systematic use of hormones resulted in an improved reproductive performance and higher economic benefit. However, no economic studies exist that compared a reproductive management program with a cow-specific hormonal treatment based on a veterinary diagnosis of ovarian dysfunction during a fertility check with a more systematic application of hormones to individual cows with a specific DIM range.

This study aimed to compare the economic impact of reproductive management programs using systematic hormonal treatments to individual cows with a specific DIM range with a reproductive management program using cow-specific hormonal treatment based on a veterinary diagnosis of ovarian dysfunction during a fertility check. A stochastic bio-economic model has been developed to estimate the net economic return (**NER**) of those reproductive management programs.

MATERIALS AND METHODS

Overview of Cow Simulation Model

The bio-economic simulation model used in this study was an adaptation and extension of the cow simulation model described by Edwardes et al. (2022). The simulation model was developed in R-studio software for Windows version 1.4.1103 (R Core Team, 2021). The model was a Monte Carlo individual cow-based dynamic and stochastic model, simulating a dairy herd of 200 cows in daily time steps. In short, the daily milk production of each cow was modeled following the Wilmink (1987) lactation curve. The daily feed requirements of each cow were expressed in the **VEM** (feed unit lactation) energy system, which are the energy requirements in feed units for lactation (Van Es, 1978; Remmelink et al., 2016). All dairy cows have a fixed dry period length of 56 d (Table 1), whereas the voluntary waiting period (**VWP**) depended on the reproductive management program. Probabilities for estrus detection and pregnancy were included (explained in the "Fertility-Related Input" section). Cows were bred a maximum of 6 times, and only when their daily milk yield was above 20 kg. Infertility culling was decided for an open cow with a daily milk yield below 15 kg. In addition to the culling decision for infertility, culling for general reasons (due to non-reproductive health disorders) was also modeled. The probability of general culling was calibrated to meet the overall culling rate of 30% (Mohd Nor et al., 2014). A mortality of 6.7% of all culled cows due to general culling was included (Rutten et al., 2014). An empty place due to a culled cow will be replaced immediately by a replacement heifer (on the following day). Input values on cow factors and their relation with milk production used in the bio-economic model are described in Table 1.

The model was adapted by adding additional reproduction dynamics including the ovarian dysfunctions: anestrus, cystic ovarian disease (**COD**) and subestrus. In addition, fertility-related events such as the probability of estrus detection and successful pregnancy based on several hormone protocols were added (Table 2). Values for the input parameters were based on scientific litera-

Table 1. Input values on cow factors used for simulating cows in the bio-economic model to evaluate different hormone-based reproductive management programs

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, 2022
Maximum parity	Assumed maximum reachable parity	10	Authors' expertise
Dry period length	Prepartum dry period length (d)	56	Inchaisri et al., 2010
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
Culling			
General culling	Probability is distributed over each daily time step:		Calibrated input to get overall annual culling rate of 30%
	Parity 1	2.74e−5	Mohd Nor et al., 2014
	Parity 2	2.74e−5	
	Parity 3	8.22e−5	
	Parity 4	1.10e−3	
	Parity ≥5	2.74e−3	
Mortality			Rutten et al., 2014
	Probability of mortality of all culled cows due to general culling	0.067	
Infertility culling	Decision to stop inseminate a cow:		Authors' expertise
	Maximum insemination	6	
	Maximum insemination after pregnancy loss	3	
	Milk yield threshold (kg)	<20	
	Daily milk yield threshold (kg) to cull cows	15	Edwardes et al., 2022
Milk loss	Milk loss due to pregnancy	$\sum_{i=30}^{n=240} -0.06 \cdot e^{0.135 \cdot \left(\frac{i}{7}\right)}$	Input to get best fitting curve on milk loss of Bohmanova et al., 2009; Inchaisri et al., 2010; Lainé et al., 2017

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

Table 2. Input values on fertility used in the bio-economic model on evaluating different hormone-based reproductive management programs

Parameter	Description	Value	Source
Voluntary waiting period	Voluntary waiting period for first insemination after calving (d)		
	Default[1] and ED+TAI[2]	65	Authors' expertise
	FTAI and FTAI+ED[3]	77	
First ovulation event	First ovulation after calving	Uniform (15–25)	Crowe et al., 2014
Subsequent estrus event	The subsequent estrous cycle	Uniform (19–26)	Remnant et al., 2018
Estrus detection			
Base probability	Base probability of estrus detection	0.5	Tippenhauer et al., 2021; Uniform-Agri, 2024; Expert
Probability after prostaglandin shot	Detection probability after estrus induction with prostaglandin	0.51	Stevenson et al., 1989
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			
Default reproductive management program			
Base probability	Base probability of successful pregnancy after insemination number 1 to ≥6	cow-specific	Inchaisri et al., 2011a
Risk factors	Relative risk on conditions		
	Anestrus	no: 1, yes: 0.6	Santos et al., 2009
	COD	no: 1, yes: 0.88	Fourichon et al., 2000
Systematic reproductive management programs			
Base probability	Successful pregnancy probability based on previous hormonal protocol treatments		
	Double-Ovsynch	0.45	Santos et al., 2017
	Ovsynch, PRIDsynch	0.35	Santos et al., 2016
	PG estrus induction	0.414	McDougall et al., 2021
Risk factors	Relative risk on systematic reproductive management program		
	Parity: 1 and ≥2	1.2, 1	Santos et al., 2009
	Calving season: summer, autumn, winter, spring	1, 0.98, 1.13, 1.7	Santos et al., 2009
Pregnancy loss	Probability of pregnancy loss from 60 d of gestation until calving	0.02	Albaaj et al., 2023

[1]Default reproductive management program reflecting the current Dutch situation regarding reproductive management with PRIDsynch being applied to an anestrus cow, Ovsynch to a cystic cow, and prostaglandin to a subestrus cow.

[2]Detection of estrus followed by timed artificial insemination (ED+TAI): PRIDsynch was applied to cows without estrus and nonpregnant cows without CL, and Ovsynch to nonpregnant cows with CL.

[3]Fixed-Time Artificial Insemination (FTAI) and FTAI with estrus detection (FTAI+ED): Double-Ovsynch was applied to all cows and ended with FTAI, Ovsynch was applied to nonpregnant cows with a corpus luteum (CL), and PRIDsynch to nonpregnant cows without CL.

ture as much as possible. The following sections describe the extensions of the cow simulation model in terms of simulation procedures and model inputs and explain the hormone-based reproductive management programs evaluated.

Simulation of Reproduction Events and Reproductive Conditions

The estrous cycle of a cow was modeled as a scheduling event, and the first ovulation event after calving was simulated by a uniform distribution of 15 to 25 d (Crowe et al., 2014). The subsequent estrus event was then modeled by a uniform distribution every 19 to 26 d (Remnant et al., 2018). After a VWP of 65 d, the detection of estrus was simulated for a cow that had a scheduled estrus event based on the cow estrous cycle. Given the probability of an estrus detection to an estrus cow, the cow was inseminated and with a certain probability of successful pregnancy subsequently checked for pregnancy by a veterinarian 32 ± 3 d later. Pregnant cows continued their lactation until dry off or were culled for general reasons, whereas nonpregnant cows went for the next estrous cycle or were culled because of general reasons or infertility.

Ovarian Dysfunctions

The probability of a cow having an ovarian dysfunction was determined by its incidence rate and attributed risk factors (Table 3). During the time window of occurrence (DIM) that the condition could occur, the cow had a probability to develop an ovarian dysfunction. Cows having an ovarian dysfunction did not express estrus and were not detected when the cow was at the scheduled day of the estrus event. The condition of a cow having an ovarian dysfunction was modeled according to the definitions introduced by Peter et al. (2009): The first condition was true anestrus due to inactive ovaries (anestrus type I and II), which was defined as inactive ovaries or less active ovaries that have follicular growth and deviation, followed by either atresia or regression. This causes delay of cyclicity in the next following estrous cycle. The second condition was cystic ovarian disease (anestrus type III or COD), which was defined as a deviation, growth, and establishment of a dominant follicle (>20–25 mm in the absence of a palpable corpus luteum [**CL**], which exists for >14 d), but it fails to ovulate and becomes a persistent follicular structure/cystic (follicular or luteal cyst). The third condition was subestrus, which was defined as a normal cycling cow with ovulation but having a suboptimal estrus expression and lack of estrus detection for insemination. This condition causes a nondetection of estrus and can be diagnosed by the presence of CL in the ovaries.

The probability for a cow to resume cyclicity (P_{rc}) at the day of the scheduled event of estrus after a VWP of 65 d was defined by a binomial (*B*) process:

$$P_{rc} = B\,(1, [1 - P_{anoest}] \times R_{par} \times R_{mp} \times R_{cs}),$$

where P_{anoest} is the base risk of anestrus, R_{par} the parity related risk factor, R_{mp} the milk production level related risk factor, and R_{cs} the calving season related risk factor (Table 3). The probability of a cow having COD (P_{cod}) at the day of the scheduled event of estrus after a VWP of 65 d, was modeled by a binomial process:

$$P_{cod} = B\,(1, I_{cod} \times R_{par} \times R_{cs}),$$

where I_{cod} is the base risk of COD, and R_{par} and R_{cs} the parity and calving season related risk factors, respectively (Table 3). For the rest of the cows that were not having anestrus or COD conditions, a subestrus condition probability of 15% was assigned, as determined by a calibration process to have an overall visual estrus detection rate

Table 3. Input values on ovarian dysfunctions and fertility diagnosis used in the bio-economic model on evaluating different hormone-based reproductive management programs

Parameter	Description	Value	Source
Anestrus[1]			
Incidence	Base rate	0.215	Opsomer et al., 2000
Occurrence	Time window of occurrence (DIM)	Uniform (42–65)	Peter et al., 2009
Risk factors	Relative risk on resuming cyclicity:		
	Parity: 1 and ≥2	0.83, 1	Santos et al., 2009
	Relative production level: ≤0.25%, 0.26–0.50%, 0.51–0.75%, ≥0.76%	1, 1.07, 1.08, 1.05	Santos et al., 2009
	Calving season: summer, autumn, winter, spring	1, 0.97, 0.88, 0.92	Santos et al., 2009
Cystic ovarian disease[2]			
Incidence	Base rate	0.085	Laporte et al., 1994
Occurrence	Time window of occurrence (DIM)	Uniform (42–105)	Inchaisri et al., 2011b, Rhodes et al., 2003
Risk factors	Relative risk		
	Parity: 1, 2, 3, 4, 5, 6, ≥ 7	1, 1.37, 0.95, 0.9, 0.73, 0.47, 0.23, 0.2	Laporte et al., 1994
	Calving season: summer, autumn, winter, spring	1, 1.8, 1, 0.54	Laporte et al., 1994
Subestrus[3]			
Incidence	Base rate	0.15	Calibrated input; van Eerdenburg et al., 2002
Veterinarian diagnosis			
Pregnancy check	Timing for pregnancy check after insemination (d)	30	Authors' expertise
First fertility check (default reproductive management program)	Timing for the first fertility check after the end of voluntary waiting period (d)	60	Authors' expertise
Next fertility check (default reproductive management program)	Timing for the next fertility check after insemination (d)	30	Authors' expertise
Corpus luteum (CL) check (systematic reproductive management program)	Probability based on CL status: CL+, CL−	0.7, 0.3	Wijma et al., 2018

[1]Inactive ovaries or less active ovaries that have follicular growth and deviation, followed by either atresia or regression causing the delay of cyclicity.

[2]There is deviation, growth, and establishment of a dominant follicle (>20–25 mm in the absence of a palpable CL, which exists for >14 d), but it fails to ovulate and becomes a persistent follicular structure/cystic (follicular or luteal cyst).

[3]The cow is normal cyclic including ovulation but with suboptimality of estrus detection or estrus expression causing a nondetection of estrus.

of 50% (Tippenhauer et al., 2021; Uniform-Agri, 2024; P. L. A. M. Vos, Utrecht University, the Netherlands, personal communication).

Fertility-Related Input

All fertility-related model inputs are shown in Table 2. Estrus detection was assumed to be visually performed by the farmer and was corrected for the relative production value of the cow (Inchaisri et al., 2010). Estrus detection rate was defined as the number of cows with a detected estrus over cows with a scheduled estrus event based on the cow estrous cycle. Estrus detection (P_{od}) was modeled by a binomial distribution:

$$P_{od} = B\ (1, B_{od} \times R_{rpl}),$$

where B_{od} is the base risk of estrus detection and R_{rpl} the relative production level related risk factor (Table 2).

After estrus detection, cows were artificially inseminated with conventional semen. In the default scenario, the diagnosis-based reproductive management program (van der Laan et al., 2021; explained later in detail), the probability of a successful pregnancy was based on a previous observational Dutch study, in which a successful pregnancy was defined as a successful insemination until a calf is born following Inchaisri et al. (2011a). The final multivariable logistic regression model from that study was incorporated in the current bio-economic model to calculate the base risk of successful pregnancy as determined by the characteristics of each simulated cow (i.e., number of inseminations, parity, season of AI, time of AI related to peak milk yield, DIM at AI time, milk yield at AI time and 4 interaction terms with DIM; Inchaisri et al., 2011a). The risk of successful pregnancy for each number of inseminations (Inchaisri et al., 2011a) is described in Appendix A. Pregnancy ($P_{preg\text{-}default}$) in the default reproductive management program was determined by a binomial process congruent to the base risk of successful pregnancy and relative risks for anestrus and COD risk factors as follows:

$$P_{preg\text{-}default} = B\ (1, B_{preg\text{-}default} \times R_{anoest} \times R_{cod}),$$

where $B_{preg\text{-}default}$ is the base risk of successful pregnancy after insemination in the default reproductive management program based on Inchaisri et al. (2011a), and R_{anoest} and R_{cod} the risk factors on the occurrence of previous anestrus and COD, respectively (Table 2).

In the reproductive management programs in which hormones were systematically applied (explained later), the pregnancies per insemination estimates of randomized controlled trials applying several hormone protocols (Santos et al., 2016, 2017; authors' expertise; Table 3) were used to define the base probability of successful pregnancy. Pregnancy in the reproductive management programs with a systematic hormone use ($P_{preg\text{-}systematic}$) was subsequently adjusted by several cow-level risk factors, namely parity, calving season, and the occurrences of anestrus and COD, and was modeled by a binomial distribution:

$$P_{preg\text{-}systematic} = B\ (1, B_{preg\text{-}systematic} \times R_{par} \times R_{cs} \times R_{anoest} \times R_{cod}),$$

where $B_{preg\text{-}systematic}$ is the base risk of successful pregnancy after insemination for the systematic reproductive management programs based on hormone protocol applications, R_{par} and R_{cs} the parity and calving season related risk factors, respectively. R_{anoest} and R_{cod} represent the risk factors on the occurrence of anestrus and COD, respectively (Table 2). For the systematic reproductive management program which involves detection of estrus (explained in the next section), the base risk of successful pregnancy followed the default reproductive management program.

Pregnancy loss was simulated with a probability of 2% during the period 60 d of gestation until calving (Albaaj et al., 2023). The probability was set to 0% during the first 60 d because pregnancy losses were included in the reported pregnancies per AI (Santos et al., 2016, 2017) in this time period. A cow with a pregnancy loss had afterward a maximum of 3 inseminations. If the third insemination was not successful, the cow was culled for infertility.

Reproduction Dynamics with Hormone-Based Reproductive Management Programs

Four hormone-based reproductive management programs were defined and modeled. The default reproductive management program reflects the current reproductive management of Dutch dairy herds, in which hormones are only administered to individual cows based on a veterinary diagnosis of ovarian dysfunction during a fertility check (van der Laan et al., 2021). The second to fourth reproductive management programs reflect systematic hormone use by administration of hormones to individual cows at a specific DIM range, namely the fixed-time artificial insemination (**FTAI**) reproductive management program, FTAI with detection of estrus reproductive management program (**FTAI+ED**), and detection of estrus followed by TAI (**ED+TAI**) reproductive management program.

Default Reproductive Management Program

Cows that were detected in estrus after the end of the VWP were inseminated and then subjected to a pregnancy check by a veterinarian (Figure 1a). Cows that showed estrus after a previous insemination will be re-inseminated. Cows that did not show estrus or were not detected until 60 d after the end of the VWP were assigned a fertility check by a veterinarian. To a nondetected cow, hormone protocols were applied based on a veterinary diagnosis during a fertility check (based on the definitions of ovarian dysfunctions provided above) and following the fertility treatment guidelines as developed by the Dutch society of cattle veterinarians on optimizing hormone use and reproduction management (KNMvD, 2020). A schematic representation of each hormone protocol can be found in Figure 2, while detailed descriptions can be found in Appendix B. The PRIDsynch protocol was applied to an anestrus cow, whereas the Ovsynch protocol was applied to a cow with COD. Both treatments were followed by a TAI. To a subestrus cow, luteolysis was attempted with prostaglandin, after which estrus had to be detected again with a given probability. If estrus was detected after prostaglandin treatment, the cow was inseminated. If estrus was not detected in a cyclic cow, the next veterinary check was modeled in 32 ± 3 d.

FTAI Reproductive Management Program

For each cow, the FTAI reproductive management program started at 50 ± 3 DIM, ended at 77 ± 3 DIM, and involved FTAI after calving using the Double-Ovsynch protocol (Souza et al., 2008; Santos et al., 2017) for all cows regardless of their reproductive cyclicity (Figure 1b). An inseminated cow was checked for its pregnancy and continued its lactation until the next calving when pregnant. A nonpregnant cow was checked for the presence of a CL by a veterinarian. The positive CL cow, with a probability of 70% (Wijma et al., 2018), was assigned to the Ovsynch protocol, whereas the negative CL cow was assigned to the PRIDsynch protocol. Both protocols were followed by insemination until the enabled maximum number of inseminations (Table 1).

FTAI+ED Reproductive Management Program

In the FTAI+ED reproductive management program, Double-Ovsynch was applied for each cow for first AI as for the FTAI program. Then the estrus detection probability for consecutive inseminations was applied (Figure 1c). After the insemination following estrus detection, there were 2 options. First, when no signs of estrus were detected, a pregnancy check followed 32 ± 3 d after insemination. The CL check was modeled for the nonpregnant cow similar to the FTAI reproductive management program. Second, when estrus was observed 19 to 26 d after insemination, the cow was subjected to a next insemination.

ED+TAI Reproductive Management Program

Figure 1d illustrates the reproduction dynamics in the ED+TAI reproductive management program. As in the default reproductive management program, the estrus and the ovarian dysfunctions were simulated after the VWP period of 65 d. The cow detected in estrus was inseminated. The nondetected cow for the first scheduled estrus event 26 d after the end of the VWP period of 65 d (due to anestrus, COD or subestrus) was submitted to a PRIDsynch protocol. This was performed at the maximum DIM of 91 d, and it was followed by an insemination at the end of the hormone protocol (after 10 d). Thereafter, 3 options were possible. First, a pregnancy check was assigned when the cow did not show any estrus signs within 32 ± 3 d after insemination, after which pregnancy was diagnosed and cows would have their next parity. Second, a CL check was performed for the nondetected estrus cow within 32 ± 3 d and followed by a specific hormone protocol based on the CL status, as in the FTAI reproductive management program. Third, the cow was re-inseminated after estrus was detected within 19 to 26 d.

Economic Calculations and Analysis

Based on the biological outputs that were derived from the model, the economic outputs were calculated. The economic outputs were then used to determine the net partial economic results of the 4 hormone-based reproductive management programs. The economic in- and outflows were calculated for all cows in daily time steps throughout a 1-yr time period and were summed the year. The economic calculations included milk returns, feed cost, culling costs, and different kinds of costs related to reproduction and hormone use.

Milk returns, feed costs, and culling costs were explained in detail by Edwardes et al. (2022). In short, the milk revenues were estimated based on the daily milk production with average fat and protein percentages and followed the lactation curve, which was modeled according to Wilmink (1987). Daily milk revenue was corrected in case of a pregnancy, and included a loss in milk production from the fifth month of pregnancy onward (Bohmanova et al., 2009; Lainé et al., 2017). Feed costs were calculated based on the daily feed requirements of each cow and expressed in VEM (Van Es, 1978; Remmelink et al., 2016). A depreciation method was used to calculate the culling costs (Edwardes et al., 2022),

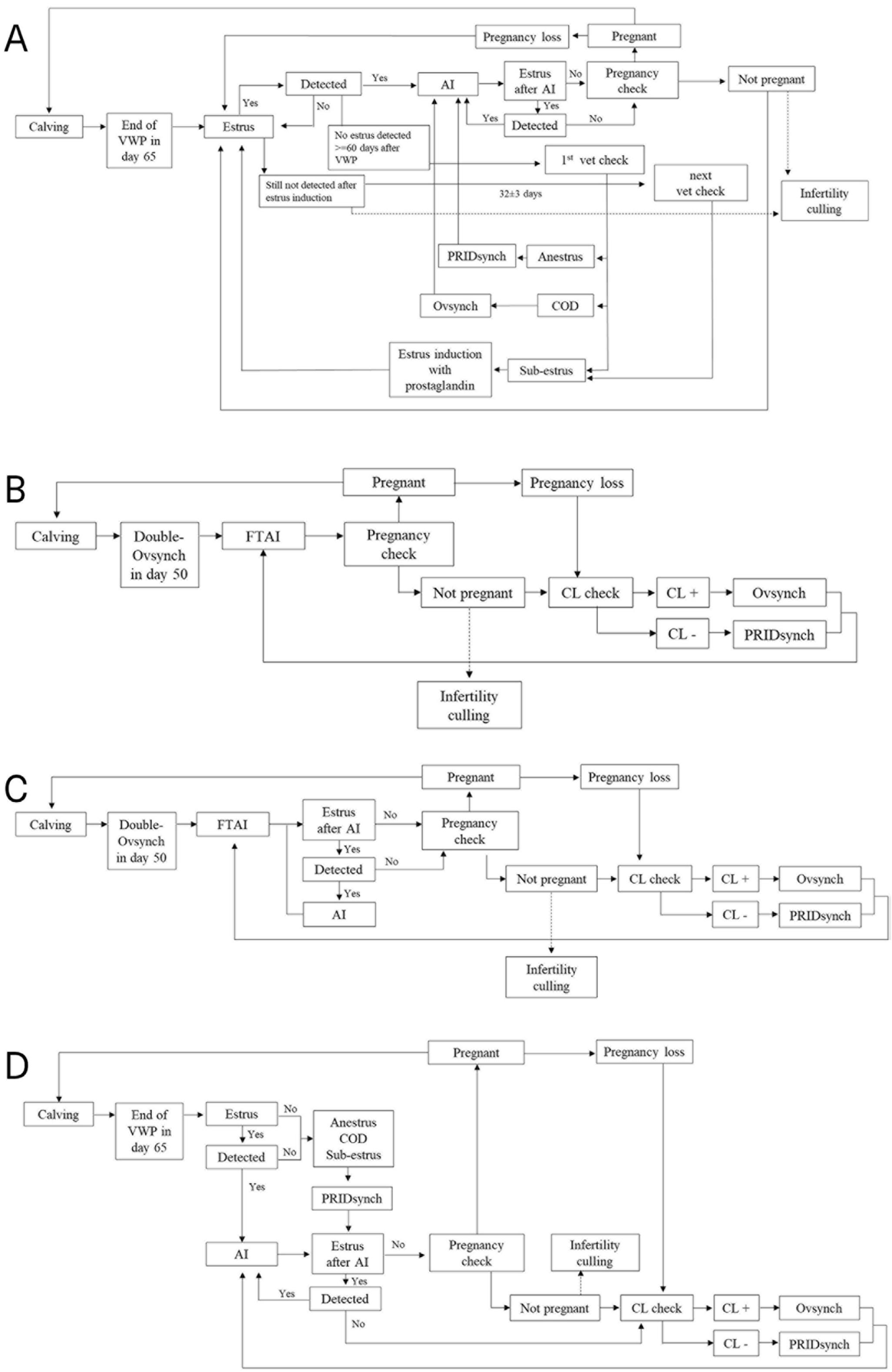

Figure 1. Reproduction dynamics of the cow simulation model according to the 4 hormone-based reproductive management programs: (A) the default reproductive management program; (B) the fixed time insemination reproductive management program; (C) the fixed time insemination with detection of estrus reproductive management program; and (D) the detection of estrus reproductive management program. VWP = voluntary waiting period; COD = cystic ovarian disease; FTAI = fixed-time artificial insemination; CL = corpus luteum. Infertility culling = open cows with a daily milk yield below 15 kg were culled for infertility reasons.

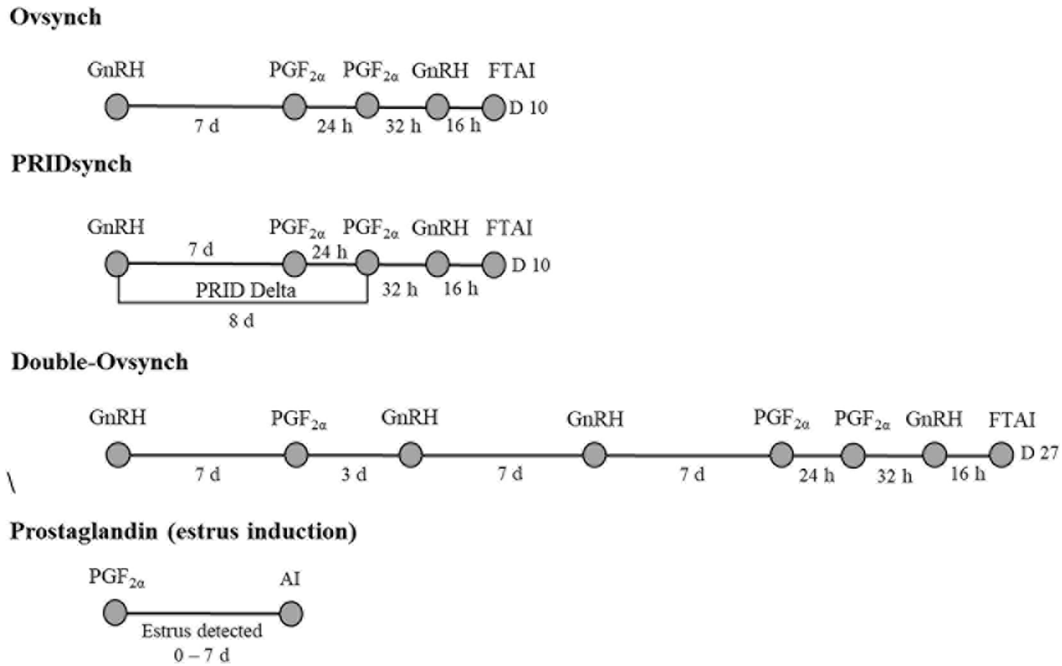

Figure 2. Schematic description of each reproductive hormone use protocol as applied in the different hormone-based reproductive management programs (PRID Delta = progesterone; FTAI = fixed-time artificial insemination). The second prostaglandin dose (in Ovsynch and PRIDsynch) was only applied in the systematic hormone-based reproductive management programs.

including the replacement heifer rearing cost to replace the culled cow and the revenue from the slaughter weight of the culled cow. Cost of mortality was incorporated in the culling cost, including the replacement heifer rearing cost to replace the dead cow, the opportunity cost from the slaughter weight of the dead cow, and the carcass removal cost. All economic related input values used in the simulation model are shown in Table 4. The calculation of different costs related to reproduction and hormone use were added to the model and explained in the following sections.

Hormone and Insemination Costs

Costs of hormones were calculated based on the applied hormone protocol. It accounted for the number of hormone doses (Appendix B) multiplied by the hormone protocol-specific prices per dose (or unit in case of progesterone; Table 4). Similarly, insemination costs were estimated by multiplying the number of inseminations by the price of semen per insemination. Labor costs were included for the implementation of hormone protocols and the application of inseminations, which both were assumed to be performed by the farmer. These costs were expressed by the hourly wage rate of the farmer and the duration of hormone application or insemination, including the preparation and administration time.

Veterinary Service Costs

Costs for veterinary services included time for pregnancy checks (all reproductive management programs), ovarian dysfunction diagnoses (default and ED+TAI reproductive management programs) and CL checks (FTAI, FTAI+ED, and ED+TAI reproductive management programs). These costs were calculated considering the call out fee price on a per visit basis, added by the veterinarian hourly rate and the veterinary check duration on a per cow basis.

Calving Costs

Costs of calving included the calving management costs, the rearing costs for the survived calves and the carcass removal for the dead calves. In agreement with Dutch legislation regarding the transport of young animals, the rearing duration of survived calves in a dairy herd was 14 d. Thereafter, female calves moved to the young stock unit of the dairy herd and male calves were sold. The calving management costs were accounted in every calving event and accommodated the costs of labor, peri- and postpartum disorders, and disease and dry-off treatments (Inchaisri et al., 2010). The probability of calves to survive until 14 d of age was modeled by a binomial process. For the surviving calves, the

Table 4. Economic input values used in the bio-economic model on evaluating different hormone-based reproductive management programs

Parameter	Description or unit	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
Hormone costs			
GnRH price	€/dose	3.5	Authors' expertise
Prostaglandin price	€/dose	3.5	
Progesterone price	€/unit	14.55	
Insemination costs			
Conventional semen price	€/insemination	20	Blanken et al., 2022
Farmer labor costs			
Hourly wage	€/h	23	Blanken et al., 2022
Insemination time	Farmer time for insemination (min/cow) including preparation and administration	10	Authors' expertise
Protocol duration			
Double-Ovsynch	Accumulative time (in minutes) per treatment per cow with 1 min per hormone injection, including preparation and administration	7	Authors' expertise
Ovsynch		4	
PRIDsynch		4	
$PGF_{2\alpha}$ (estrus induction)		1	
Veterinary costs			
Hourly wage	€/h	139.2	Edwardes et al., 2022
Call out fee	€/visit	31.35	
Diagnosing time	Veterinarian time for diagnosing pregnancy or reproductive conditions (min/cow)	5	Edwardes et al., 2022; authors' expertise
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 2021–2023	3.3	Wageningen Economic Research, 2023
	Carcass removal price (€/animal)	47	Rendac, 2023
Calving cost	Calving management cost (€/calving)	152	Inchaisri et al., 2010
	BW (kg) for milk replacement	42	Mohd Nor et al., 2012
	Milk replacement (kg)	4	Mohd Nor et al., 2012
	Milk replacement price (€/kg)	2.25	Blanken et al., 2022

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

rearing costs for 14 d included the farmer's labor to rear the calves and the milk replacement cost. For the dead calves, the calving management costs and the cost of carcass removal were accounted.

Economic Analysis

To compare the economic effect of the 4 hormone-based reproductive management programs, the mean annual NER was estimated for all 4 reproductive management programs using a partial approach. The annual NER for each program was determined as follows:

$$NER_{n,s} = \sum_{i=1}^{200}\sum_{t=1}^{362} R_{i,t,n,s}^{(total)} - \sum_{i=t}^{200}\sum_{t=1}^{365} C_{i,t,n,s}^{(total)},$$

where $NER_{n,s}$ is the annual net economic return for iteration n in the hormone-based reproductive management program s, $R_{i,t,n,s}^{(total)}$ the total annual revenue for cow i in time step t consisting of milk yield revenues and calf revenues, and $C_{i,t,n,s}^{(total)}$ is the annual total costs consisting of several costs, namely: feed, insemination, hormones, labor, veterinary services, calving, and culling. Economic outputs were expressed by the mean and 5th and 95th percentiles. In addition, the difference in NER between the 3 systematic hormone-based reproductive management programs with the default diagnosed-based reproductive management program was calculated.

Model Simulation

Model Calibration and Validation. Parameters were calibrated to ensure the accuracy of model inputs. Model outputs were then internally and externally validated. The validation of calibrated inputs was conducted in 5 rounds by the authors. For internal validation, the processes included an output reliability check after adjusting several inputs, the trace and track on the outputs of individual cows during each time step, and the face validity assessment to the model. An external validation

Table 5. Average (and 5th and 95th percentiles) annual reproduction and production levels for different hormone-based reproductive management programs in a 200-cow dairy herd

		Systematic hormone-based reproductive management program		
Parameter	Default[1]	FTAI[2]	FTAI+ED[3]	ED+TAI[4]
Calving interval (d)	419 (350; 522)	377 (352; 480)	374 (352; 450)	395 (349; 469)
Calving to first AI (d)	115 (69; 159)	77 (74; 80)	77 (74; 80)	93 (68; 101)
Calving to pregnancy (d)	170 (100; 269)	126 (104; 194)	122 (104; 191)	145 (99; 216)
Number of AI to pregnancy	1.6 (1.0; 3.0)	1.4 (1.0; 3.0)	1.5 (1.0; 3.0)	1.6 (1.0; 3.0)
Number of culled cows	49 (38; 60)	44 (35; 54)	43 (34; 54)	41 (32; 52)
Number of hormone protocol applications	188 (162; 216)	307 (286; 329)	256 (243; 270)	224 (200; 250)
Number of Double-Ovsynch applications	—	206 (197; 216)	210 (201; 219)	—
Number of Ovsynch applications	14 (8; 21)	71 (55; 87)	32 (23; 42)	78 (62; 95)
Number of PRIDsynch applications	46 (37; 56)	30 (21; 40)	14 (8; 20)	146 (123; 170)
Number of estrus induction by prostaglandin	128 (104; 153)	—	—	—
Number of cows submitted to hormone protocols[5]	110 (98; 121)	200 (198; 200)	197 (194; 199)	139 (129; 150)
Labor time on hormone protocol (min)	155 (108; 210)	922 (340; 1,491)	827 (144; 1,519)	897 (780; 1,000)
Labor time on AI (min)	3,011 (2,780; 3,240)	3,041 (2,840; 3,260)	3,110 (2,910; 3,340)	3,145 (2,930; 3,360)
Total number of calves born	148 (138; 158)	170 (161; 179)	173 (165; 182)	161 (152; 170)
Net milk yield (kg)	1,700,431 (1,669,436; 1,733,443)	1,759,751 (1,729,595; 1,788,085)	1,767,967 (1,739,248; 1,793,473)	1,744,099 (1,716,636; 1,775,401)

[1]Default reproductive management program reflecting the current Dutch situation regarding reproductive management with PRIDsynch being applied to an anestrus cow, Ovsynch to a cystic cow, and prostaglandin to a subestrus cow.

[2]FTAI = fixed-time artificial insemination.

[3]FTAI with estrus detection (FTAI+ED): Double-Ovsynch was applied to all cows and ended with FTAI, Ovsynch was applied to nonpregnant cows with a corpus luteum (CL), and PRIDsynch to nonpregnant cows without CL.

[4]Detection of estrus followed by timed artificial insemination (ED+TAI): PRIDsynch was applied to cows without estrus and nonpregnant cows without CL, and Ovsynch to nonpregnant cows with CL.

[5]Number of individual cows that received at least one hormone protocol.

was conducted by the comparison of model outputs to relevant literature.

Model Convergence. Model convergence was analyzed by running the model in which the variance of the incidence of anestrus, COD, and subestrus; the estrus detection rate; and the total number of milk yield and cows culled were graphically observed. This procedure showed that the model equilibrated at around 400 iterations. Five hundred iterations were consequently run in each simulation to ensure stability. Parity distributions stabilized at the end of yr 7; entailing a 7-yr burn-in period. Reproductive management programs were therefore implemented in yr 8 and model output was derived in yr 9 to allow a full implementation of the reproductive management programs across all cows in the herd.

Sensitivity Analysis

To evaluate the sensitivity of the NER for different input values, sensitivity analyses were conducted for each hormone-based reproductive management program. The NER of each reproductive management program was calculated for every adjusted value in the sensitivity analysis, and their difference with the default reproductive management program was determined afterward. Additionally, this value was compared with the difference in NER based on the original parameter value (Tables 5 and 6).

The biological input parameters included in the sensitivity analysis were the probability of successful pregnancy, ovarian dysfunctions' incidence rates, and estrus detection probability. Values used in the sensitivity analysis were based on literature findings and authors' expertise. The probability of pregnancy of the Double-Ovsynch protocol was changed from 45% to 42% and 52.7%, representing the minimum and the maximum probability of pregnancy of the Double-Ovsynch protocol (Santos et al., 2017) and of the Ovsynch/PRIDsynch protocol from 35% to 31.7% and 38.9%, representing the minimum and the maximum probability of pregnancy of the Ovsynch/PRIDsynch protocol (Santos et al., 2016). For values that were uncertain and had no reference, such as the incidence of ovarian dysfunctions, fixed intervals (i.e., ± 20%) were used. The estrus detection rate was

Table 6. Average (5th and 95th percentiles in parentheses) annual economic (€) simulation results for different hormone-based reproductive management programs in a 200-cow dairy herd

Parameter	Default[1]	Systematic hormone-based reproductive management program					
		FTAI[2]	Δ€[5]	FTAI+ED[3]	Δ€	ED+TAI[4]	Δ€
Revenues							
Milk revenues	782,198 (767,941; 797,384)	809,486 (795,614; 822,519)	27,288	813,265 (800,054; 824,998)	31,067	802,286 (789,653; 816,685)	20,088
Calf revenues	8,993 (8,320; 9,685)	10,370 (9,685; 11,050)	1,377	10,580 (9,945; 11,245)	1,587	9,825 (9,165; 10,530)	832
Costs							
Feed cost	247,537 (246,094; 249,059)	251,523 (250,050; 252,836)	3,986	252,055 (250,739; 253,254)	4,518	250,318 (248,972; 251,806)	2,781
Calving cost	43,950 (40,973; 46,852)	50,440 (47,675; 53,033)	6,490	51,362 (48,818; 53,866)	7,412	47,892 (44,981; 50,711)	3,942
Semen cost	6,023 (5,559; 6,480)	6,082 (5,680; 6,520)	59	6,220 (5,819; 6,680)	197	6,291 (5,860; 6,720)	268
Labor cost on AI	1,154 (1,065; 1,242)	1,166 (1,089; 1,250)	12	1,192 (1,115; 1,280)	38	1,206 (1,123; 1,288)	52
Hormone cost	1,761 (1,496; 2,019)	6,895 (6,501; 7,364)	5,134	5,992 (5,716; 6,300)	4,231	5,269 (4,632; 5,960)	3,508
Labor cost on hormone	119 (103; 135)	707 (672; 745)	558	634 (607; 662)	515	344 (307; 383)	215
Veterinary service cost	6,479 (6,003; 6,978)	5,061 (4,824; 5,296)	−1,418	4,451 (4,290; 4,600)	−2,028	9,205 (8,695; 9,707)	2,726
Culling cost	21,069 (15,294; 27,173)	15,367 (11,352; 19,481)	−5,702	15,137 (11,206; 19,294)	−5,932	14,195 (10,035; 18,208)	−6,874
Total cost	328,093 (322,227; 333,612)	337,241 (333,019; 341,724)	9,148	337,046 (333,002; 341,036)	8,953	334,728 (330,369; 339,466)	6,635
Net economic return	463,070 (449,242; 477,575)	482,620 (470,532; 494,533)	19,550	486,834 (474,378; 497,519)	23,764	477,384 (465,485; 489,641)	14,314

[1]Default reproductive management program reflecting the current Dutch situation regarding reproductive management with PRIDsynch being applied to an anestrus cow, Ovsynch to a cystic cow, and prostaglandin to a subestrus cow.

[2]FTAI = fixed-time artificial insemination.

[3]FTAI with detection of estrus (FTAI+ED): Double-Ovsynch was applied to all cows and ended with FTAI, Ovsynch was applied to nonpregnant cows with a corpus luteum (CL), and PRIDsynch to nonpregnant cows without CL.

[4]Detection of estrus followed by timed artificial insemination (ED+TAI): PRIDsynch was applied to cows without estrus and nonpregnant cows without CL, and Ovsynch to nonpregnant cows with CL.

[5]Difference of the economic results in € between systematic and default hormone-based reproductive management program.

adjusted to 30%, representing a poor visual detection by farmers (Inchaisri et al., 2010), and 80%, representing an enhanced estrus detection rate when sensors are used (Kamphuis et al., 2012; Rutten et al., 2014).

Sensitivity analyses were also performed for the economic input parameters namely milk, calf, and hormone prices. Values used in the sensitivity analysis were adjusted to low and high values based on authors' expertise or on lowest and highest market prices in the Netherlands in the last 5 yr (Wageningen Economic Research, 2023).

RESULTS

Reproduction and Production Effects

The mean annual simulation results regarding reproduction and production outcomes for the different hormone-based reproductive management programs are presented in Table 5. The mean calving interval was 419 d for the default reproductive management program, whereas the systematic hormone-based reproductive management programs resulted in shorter average calving intervals (FTAI+ED = 374 d, FTAI = 377 d, ED+TAI = 395 d). The same trends were shown for other reproductive performance outputs (i.e., calving to first AI and calving to pregnancy). The highest mean total number of culled cows was obtained from the default reproductive management program (49 cows), whereas the systematic hormone-based reproductive management programs gave less culled cows on average (FTAI+ED = 43 cows, FTAI = 44 cows, ED+TAI = 41 cows). The systematic hormone-based reproductive management programs submitted more cows to hormone protocols, and the highest mean number of rounds of hormone protocols used was obtained from the FTAI reproductive management program (307 rounds of hormone protocols applied to 200 cows). In the systematic programs that includes estrus detection, the proportion of the open cows after first AI which were detected in estrus and being re-inseminated before the pregnancy check, was 21.5% and 40.4% for the FTAI+ED and ED+TAI programs, respectively.

For the production output, the default reproductive management program resulted in 148 calves (incorporated both male and female calves) and 8,502 kg/cow of milk on average, whereas the systematic hormone-based reproductive management programs resulted in a higher net production of calves and milk with the FTAI+ED reproductive management program having the highest mean values (173 calves and 8,840 kg of milk/cow), followed by FTAI program (170 calves and 8,799 kg of milk/cow) and ED+TAI program (161 calves and 8,720 kg of milk/cow).

Economic Effects

Table 6 describes the mean total annual economic outcomes of the 4 hormone-based reproductive management programs. The default reproductive management program gave the lowest milk and calf revenues with a difference of €31,067 and €1,587 for the milk and calf revenues, respectively, compared with the FTAI+ED reproductive management program, which gave the highest revenues. In terms of costs, the default reproductive management program gave the lowest cost on some cost parameters when compared with the systematic hormone-based reproductive management programs, including feed, calving, semen, hormones, and labor on AI and hormones. However, different results were obtained for the costs on veterinary service and culling, where the default reproductive management program gave the highest costs. The FTAI reproductive management program gave €9,148 higher costs compared with the default reproductive management program, followed by the FTAI+ED (€8,953) and ED+TAI (€6,635), respectively. Despite these higher costs, the highest NER was observed for the FTAI+ED reproductive management program with €23,764 higher net revenues, followed by the FTAI and the ED+TAI reproductive management programs with €19,550 and €14,314 higher net revenues, respectively, compared with the default reproductive management program.

Sensitivity Analysis Outputs

The sensitivity analysis showed that the most influential parameter for the NER was the estrus detection rate (Table 7). Increasing the estrus detection rate to 80% resulted in a difference in NER that was €8,563; €10,432; €7,621 lower for the FTAI, FTAI+ED, and ED+TAI reproductive management programs, respectively, when compared with the base value of 50%. Decreasing this rate to 30% resulted in an increased difference in NER on the systematic hormone-based reproductive management programs. The economic parameter to which the NER was the most sensitive was milk price. Decreasing the milk price resulted in a lower difference in NER between the FTAI (€7,741), FTAI+ED (€8,471), and ED+TAI (€5,574) reproductive management programs compared with the default reproductive management program, whereas increasing this parameter resulted in a higher difference in NER for the systematic hormone-based reproductive management programs. In contrast, changing the incidence rate of ovarian dysfunctions with 20% resulted only in a small change in the difference in NER for the systematic hormone-based reproductive management programs compared with the default reproductive

Table 7. Sensitivity of the net economic return (NER; €) for different biological and economic input values of systematic hormone-based reproductive management programs compared with the base parameter value

Parameter	Adjusted value for sensitivity analysis	Base parameter value	Average NER of default reproductive management program when using adjusted values (€)	Difference in NER of systematic reproductive management programs with the default reproductive management program when using adjusted values (€)			Change in difference in NER (in €) compared with the base value[1]		
				FTAI[2]	FTAI+ED[3]	ED+TAI[4]	FTAI	FTAI+ED	ED+TAI
Estrus detection rate[5] (%)	30	50	450,610	32,010	39,292	25,736	12,460	15,528	11,422
	80	50	471,633	10,987	13,332	6,693	−8,563	−10,432	−7,621
Milk price (€/kg)	0.32	0.46	224,464	11,809	15,293	8,740	−7,741	−8,471	−5,574
	0.63	0.46	751,242	30,762	36,743	22,725	11,212	12,979	8,411
Successful pregnancy probability Double-Ovsynch[6] (%)	42	45	463,070	16,522	22,510	14,314	−3,028	−1,254	0
	52.7	45	463,070	25,299	28,412	14,314	5,749	4,648	0
Hormone price (€)	Low[7]	Base[8]	463,000	22,610	26,870	16,274	3,060	3,106	1,960
	High[9]	Base[8]	461,677	18,808	23,751	13,778	−742	−13	−536
Successful pregnancy probability Ovsynch and PRIDsynch (%)	31.7	35	462,363	18,917	23,994	15,056	−633	230	742
	38.9	35	462,363	21,801	24,765	15,056	2,251	1,001	742
Calf price (€/calf)	23	65	456,579	19,440	23,951	14,492	−110	187	178
	109	65	468,423	21,341	26,058	15,646	1,791	2,294	1,332
Incidence rate cystic ovarian disease[10] (%)	6.8	8.5	461,827	20,793	25,007	14,904	1,243	1,243	590
	10.2	8.5	461,625	20,994	25,208	15,667	1,444	1,444	1,353
Incidence rate subestrus[10] (%)	12	15	463,252	19,367	23,581	13,747	−183	−183	−567
	18	15	461,088	21,532	25,746	16,276	1,982	1,982	1,962
Incidence rate anestrus[10] (%)	17.2	21.5	463,511	19,109	23,323	14,283	−441	−441	−31
	25.8	21.5	461,700	20,920	25,134	15,330	1,370	1,370	1,016

[1]Table 6.

[2]FTAI = fixed-time artificial insemination.

[3]FTAI with detection of estrus (FTAI+ED): Double-Ovsynch was applied to all cows and ended with FTAI, Ovsynch was applied to nonpregnant cows with a corpus luteum (CL), and PRIDsynch to nonpregnant cows without CL.

[4]Detection of estrus followed by timed artificial insemination (ED+TAI): PRIDsynch was applied to cows without estrus and nonpregnant cows without CL, and Ovsynch to nonpregnant cows with CL.

[5]Adjusted values on estrus detection rate only applied for default, FTAI+ED and ED program.

[6]Adjusted values on successful pregnancy probability Double-Ovsynch only applied for FTAI and FTAI+ED program.

[7]Low hormone prices: GnRH 2 €/dose, prostaglandin 2 €/dose, progesterone 11 €/unit.

[8]Base hormone prices: GnRH 3.5 €/dose, prostaglandin 3.5 €/dose, progesterone 14.55 €/unit.

[9]High hormone prices: GnRH 4.3 €/dose, prostaglandin 5 €/dose, progesterone 21 €/unit.

[10]Adjusted values on incidence rate cystic ovarian disease, subestrus and anestrus only applied for default and ED+TAI program.

management program, making those parameters the least influential (Table 7).

DISCUSSION

The developed stochastic bio-economic simulation model described for the first time the economic consequences of systematic hormone-based reproductive management programs in comparison with the default diagnosis-based reproductive management program that is currently applied in Dutch dairy farms. Compared with the default reproductive management program, the highest NER was observed for the FTAI+ED reproductive management program with €23,764 higher net revenues, followed by the FTAI and the ED+TAI reproductive management programs with €19,550 and €14,314 higher net revenues in a 200-cow dairy herd, respectively. Results indicated that reproductive management programs with a more systematic use of hormones give economic advantages over the default hormone-based reproductive management program in dairy farms. These differences were predominantly caused by less culling of lactating cows due to fertility and more milk and calves produced per cow per year. These findings might give dairy farmers economic considerations to start implementing systematic reproductive management programs to gain more profit for their business.

The findings in this study were in agreement with other studies that simulated several hormone-based reproductive management programs based on individual cow-based treatments. These studies, simulating populations of dairy cows (Ricci et al., 2020) and heifers and lactating cows combined (Li et al., 2023), showed an economic benefit when hormones were applied more systematically. Moreover, the current study corroborated with a previous simulation study whereby combining the FTAI and detection of estrus (which was applied in FTAI+ED reproductive management program) gave a higher profit compared with applying the FTAI or detection of estrus only (Galvão et al., 2013). Those studies were only comparing the economic effect among systematic hormone-based reproductive management programs, whereas this simulation study also compared systematic reproductive management programs with the default reproductive management program in which hormones were used only based on the veterinary diagnosis of ovarian dysfunctions during a fertility check (i.e., reproductive treatments or estrus induction), which is current practice in many countries. In addition, 3 different reproductive disorders—true anestrus, COD, and subestrus—were modeled, whereas they were not included in the previous simulation studies.

The simulation model showed that a systematic use of hormones, relying in the combination of different protocols, resulted in better reproductive performances (i.e., shorter calving interval, calving to first AI, and calving to pregnancy) compared with the default reproductive management program. This was confirmed by a randomized clinical trial determining that hormone treatments result in better reproductive performance at cow level (Galvão et al., 2009; Santos et al., 2017). The model results were also supported by a recent Dutch ecological study suggesting that a higher use of hormones was associated with better reproductive performance at herd level (Wicaksono et al., 2023).

The FTAI+ED program gave the best technical outputs (i.e., calving interval, calving to first AI and calving to pregnancy) with a slight difference in results compared with FTAI, and followed by ED+TAI. The application of the Double-Ovsynch protocol at 50 ± 3 DIM in the FTAI+ED and FTAI programs ensured that the cow had her first AI within 77 DIM. This reduced the interval of calving to first AI by respectively 16 and 38 d compared with the ED+TAI and default programs. The reduction of the calving to pregnancy interval was as expected because the Double-Ovsynch protocol resulted in a higher probability of successful pregnancy, as well as a 100% service rate through TAI (Nowicki et al., 2017; Santos et al., 2017). Compared with the systematic programs, the default program did not use any resynchronization of estrus for the nonpregnant cows after a pregnancy check. Hormones were only applied based on a veterinary diagnosis for the nondetected cows. Consequently, with the default management program cows are re-inseminated later, thus resulting in a lower reproductive performance.

The 3 systematic hormone-based reproductive management programs gave a higher NER than the default reproductive management program, with FTAI+ED being the most beneficial. More systematic reproductive program that use more hormonal treatments gave the highest economic benefit than less systematic program (Ricci et al., 2020). Based on Giordano et al. (2011), the 2 reproductive programs using 100% TAI were more beneficial than the reproductive programs using 100% ED. Another study showed that TAI combined with the detection of estrus gave a higher economic benefit than FTAI or detection of estrus only (Galvão et al., 2013). However, some of the costs within the systematic hormone-based reproductive management programs of the current study were higher. Calving cost was higher than in the default reproductive management program because more cows were pregnant, resulting in more calves produced. This subsequently raised the feed cost. Obviously, because more hormones were used, hormone cost and cost of labor associated with hormone administration were also higher. Therefore, the total costs were higher for the systematic hormone-based reproductive management programs compared with the default reproductive management program. Nevertheless, the additional revenues of milk and calves in the systematic hormone-based reproductive management programs outweighed the total costs, giving a higher annual NER compared with the default reproductive management program.

Model input parameters were acquired from particular references, which may result in model outcomes that differ from other situations. These include the probability of successful pregnancy after the application of hormone protocols and the incidence of ovarian dysfunctions. To solve this limitation, sensitivity analyses were conducted to evaluate possible different input parameters. Through this method, different possible outputs could be obtained, which would be applicable to various situations (Kirkeby et al., 2021). In addition, to generate outputs that mimic real situations, accurate farm-specific input parameters need to be considered to help farmers make their own decisions based on the model's outcomes.

As any other simulation model, this study had some limitations. This study simulated the reproductive management program of a dairy farm under Dutch circumstances, which implements an individual cow-based approach for hormone applications. This may also be common to dairy herds with a year-round calving pattern in other European countries. The results of this study therefore only represent those given conditions and cannot be directly compared with herds implementing a group-based approach in other countries. Also, modeling the occurrence of general culling was simplified by using a constant daily probability. This probability was, however, made cow-specific based on the parity of the cow, and final results indicated a realistic overall culling probability (similar to the overall culling rate of 28% in the Netherlands (Kulkarni et al., 2023). In the systematic programs that include estrus detection, the proportion of open cows after first AI that were detected in estrus and re-inseminated before the pregnancy check (21.5% for the FTAI+ED program and 40.4% for the ED+TAI program), can be considered low (Tippenhauer et al., 2021; Uniform-Agri, 2024). This likely results in an underestimation of the true effect of the 2 systematic reproductive management programs. The proportion of cows open might be improved when a higher visual estrus detection rate is achieved. In the default program, a waiting period of 60 d after the end of the VWP to conduct a "fertility check" was included. This suggested interval can be considered as being long. This assumption also partly explains the poor reproductive performance in comparison with the systematic reproductive management programs. In contrast, this specific management is promoted in the current Dutch hormone use guideline (KNMvD, 2020), encouraging dairy farmers to prudently apply reproductive hormones.

The estrus detection rate was the most influential parameter for the annual NER in the sensitivity analysis. As such, it plays an important role in the decision to implement the systematic hormone-based reproductive management programs in dairy herds. Decreasing the estrus detection rate to 30% resulted in an increased difference in NER for the systematic hormone-based reproductive management programs. It thus indicates that systematic hormone-based reproductive management programs would be more beneficial for dairy farms with poor estrus detection (e.g., those with poor visual detection by the farmer). Meanwhile, systematic hormone-based reproductive management programs would be less cost-effective in dairy farms which already have a high estrus detection rate. Herds with a low submission risk due to a low detection rate would economically benefit more from the systematic hormone-based reproductive management programs than herds with high submission risk (Archer et al., 2015). A better estrus detection could be achieved through enhancing visual estrus detection by farmers or using sensors (Crowe et al., 2018). However, the reproductive management program with systematic use of reproductive hormones still gave the best reproductive performance outputs thus maximizing its economic performance.

Optimizing hormone use in dairy farms is a complex decision-making process that involves several aspects. Here we investigated the relationship between a systematic hormone-based reproductive management program, the reproductive performance of the cow and the associated economic benefits. Although allowed (Lane et al., 2008), there is societal pressure to reduce hormone use in dairy farms (Pieper et al., 2016; Higgins et al., 2013). The weight of these aspects may differ between countries and stakeholders but must be taken into account when trying to improve reproductive performance in dairy herds alongside other management strategies such as adequate feeding and proper housing, good heat detection, and a correct insemination moment.

CONCLUSIONS

Reproductive management programs with a more systematic use of hormones (i.e., administrating hormones to individual cows at a specific DIM range) provided substantial economic advantages over the current default reproductive management program for Dutch conditions in which hormones are administered to individual cows based on a veterinary diagnosis of ovarian dysfunctions during a fertility check. The differences are predominantly caused by a reduced culling of lactating cows due to fertility and more milk and calves produced per cow per year because of a shorter calving interval. Result of the sensitivity analysis showed that systematic hormone-based reproductive management programs were less economically beneficial in herds with a high estrus detection rate. Decisions to implement more systematic reproductive management programs, therefore, will be dependent on the reproductive performance of those farms and need to be made farm specific.

NOTES

This research was funded by the Indonesia Endowment Fund for Education (LPDP, Jakarta, Indonesia) through a PhD scholarship (grant number: 202001221915982) awarded to the first author and CEVA Santé Animale (Libourne, France) for the project. No human or animal subjects were used, so this analysis did not require approval by an Institutional Animal Care and Use Committee or Institutional Review Board. PP and FR are employees of CEVA Santé Animale. The authors have not stated any other conflicts of interest.

Nonstandard abbreviations used: CL = corpus luteum; COD = cystic ovarian disease; ED+TAI = detection of estrus followed by TAI; FTAI = fixed-time AI; FTAI+ED = FTAI with detection of estrus; HF = Holstein Friesian; MRY = Dutch Red-and-White; NER = net economic return; NS = nonsignificant; PRID = progesterone-releasing intravaginal device; TAI = timed AI; VEM = feed unit lactation; VWP = voluntary waiting period.

REFERENCES

Albaaj, A., J. Durocher, S. J. LeBlanc, and S. Dufour. 2023. Meta-analysis of the incidence of pregnancy losses in dairy cows at different stages to 90 days of gestation. JDS Commun. 4:144–148. https://doi.org/10.3168/jdsc.2022-0278.

Archer, S. C., C. D. Hudson, and M. J. Green. 2015. Use of stochastic simulation to evaluate the reduction in methane emissions and improvement in reproductive efficiency from routine hormonal interventions in dairy herds. PLoS One 10:e0127846. https://doi.org/10.1371/journal.pone.0127846.

Blanken, K., F. de Buisonje, A. Evers, W. Ouweltjes, J. Verkaik, I. Vermeij, and H. Wemmenhove. 2022. Kwantitatieve informatie veehouderij 2022–2023. Chapter 1 and 2 in KWIN 2022–2023. Wageningen Livestock Research, Wageningen, the Netherlands.

Bohmanova, J., J. Jamrozik, and F. Miglior. 2009. Effect of pregnancy on production traits of Canadian Holstein cows. J. Dairy Sci. 92:2947–2959. https://doi.org/10.3168/jds.2008-1782.

Caraviello, D. Z., K. A. Weigel, P. M. Fricke, M. C. Wiltbank, M. J. Florent, N. B. Cook, K. V. Nordlund, N. R. Zwald, and C. L. Rawson. 2006. Survey of management practices on reproductive performance of dairy cattle on large US commercial farms. J. Dairy Sci. 89:4723–4735. https://doi.org/10.3168/jds.S0022-0302(06)72522-X.

Colazo, M. G., and R. J. Mapletoft. 2014. A review of current timed-AI (TAI) programs for beef and dairy cattle. Can. Vet. J. 55:772–780.

Crowe, M. A., M. G. Diskin, and E. J. Williams. 2014. Parturition to resumption of ovarian cyclicity: comparative aspects of beef and dairy cows. Animal 8:40–53. https://doi.org/10.1017/S1751731114000251.

Crowe, M. A., M. Hostens, and G. Opsomer. 2018. Reproductive management in dairy cows—The future. Ir. Vet. J. 71:1. https://doi.org/10.1186/s13620-017-0112-y.

CRV. 2022. Jaarstatistieken 2021 voor Nederland. Accessed Jul. 16, 2022. https://www.cooperatie-crv.nl/wp-content/uploads/2022/03/Jaarstatistieken-2021-NL.pdf.

Edwardes, F., M. van der Voort, T. Halasa, M. Holzhauer, and H. Hogeveen. 2022. Simulating the mechanics behind sub-optimal mobility and the associated economic losses in dairy production. Prev. Vet. Med. 199:105551. https://doi.org/10.1016/j.prevetmed.2021.105551.

Fourichon, C., H. Seegers, and X. Malher. 2000. Effect of disease on reproduction in the dairy cow: A meta-analysis. Theriogenology 53:1729–1759. https://doi.org/10.1016/S0093-691X(00)00311-3.

Fricke, P. M., J. O. Giordano, A. Valenza, G. Lopes Jr., M. C. Amundson, and P. D. Carvalho. 2014. Reproductive performance of lactating dairy cows managed for first service using timed artificial insemination with or without detection of estrus using an activity-monitoring system. J. Dairy Sci. 97:2771–2781. https://doi.org/10.3168/jds.2013-7366.

Fricke, P. M., and M. C. Wiltbank. 2022. Symposium review: The implications of spontaneous versus synchronized ovulations on the reproductive performance of lactating dairy cows. J. Dairy Sci. 105:4679–4689. https://doi.org/10.3168/jds.2021-21431.

Galvão, K. N., P. Federico, A. De Vries, and G. M. Schuenemann. 2013. Economic comparison of reproductive programs for dairy herds using estrus detection, timed artificial insemination, or a combination. J. Dairy Sci. 96:2681–2693. https://doi.org/10.3168/jds.2012-5982.

Galvão, K. N., M. Frajblat, S. B. Brittin, W. R. Butler, C. L. Guard, and R. O. Gilbert. 2009. Effect of prostaglandin F2α on subclinical endometritis and fertility in dairy cows. J. Dairy Sci. 92:4906–4913. https://doi.org/10.3168/jds.2008-1984.

Giordano, J. O., P. M. Fricke, M. C. Wiltbank, and V. E. Cabrera. 2011. An economic decision-making support system for selection of reproductive management programs on dairy farms. J. Dairy Sci. 94:6216–6232. https://doi.org/10.3168/jds.2011-4376.

Giordano, J. O., A. S. Kalantari, P. M. Fricke, M. C. Wiltbank, and V. E. Cabrera. 2012. A daily herd Markov-chain model to study the reproductive and economic impact of reproductive programs combining timed artificial insemination and estrus detection. J. Dairy Sci. 95:5442–5460. https://doi.org/10.3168/jds.2011-4972.

Herlihy, M. M., D. P. Berry, M. A. Crowe, M. G. Diskin, and S. T. Butler. 2011. Evaluation of protocols to synchronize estrus and ovulation in seasonal calving pasture-based dairy production systems. J. Dairy Sci. 94:4488–4501. https://doi.org/10.3168/jds.2010-4126.

Herlihy, M. M., J. O. Giordano, A. H. Souza, H. Ayres, R. M. Ferreira, A. Keskin, A. B. Nascimento, J. N. Guenther, J. M. Gaska, S. J. Kacuba, M. A. Crowe, S. T. Butler, and M. C. Wiltbank. 2012. Presynchronization with Double-Ovsynch improves fertility at first postpartum artificial insemination in lactating dairy cows. J. Dairy Sci. 95:7003–7014. https://doi.org/10.3168/jds.2011-5260.

Higgins, H. M., E. Ferguson, R. F. Smith, and M. J. Green. 2013. Using hormones to manage dairy cow fertility: The clinical and ethical beliefs of veterinary practitioners. PLoS One 8:e62993. https://doi.org/10.1371/journal.pone.0062993.

Hölper, M., L. Bretzinger, F. Randi, W. Heuwieser, and S. Borchardt. 2023. Effect of a progesterone-releasing intravaginal device (PRID) for 8 days during a modified Ovsynch protocol on pregnancy outcomes in lactating Holstein cows. JDS Commun. 4:303–307. https://doi.org/10.3168/jdsc.2022-0314.

Inchaisri, C., R. Jorritsma, J. C. M. Vernooij, P. L. A. M. Vos, G. C. van der Weijden, and H. Hogeveen. 2011a. Cow effects and estimation of success of first and following inseminations in Dutch dairy cows. Reprod. Domest. Anim. 46:1043–1049. https://doi.org/10.1111/j.1439-0531.2011.01782.x.

Inchaisri, C., R. Jorritsma, P. L. A. M. Vos, G. C. van der Weijden, and H. Hogeveen. 2010. Economic consequences of reproductive performance in dairy cattle. Theriogenology 74:835–846. https://doi.org/10.1016/j.theriogenology.2010.04.008.

Inchaisri, C., R. Jorritsma, P. L. A. M. Vos, G. C. van der Weijden, and H. Hogeveen. 2011b. Analysis of the economically optimal voluntary waiting period for first insemination. J. Dairy Sci. 94:3811–3823. https://doi.org/10.3168/jds.2010-3790.

Kamphuis, C., B. DelaRue, C. R. Burke, and J. Jago. 2012. Field evaluation of 2 collar-mounted activity meters for detecting cows in estrus on a large pasture-grazed dairy farm. J. Dairy Sci. 95:3045–3056. https://doi.org/10.3168/jds.2011-4934.

Kirkeby, C., V. J. Brookes, M. P. Ward, S. Dürr, and T. Halasa. 2021. A practical introduction to mechanistic modeling of disease transmission in veterinary science. Front. Vet. Sci. 7:546651. https://doi.org/10.3389/fvets.2020.546651.

KNMvD (Koninklijke Nederlandse Maatschappij voor Diergeneeskunde). 2020. Richtlijn Vruchtbaarheidsbehandelingen als onderdeel van de veterinairebegeleiding van melkveebedrijven. Accessed Jun. 6, 2021. https://www.knmvd.nl/app/uploads/2021/04/Richtlijn-Vruchtbaarheidsbehandelingen_april2021.pdf.

Kok, A., C. E. Van Middelaar, P. F. Mostert, A. T. M. Van Knegsel, B. Kemp, I. J. M. De Boer, and H. Hogeveen. 2017. Effects of dry period length on production, cash flows and greenhouse gas emissions of the dairy herd: A dynamic stochastic simulation model. PLoS One 12:e0187101. https://doi.org/10.1371/journal.pone.0187101.

Kulkarni, P. S., M. Mourits, M. Nielen, and W. Steeneveld. 2023. Associations between dairy farm performance indicators and culling rates under policy-driven herd size constraints. Front. Vet. Sci. 10:1062891. https://doi.org/10.3389/fvets.2023.1062891.

Lainé, A., C. Bastin, C. Grelet, H. Hammami, F. G. Colinet, L. M. Dale, A. Gillon, J. Vandenplas, F. Dehareng, and N. Gengler. 2017. Assessing the effect of pregnancy stage on milk composition of dairy cows using mid-infrared spectra. J. Dairy Sci. 100:2863–2876. https://doi.org/10.3168/jds.2016-11736.

Lane, E. A., E. J. Austin, and M. A. Crowe. 2008. Oestrous synchronisation in cattle—Current options following the EU regulations restricting use of oestrogenic compounds in food-producing animals: A review. Anim. Reprod. Sci. 109:1–16. https://doi.org/10.1016/j.anireprosci.2008.08.009.

Laporte, H. M., H. Hogeveen, Y. H. Schukken, and J. P. T. M. Noordhuizen. 1994. Cystic ovarian disease in Dutch dairy cattle, I. Incidence, risk factors and consequences. Livest. Prod. Sci. 38:191–197. https://doi.org/10.1016/0301-6226(94)90170-8.

Li, M., K. F. Reed, M. R. Lauber, P. M. Fricke, and V. E. Cabrera. 2023. A stochastic animal life cycle simulation model for a whole dairy farm system model: Assessing the value of combined heifer and lactating dairy cow reproductive management programs. J. Dairy Sci. 106:3246–3267. https://doi.org/10.3168/jds.2022-22396.

McDougall, S., R. Castle, E. Blythe, Y. Macpherson, and A. Karkaba. 2021. Increasing conception rate by addition of a second prostaglandin injection in an Ovsynch and progesterone treatment programme for dairy cows not detected in oestrus before the start of the seasonal mating period. N. Z. Vet. J. 69:211–223. https://doi.org/10.1080/00480169.2021.1906343.

Meadows, C., P. J. Rajala-Schultz, and G. S. Frazer. 2005. A spreadsheet-based model demonstrating the nonuniform economic effects of varying reproductive performance in Ohio dairy herds. J. Dairy Sci. 88:1244–1254. https://doi.org/10.3168/jds.S0022-0302(05)72791-0.

Mohd Nor, N., W. Steeneveld, T. H. J. Derkman, M. D. Verbruggen, A. G. Evers, M. H. A. De Haan, and H. Hogeveen. 2015. The total cost of rearing a heifer on Dutch dairy farms: Calculated versus perceived cost. Ir. Vet. J. 68:29. https://doi.org/10.1186/s13620-015-0058-x.

Mohd Nor, N., W. Steeneveld, and H. Hogeveen. 2014. The average culling rate of Dutch dairy herds over the years 2007 to 2010 and its association with herd reproduction, performance and health. J. Dairy Res. 81:1–8. https://doi.org/10.1017/S0022029913000460.

Mohd Nor, N., W. Steeneveld, M. C. M. Mourits, and H. Hogeveen. 2012. Estimating the costs of rearing young dairy cattle in the Netherlands using a simulation model that accounts for uncertainty related to diseases. Prev. Vet. Med. 106:214–224. https://doi.org/10.1016/j.prevetmed.2012.03.004.

Nowicki, A., W. Barański, A. Baryczka, and T. Janowski. 2017. OvSynch protocol and its modifications in the reproduction management of dairy cattle herds—An update. J. Vet. Res. 61:329–336. https://doi.org/10.1515/jvetres-2017-0043.

Opsomer, G., Y. T. Grohn, J. Hertl, M. Coryn, H. Deluyker, and A. de Kruif. 2000. Risk factors for post partum ovarian dysfunction in high producing dairy cows in Belgium: A field study. Theriogenology 53:841–857. https://doi.org/10.1016/S0093-691X(00)00234-X.

Peter, A. T., P. L. A. M. Vos, and D. J. Ambrose. 2009. Postpartum anestrus in dairy cattle. Theriogenology 71:1333–1342. https://doi.org/10.1016/j.theriogenology.2008.11.012.

Pieper, L., M. G. Doherr, and W. Heuwieser. 2016. Consumers' attitudes about milk quality and fertilization methods in dairy cows in Germany. J. Dairy Sci. 99:3162–3170. https://doi.org/10.3168/jds.2015-10169.

Pursley, J. R., M. O. Mee, and M. C. Wiltbank. 1995. Synchronization of ovulation in dairy cows using $PGF_{2\alpha}$ and GnRH. Theriogenology 44:915–923. https://doi.org/10.1016/0093-691X(95)00279-H.

R Core Team. 2021. R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. Accessed Apr. 1, 2021. http://www.r-project.org/index.html.

Remmelink, G., H. J. Curth-van Dooren, J. van Middelkoop, W. Ouweltjes, and H. Wemmenhove. 2016. Handboek melkveehouderij. Chapter 6 in Handboek/Wageningen Livestock Research; No. 32. Wageningen University and Research, Wageningen, the Netherlands. https://doi.org/10.18174/391823.

Remnant, J. G., M. J. Green, J. N. Huxley, and C. D. Hudson. 2018. Associations between dairy cow inter-service interval and probability of conception. Theriogenology 114:324–329. https://doi.org/10.1016/j.theriogenology.2018.03.029.

Rendac. 2023. Kadavertarieven. Accessed Feb. 15, 2024. https://www.rendac.nl/faq/kadavertarieven.

Rhodes, F. M., S. McDougall, C. R. Burke, G. A. Verkerk, and K. L. Macmillan. 2003. Invited review: Treatment of cows with an extended postpartum anestrous interval. J. Dairy Sci. 86:1876–1894. https://doi.org/10.3168/jds.S0022-0302(03)73775-8.

Rial, C., A. Laplacette, and J. O. Giordano. 2022. Effect of a targeted reproductive management program designed to prioritize insemination at detected estrus and optimize time to insemination on the reproductive performance of lactating dairy cows. J. Dairy Sci. 105:8411–8425. https://doi.org/10.3168/jds.2022-22082.

Ricci, A., M. Li, P. M. Fricke, and V. E. Cabrera. 2020. Short communication: Economic impact among 7 reproductive programs for lactating dairy cows, including a sensitivity analysis of the cost of hormonal treatments. J. Dairy Sci. 103:5654–5661. https://doi.org/10.3168/jds.2019-17658.

Rutten, C. J., W. Steeneveld, C. Inchaisri, and H. Hogeveen. 2014. An ex ante analysis on the use of activity meters for automated estrus detection: To invest or not to invest? J. Dairy Sci. 97:6869–6887. https://doi.org/10.3168/jds.2014-7948.

Santos, J. E. P., H. M. Rutigliano, and M. F. S. Filho. 2009. Risk factors for resumption of postpartum estrous cycles and embryonic survival in lactating dairy cows. Anim. Reprod. Sci. 110:207–221. https://doi.org/10.1016/j.anireprosci.2008.01.014.

Santos, V. G., P. D. Carvalho, C. Maia, B. Carneiro, A. Valenza, P. M. Crump, and P. M. Fricke. 2016. Adding a second prostaglandin F2α treatment to but not reducing the duration of a PRIDsynch protocol increases fertility after resynchronization of ovulation in lactating Holstein cows. J. Dairy Sci. 99:3869–3879. https://doi.org/10.3168/jds.2015-10557.

Santos, V. G., P. D. Carvalho, C. Maia, B. Carneiro, A. Valenza, and P. M. Fricke. 2017. Fertility of lactating Holstein cows submitted to a Double-Ovsynch protocol and timed artificial insemination versus artificial insemination after synchronization of estrus at a similar day in milk range. J. Dairy Sci. 100:8507–8517. https://doi.org/10.3168/jds.2017-13210.

Souza, A. H., H. Ayres, R. M. Ferreira, and M. C. Wiltbank. 2008. A new presynchronization system (Double-Ovsynch) increases fertility at first postpartum timed AI in lactating dairy cows. Theriogenology 70:208–215. https://doi.org/10.1016/j.theriogenology.2008.03.014.

Stevenson, J. S. 2016. Synchronization and Artificial Insemination Strategies in Dairy Herds. Vet. Clin. North Am. Food Anim. Pract. 32:349–364. https://doi.org/10.1016/j.cvfa.2016.01.007.

Stevenson, J. S., and J. H. Britt. 2017. A 100-Year Review: Practical female reproductive management. J. Dairy Sci. 100:10292–10313. https://doi.org/10.3168/jds.2017-12959.

Stevenson, J. S., M. O. Mee, and R. E. Stewart. 1989. Conception rates and calving intervals after prostaglandin F2α or prebreeding progesterone in dairy cows. J. Dairy Sci. 72:208–218. https://doi.org/10.3168/jds.S0022-0302(89)79099-8.

Tippenhauer, C. M., J.-L. Plenio, A. M. L. Madureira, R. L. A. Cerri, W. Heuwieser, and S. Borchardt. 2021. Factors associated with estrous expression and subsequent fertility in lactating dairy cows using automated activity monitoring. J. Dairy Sci. 104:6267–6282. https://doi.org/10.3168/jds.2020-19578.

Uniform-Agri. 2024. Reproductive performance of dairy farms in the last 3 years in Europe. Accessed May 22, 2024. https://www.uniform-agri.com/blog/reproductive-performance-of-dairy-farms-in-the-last-3-years-in-europe/.

van der Laan, J. S. M., P. L. A. M. Vos, B. H. P. van den Borne, H. Aardema, and T. van Werven. 2021. Reproductive hormone use and its association with herd-level factors on Dutch dairy farms. J. Dairy Sci. 104:10854–10862. https://doi.org/10.3168/jds.2020-19786.

van Eerdenburg, F. J. C. M., D. Karthaus, M. A. M. Taverne, I. Merics, and O. Szenci. 2002. The relationship between estrous behavioral score and time of ovulation in dairy cattle. J. Dairy Sci. 85:1150–1156. https://doi.org/10.3168/jds.S0022-0302(02)74177-5.

Van Es, A. J. H. 1978. Feed evaluation for ruminants. I. The systems in use from May 1977-onwards in the Netherlands. Livest. Prod. Sci. 5:331–345. https://doi.org/10.1016/0301-6226(78)90029-5.

Wageningen Economic Research. 2023. Agricultural prices. Accessed Dec. 15, 2023. https://agrimatie.nl/Prijzen.aspx?ID=15125.

Wageningen Livestock Research. 2023. Feed value prices: Cattle. Accessed Dec. 15, 2023. https://www.wur.nl/nl/Onderzoek-Resultaten/Onderzoeksinstituten/livestock-research/Producten/Voederwaardeprijzen-Rundvee.htm.

Wicaksono, A., B. H. P. van den Borne, W. Steeneveld, T. van Werven, and H. Hogeveen. 2023. Hormone use for reproductive diseases and heat induction in relation to herd-level reproductive performance in Dutch dairy farms. Prev. Vet. Med. 211:105832. https://doi.org/10.1016/j.prevetmed.2022.105832.

Wijma, R., M. M. Pérez, M. Masello, M. L. Stangaferro, and J. O. Giordano. 2018. A resynchronization of ovulation program based on ovarian structures present at nonpregnancy diagnosis reduced time to pregnancy in lactating dairy cows. J. Dairy Sci. 101:1697–1707. https://doi.org/10.3168/jds.2017-13489.

Wilmink, J. B. M. 1987. Adjustment of test-day milk, fat and protein yield for age, season and stage of lactation. Livest. Prod. Sci. 16:335–348. https://doi.org/10.1016/0301-6226(87)90003-0.

ORCIDS

A. Wicaksono https://orcid.org/0000-0002-0682-9384
F. Edwardes https://orcid.org/0000-0002-7908-7596
W. Steeneveld https://orcid.org/0000-0002-8329-0466
B. H. P. van den Borne https://orcid.org/0000-0001-6248-4707
P. Pinho https://orcid.org/0000-0002-9664-3865
F. Randi https://orcid.org/0000-0001-6400-7429
H. Hogeveen https://orcid.org/0000-0002-9443-1412

APPENDIX A

Explanation on Calculating the Probability of Successful Pregnancy Based on Inchaisri et al. (2011a)

The probability of successful pregnancy was determined by the characteristics of each simulated cow using the final multivariable logistic regression model output from Inchaisri et al. (2011a). The output of that multivariable logistic regression is shown in Table A1. From that output, after correcting for cow characteristic parameters and interactions, the mean probability of successful pregnancy based on the number of inseminations was 0.45 (95% CI = 0.43–0.46), 0.42 (95% CI = 0.40–0.43), 0.41 (95% CI = 0.39–0.43), 0.38 (95% CI = 0.35–0.41), 0.33 (95% CI = 0.29–0.37), and 0.27 (95% CI = 0.21–0.34) for the first, second, third, fourth, fifth, and sixth insemination, respectively.

APPENDIX B

Hormone Protocols Specification

Four reproductive hormone protocols (Double-Ovsynch, Ovsynch, PRIDsynch, and estrus induction) were incorporated into the reproduction part of the simulation model. Figure 2 specifies details of each hormone protocol on the type of injections, its time order, and insemination strategy at the end of the protocol. The Ovsynch protocol was described in a previous study (Wijma et al., 2018). It is included in the current Dutch hormone use guideline (KNMvD, 2020) and represents the default hormone-based treatment. In this protocol, hormone treatment is followed by a FTAI on d 10. In the systematic hormone-based reproductive management programs, the Ovsynch protocol had an additional second prostaglandin injection 24 h after the first administration. The PRIDsynch protocol had a similar sequence compared with the Ovsynch protocol but with an additional intravaginal progesterone hormone implant (PRID Delta) inserted at the first 7 or 8 d of the protocol (Santos et al., 2016; Wijma et al., 2018; KNMvD, 2020). The Double-Ovsynch protocol, based on Santos et al. (2017), was modeled as a systematic reproductive management program, and ended with a FTAI on d 27. The last protocol represents the common Dutch herd reproductive management program and the estrus induction procedure with prostaglandin administration followed by an artificial insemination if estrus was detected during some time period (KNMvD, 2020).

Table A1. Output of the multivariable logistic regression analysis on parameters affecting the probability of successful pregnancy (Inchaisri et al., 2011a)[1]

Variable	*B*	SE	*P*-value
Intercept	−0.30		
A serial number of inseminations			<0.01
The first insemination	Referent[a]	—	—
The second insemination	0.13[b]	0.06	<0.05
The third insemination	0.08[b]	0.08	NS[2]
The fourth insemination	−0.02[c]	0.12	NS
The fifth insemination	−0.37[d]	0.18	<0.05
The sixth insemination	−0.76[d]	0.29	<0.01
Parity			<0.01
Parity 1	0.21[a]	0.05	<0.01
Parity 2	0.15[a]	0.05	<0.01
Parity 3	0.11[a]	0.06	<0.05
Parity 4	0.03[a]	0.06	NS
Parity ≥5	Referent[b]	—	—
Breed[3]			
100% HF	Referent[a]	—	—
50% to <100% HF	0.09[b]	0.01	<0.01
51% to 100% MRY	0.22[c]	0.04	<0.01
Others	0.37[d]	0.06	<0.01
Last calf[3]			<0.01
Female	Referent[a]	—	—
Male	−0.05[b]	0.01	<0.01
Twin	−0.16[c]	0.04	<0.01
Still birth	−0.28[d]	0.03	<0.01
Season of insemination			NS
Spring	0.02[a]	0.04	NS
Summer	−0.05[b]	0.05	NS
Autumn	0.04[a]	0.04	NS
Winter	Referent[c]		
Time of inseminations related to time of peak milk			
Insemination before peak yield	−0.28[a]	0.03	<0.01
Insemination after peak yield	Referent[b]	—	—
DIM at insemination date (d)	0.005	0.001	<0.01
Daily milk yield at insemination date (kg)	−0.00009	0.00002	NS
Interaction			
Daily milk yield at insemination date × DIM	−0.00007	0.00003	<0.01
Season of insemination × DIM			<0.01
Spring × DIM	−0.0006	0.0003	<0.1
Summer × DIM	−0.0011	0.0003	<001
Autumn × DIM	−0.001	0.0003	<0.01
Winter × DIM	Referent	—	—
A serial number of inseminations × DIM			<0.01
The first insemination × DIM	Referent	—	—
The second insemination × DIM	−0.0022	0.0006	<0.01
The third insemination × DIM	−0.0021	0.0006	<0.01
The fourth insemination × DIM	−0.0022	0.0007	<0.01
The fifth insemination × DIM	−0.0011	0.0009	NS
The sixth insemination × DIM	−0.0001	0.0012	NS
Parity × DIM			<0.05
Parity 1 × DIM	−0.0007	0.0004	<0.1
Parity 2 × DIM	−0.0001	0.0004	NS
Parity 3 × DIM	0.0003	0.0004	NS
Parity 4 × DIM	0.0006	0.0005	NS
Parity ≥5 × DIM	Referent	—	—

[a–d]Indicate significant ($P < 0.05$) differences of estimated mean probabilities of successful inseminations between parameter classes after adjusting for other parameters in the final multivariable model.

[1]The ratio of generalized chi-squared statistic and its df equals 1.00 and estimated coefficients (b), SE for the coefficient and significant level are given for each cow-specific factor. HF = Holstein Friesian; MRY = Dutch Red-and-White.

[2]NS = nonsignificant.

[3]In this simulation model 100% HF breed, and half male and half female calf for the last calf were assumed.