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Determining the optimal replacement and culling strategy for dairy cows affected by lameness

Sarah Taheri¹, Reza Seyedsharifi^{1*}, Jamal Seifdavati¹, Nemat Hedayat¹, Hossein Abdi-Benemar¹, Abdelfattah Zeidan Salem²

¹Department of Animal Sciences, Faculty of Agriculture and Natural Resources, University of Mohaghegh Ardabili, Ardabil, Iran

²Investigador, Depto. de Nutrición Animal, Facultad de Medicina Veterinaria y Zootecnia, Universidad Autonoma del Estado de México, Estado de México; email: salem@uaemex.mx

*Corresponding author,
E-mail address:
reza_seyedsharifi@yahoo.com

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ORCID

Sarah Taheri
0009-0006-8523-0893
Reza Seyedsharifi
0000-0003-4593-2058
Jamal Seifdavati
0000-0001-6794-4450
Nemat Hedayat
0000-0002-6802-6739
Hossein Abdi-Benemar
0000-0001-5318-4585
Abdelfattah Zeidan Salem
0000-0001-7418-4170

Abstract Lameness is considered the third leading cause of reduced productivity and economic losses in dairy herds, after reproductive disorders and mastitis. The objective of this study was to quantify the economic impact of lameness and determine the optimal herd life and replacement strategy for dairy cows with different production levels using a bio economic optimization model. This study was conducted using data collected from several large industrial dairy farms in Ardabil Province, Iran. A systems analysis approach was employed to decompose the dairy herd economic system into its income and cost components. Subsequently, a bio economic model was developed and simulated using mathematical modeling techniques, and optimization was performed using the Compecon toolbox in MATLAB. Dairy cows were classified according to production level into low-, medium-, and high-producing groups and according to lameness status into healthy, subclinical, and clinical lameness categories. An objective function was defined to maximize the present value of net income generated by a cow and its replacement heifer. The results showed that healthy cows were predominantly represented in the low-producing group, cows with subclinical lameness were more common in the medium-producing group, and cows with clinical lameness were primarily found among high-producing cows. Lameness reduced milk production by 0.16, 0.57, and 0.88 kg per cow per day in low-, medium-, and high-producing cows, respectively. Corresponding cumulative milk yield losses over the study period were estimated at 45, 84, and 66 kg per cow. According to the model results, the present value in the low-producing group increased until the fourth calving and declined thereafter. In contrast, although present value generally decreased with increasing parity in the medium- and high-producing groups, retaining cows remained economically optimal up to the seventh and eighth calving, respectively. The optimal culling and replacement decisions were similar across different lameness statuses within each production level. Furthermore, future economic value was influenced by age, production level, and stage of lactation. The average optimal herd life was estimated to be 4.69 years. Based on this value, the annual replacement rate was calculated at 21.32%, using the inverse of the optimal herd life.

Keywords: dairy cow, economic evaluation, lameness, dynamic programming

Introduction

Lameness is one of the most significant health and welfare challenges in dairy cattle worldwide. Beyond its detrimental effects on animal welfare, lameness has substantial economic consequences due to reduced milk

production, impaired reproductive performance, increased treatment and labor costs, and a higher risk of premature culling. Consequently, effective management of lameness is essential not only for improving animal well-being but also for enhancing the economic

sustainability of dairy production systems. Today, dairy cows are more exposed to the negative effects of environmental and management challenges. Lameness is considered one of the most important factors of economic losses in dairy herds, which is currently one of the biggest challenges facing this industry worldwide Robinson et al. (2002). Lameness is a common problem in dairy cattle and is a multifactorial condition influenced by infectious, nutritional, environmental, and management-related factors. It can result in reduced milk production, impaired reproductive performance, and an increased risk of culling, thereby imposing substantial economic losses on dairy producers (Patoliya et al., 2024; Tsousis et al., 2022). The economic loss of a disease is primarily due to the complications that the disease has on production and productivity, and treatment costs are a later stage. The impact of lameness in dairy cattle is significant not only on production performance but also on economic indicators and animal welfare. This condition is the third cause of economic losses in dairy cattle herds after infertility and mastitis. Given that lameness ranks third in causing economic losses in the dairy cattle industry, its impact on direct costs (drug treatment, veterinary costs and culling) and indirect costs (reduced milk production, reduced reproductive performance and reduced age of herd animals) is considered much less than it should be (Baran and Kamiloğlu, 1997). The majority of economic losses are related to the complications of lameness in the herd (not treatment costs). On average, in a case of lameness, 82% of the losses are related to reduced fertility and milk production, and only 1% is related to veterinary costs. The greatest economic loss from lameness is due to premature culling of the animal (Enting et al., 1997; Dolecheck and Bewley, 2018). Today, the economic loss of diseases in the herd is not only related to treatment costs, but all costs incurred to prevent a disease and losses that cause reduced production, culling and replacement of new animals in the herd, and other such losses are included in the calculation of losses.

In general, the profitability of dairy herds is related to feed costs and income from milk sales and calf or heifer sales (Hultgren et al., 2011). In most dairy herds, decisions regarding cow culling and replacement are primarily based on farmers' experience and personal judgment, and in many cases lack a structured plan founded on economic principles. When culling and replacement decisions are not made at the optimal time, and cows are removed from the herd either earlier or later than economically justified, herd profitability is adversely affected. The productive herd life of dairy cows is influenced by numerous factors, including age, stage of lactation, health status, reproductive performance, and management practices. Improving these factors can reduce culling rates, increase cow longevity within the herd, and ultimately enhance farm profitability. Conversely, premature culling and frequent replacement of cows impose substantial costs on the dairy industry.

Therefore, implementing appropriate management strategies to extend the economic herd life of dairy cows is of considerable importance. The most important cost that the culling process brings to a livestock unit is the purchase of replacement heifers, which is considered the most important factor in the cost of livestock farms after the costs related to feeding. One of the models used in simulation is mathematical modeling, in which the relationship between a series of variables and parameters in the system is defined using mathematical relationships. Mathematical models are divided into two types of dynamic and static models in terms of the time of occurrence of phenomena. In animal science, simulation has been widely used in dairy herd management, examining the economic performance of the production system, and evaluating genetic improvement and advancement programs, and much research has been conducted in these cases, since dairy cattle breeding is a complex system that includes genetic, nutritional, management factors and their interactions. And this complexity may make it difficult to accurately estimate the profitability of the system, so the most appropriate method is the bioeconomic model, which uses a set of mathematical equations. Dynamic models are models that consider time-varying events in a system and examine the relationships between system components and their changes over time (Cardoso et al., 1999; Sarttra and Kiatcharoenpol, 2025).

Dynamic programming is used to optimize production systems. This method makes the biological cycle of lactation and reproduction and management decisions of dairy farms dynamic and reversible, in which decisions are time-dependent. This programming obtains future cash flows for different states of each cow (Warner et al., 2022; Kennedy, 1986). The novelty of this study lies in the integration of lameness-related biological and economic consequences into a bio economic optimization model for dairy herd management. While previous studies have mainly focused on estimating the direct economic losses associated with lameness, the present research extends this approach by evaluating optimal culling and replacement decisions under different production levels and lameness statuses. In addition, the model was calibrated using data obtained from commercial dairy farms in Ardabil Province, providing region-specific estimates of optimal herd life, replacement rates, and the economic impact of lameness. Therefore, this study offers a practical decision-support framework for improving herd profitability and management efficiency in dairy production systems.

Materials and methods

Ethical statement

This study does not present any ethical concerns.

Dataset

This study was based on data collected from several large herds of dairy cows in industrial dairy farms in

Ardabil province. The mentioned dairy farms are recorded by the National Livestock Breeding Center, so the required data were collected from the National Livestock Breeding Center data set or by questionnaire from the dairy farms. The source of data used as input parameters of the model is based on market conditions in 2021. A systems analysis approach was employed to identify and separate the revenue and cost components of the dairy herd economic system. Total farm revenue was calculated using the following equation:

$$R = R_{milk} + R_{male\ calves} + R_{cows_age} + R_{culled\ heifer}$$

where R_{milk} represents revenue from milk sales, $R_{male\ calves}$ represents revenue from the sale of male calves, R_{cows_age} denotes revenue from culled cows, and $R_{culled\ heifer}$ represents revenue from the sale of surplus heifers. Total costs were calculated as follows:

$$C = (C_{Mmale\ calves} + C_{Fheifers} + C_{Hheifers} + C_{Rheifers} + C_{Iheifer} + C_{Mcullled\ heifers} + C_{Fcows} + C_{Hcows} + C_{Rcows} + C_{lcows} + C_{Mmilk} + C_{Mcows-age} + fixedcosts)$$

where $C_{Mmale\ calves}$ is the marketing cost of male calves; $C_{Fheifers}$ is the total feeding cost of heifers from birth until first calving; $C_{Hheifers}$ is the total health-related cost of heifers; $C_{Rheifers}$ is the reproductive cost of heifers; $C_{Iheifer}$ is the labor cost associated with heifers; $C_{Mcullled\ heifers}$ is the marketing cost of surplus heifers; C_{Fcows} is the feeding cost per cow; C_{Hcows} is the health-related cost per cow; C_{Rcows} is the reproductive cost per cow; C_{lcows} is the labor cost per cow; C_{Mmilk} is the milk marketing cost; $C_{Mcows-age}$ is the marketing cost of culled cows; and Fixed Costs represent the fixed costs of the production unit. Using the MATLAB programming language, an algorithm was designed to simulate the bio-economic system of the dairy herd (Table 1). Profit per cow per year (riyals) was defined as follows (Kahi and Nitter, 2004).

$$P = R_i - C_i$$

In this equation, P : annual profit per head of breeding cattle. R_i is the annual income per head of breeding cattle and C_i is the annual cost per head of breeding cattle.

In this study, a stochastic dynamic programming method was used to make optimal decisions for maintaining or replacing dairy cows. Optimization techniques require models that must be run multiple times to achieve the optimal solution. In this study, the planning horizon was 10 lactations. Each lactation was considered as a stage for decision-making. At each stage, dairy cows were classified by state variables including production capacity at 3 levels (low, medium and high production) and lameness status at three levels with normal, subclinical lameness and clinical lameness. Finally, an objective function was defined to maximize the present value of net income from the current cow and its replacement heifer (Cha et al., 2010).

To express the state variables, the state vector S_t was defined as follows:

$$S_t = [S_t^{parity}, S_t^{prod}, S_t^{lamin}]$$

In this vector, the number of lactation periods is characterized by S_t^{parity} a value ranging from 1 to 10. Since in the last lactation period, the cow is voluntarily replaced and the value of such a cow is obtained from the slaughter value, the value of the system at the end of the planning horizon can be considered zero because it has no effect on the decision-making process. Production capacity is characterized by S_t^{prod} a value that includes three states. 1 is for low production, 2 is for medium production, and 3 is for high production, and the characteristic is related to S_t^{lamin} the lameness state, which includes normal, subclinical, and clinical. According to studies conducted by Sprecher et al. (1997), the appearance of the cow's spine (backline) is the most important factor in diagnosing and grading cow movement problems, such that a straight backline in standing and moving positions indicates a score of 1, a slight curvature during movement and being straight in standing positions indicates a score of 2, and a curvature in both standing and moving positions indicates a score of 3 for cows.

Table 1. Biological and economic parameters used for modeling

Variable	Amount
Birth weight (kg)	36.6
Adult body weight (kg)	600
Daily weight gain before weaning (gr)	750
Daily weight gain after weaning (gr)	695
Survival rate before weaning (%)	0.95
Survival rate after weaning (%)	0.98
Survival rate at 24 hours after birth (%)	0.98
Calving interval (days)	450
Age at first calving (days)	1016
Productive lifespan (days)	1460
Milk production per cow per year (kg)	7200
Fat production per cow per year (kg)	230.4

To determine scores 4 and 5, in addition to the curvature of the backline, the position of the steps and leg movements are used. A score of 1 indicates normal condition, a score of 2 indicates uneven gait, a score of 3 indicates mild lameness, a score of 4 indicates moderate lameness, and a score of 5 indicates severe lameness. Generally, scores of 2 and 3 indicate subclinical lameness in the herd, while cows with scores of 4 and 5 indicate clinical lameness (Table 2).

The following relationship was used for the optimal decision:

$$V_t(s_t) = \max_{at} \{ \sum_k P(K_t) [R_t(s_t, a_t) + \delta V_{t+1}(s_{t+1}, a_t)] \}$$

$$t = T - 1, T - 2, \dots, 1$$

$$\sum_K P_t(k_t) = 1$$

$$V_T(S_T) = F(S_T)$$

In this regard, $V_t(s_t)$ the maximum expected value of the objective function over the planning horizon under

the optimal replacement policy is in the state s_t and lactation period (t). If the decision is made to keep or replace the livestock and the probability of transferring the random variables (production and lameness) $P(K_t)$ is, the efficiency of lactation period (t) will be as $R_t(s_t, a_t, k_t)$. In addition, the system during lactation (t+1) is transferred to state of $V_{t+1}(s_{t+1}, a_t, k_t)$. T is the length of the planning horizon and is equal to the maximum number of possible lactation periods in the model and δ is the discount rate.

Table 2. Movement score of the studied cows

Movement score	Percentage	Animal condition
1	52.45	Healthy
2	31.43	Subclinical lameness
3	12.37	Subclinical lameness
4	2.55	Clinical lameness
5	1.2	Clinical lameness

Statistical analysis

The probability of transitioning from one stage to the next of lameness states was investigated using data on lameness status in each lactation period and calculating the probabilities of each state in each lactation period using logistic regression. In this study, the GENMOD procedure of SAS software was used to estimate the probabilities of each lameness state.

Logistic regression is a widely used statistical method for modeling discrete dependent variables. When the response variable is binary, this approach is applied to estimate the probability of occurrence of each outcome. In this model, the effects of independent variables on a binomial dependent variable are described using a generalized linear model (GLM) with a logit link function. The primary objective of logistic regression is to estimate the probability that an observation belongs to a particular category. If z denotes the explanatory variable and P represents the probability of occurrence of the response variable, the logistic model can be expressed as follows, where α and β are the intercept and regression coefficient parameters, respectively:

$$\log it(P) = \alpha + \beta'Z = \log[p_i / (1 - p_i)]$$

$$p_i = e^{(\alpha + \beta'z)} / [1 + e^{(\alpha + \beta'z)}]$$

To estimate the amount of production loss and economic loss due to lameness, the percentage of cows

at each locomotion score and in each herd was determined and the information was entered into the Loss-Calculator software, which reports the results including the amount of production loss daily for each cow and for the entire herd and the economic loss daily and monthly for the entire herd (Shahinfar et al., 2021). Future value (FV) was also calculated according to the following equation. In this relation, PV is the present value, r is the interest rate in the period, and n is the number of periods in the future:

$$FV = PV(1 + r)^n$$

Results and discussion

Two types of relationships between the occurrence of lameness and milk production are possible. On the one hand, low milk production may be a consequence of lameness, and on the other hand, lower production may have a protective effect against lameness. Most healthy cows, cows with subclinical lameness, and cows with clinical lameness are in the low-producing, medium-producing, and high-producing groups, respectively. This reflects the fact that high-producing cows are more susceptible to lameness due to the metabolic pressures of high production (Robinson and Juarez, 2002). This is because high concentrate feeding in high-producing cows causes acidosis and an increase in lactic acid in the rumen, which is absorbed through the bloodstream and affects the capillaries of the hoof wall, causing lameness (Elmhadi et al., 2022). Also, since most of the cows studied have a high prevalence of subclinical lameness, this indicates that if this issue is not addressed, the possibility of their transformation into clinical lameness is very likely. Therefore, in addition to improving management issues, more attention should be paid to the factors causing this disease, such as diet formulation, bedding conditions, livestock density in the stall, etc. (Table 3).

Economic study of dairy farms can lead to better identification of the situation of these units and increase the level of awareness of policy makers and agricultural planners to make principled decisions or solve existing problems, and this approach provides a suitable perspective for livestock farmers to make better decisions by better identifying the strengths and weaknesses in dairy cattle breeding.

Table 3. The relationship between production level, locomotion score, and the probability of occurrence of subclinical and clinical lameness

Lameness severity	Movement score	Low production	Average production	High production
Healthy	1	55.1	24.3	28.5
Subclinical	2	27.44	38.55	34.55
	3	23.28	42.26	38.47
	Total	50.72	80.81	37.02
Clinical	4	1.76	2.35	3.94
	5	1.24	1.64	3.34
	Total	3	3.99	7.28

The reduction in milk production for low-, medium-, and high-producing cows was estimated at 0.16, 0.57,

and 0.88 kg per cow per day, respectively, and 45, 84, and 66 kg per day for the fresh-cow group (i.e., the

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grouped early-lactation cohort housed in the fresh-calving pen). Overall, the total reduction in milk production across the studied herds was 195 kg per day and 5,850 kg per month. Considering a milk price of 250,000 Rials per kilogram, the resulting economic losses were estimated at 48,750,000 Rials per day and 1,462,500,000 Rials per month (Table 4).

Lameness cows suffer from reduced milk production, weight loss, poor reproductive performance, increased treatment costs, and early culling in poorly maintained

herds (Boujenane et al., 2017). Lame cows are fed later than other cows, and therefore have a significant loss in quality and quantity of feed compared to cows that have earlier access to feed, resulting in weight loss. Given the importance of subclinical lameness and the economic losses it causes, in addition to improving management issues, special attention should be paid to factors that predispose cattle to lameness, such as feed composition and preparation methods, bedding conditions, and stocking density.

Table 4. Production loss and economic loss due to lameness using Loss-Calculator software

Paddock	Production reduction (kg)		Economic loss (Rials)			
	Cow per day	Paddock per day	Cow per day	Paddock per day	Paddock per month	Paddock per year
Low production	0.16	45	40000	11250000	337500000	4050000000
Average production	0.57	84	142500	21000000	630000000	7560000000
High production	0.88	66	220000	16500000	495000000	5940000000

The expected present value of each animal is given in Figure 1. Each of these numbers represents the value of the objective function in dynamic programming. If the expected present value of a dairy cow in the herd is less than a heifer, a decision to replace it is made. Otherwise, the dairy cow will remain in the herd for at least one more period until a decision is made for it at the beginning of the next period. According to the results of the model under study, in the low-production group, the present

value increases until the fourth calving, then it starts to decrease. In the medium and high-production groups, the present value starts to decrease, which is economically justified in the medium-production group until the seventh calving and in the high-production group until the eighth calving. It is also observed that the optimal decision is the same at each production level for different lameness conditions.

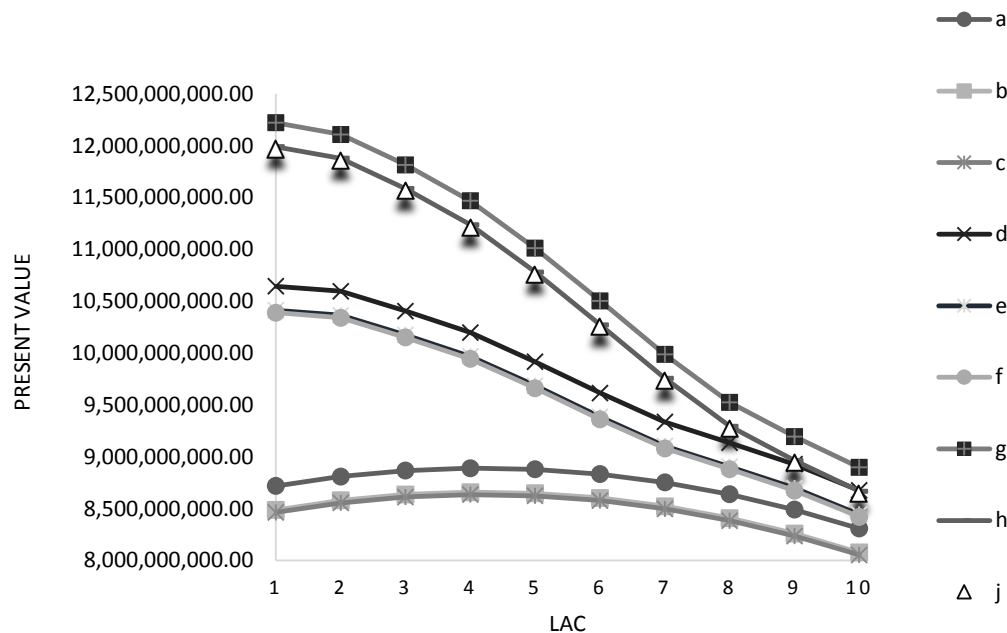


Figure 1. Expected present value for different production and lameness statuses in different lactation periods (million Rials) a = Low milk production + Normal; b = Low milk production + Subclinical lameness; c = Low milk production + Clinical lameness; d = Moderate milk production + Normal; e = Moderate milk production + Subclinical lameness; f = Moderate milk production + Clinical lameness; g = High milk production + Normal; h = High milk production + Subclinical lameness; i = High milk production + Clinical lameness; j = High milk production + Clinical lameness.

When a producer wants to decide to retain or replace a cow, it is necessary to compare the benefits and expected future income for maintaining or replacing the animal with another animal. The profit that a cow is likely to generate in the future varies during different lactation periods. Future value means a cash or asset at a specific date in the future that has a value equal to a specific

amount in the present. Therefore, with changes in age and production level and lactation stage, future value also changes. Also, in high-producing cows that had high future value, future value increased as the cow aged and became older (Figure 2). Figure 3 shows the difference between future value and present value under a 20% discount rate for different lameness situations, which represents the annual benefit.

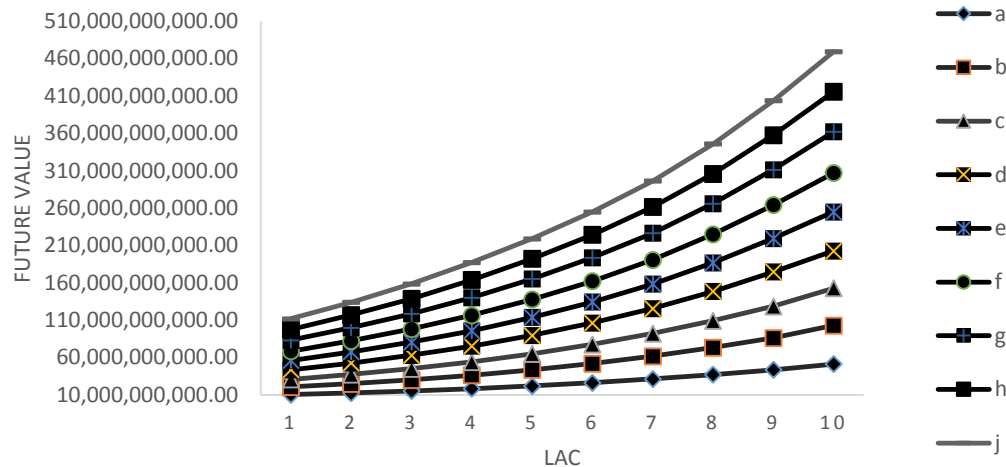


Figure 2. Future value changes for different production and lameness statuses in different lactation periods (million Rials) a = Low milk production + Normal; b = Low milk production + Subclinical lameness; c = Low milk production + Clinical lameness; d = Moderate milk production + Normal; e = Moderate milk production + Subclinical lameness; f = Moderate milk production + Clinical lameness; g = High milk production + Normal; h = High milk production + Subclinical lameness; j = High milk production + Clinical lameness.

The difference between present value and future value increases with increasing production level. Therefore, as the age of the cow and the lactation period or calving period increase, the annual benefit also increases. The method of calculating the annual benefit is as follows: if the net present value of a low-producing cow in the first lactation period in the lameness model is assumed to be 8717313073.2 Rials and its future value will be 10,460,775,687.84 Rials one year later, then the annual benefit of the cow is equal to 1,743,462,614.64 Rials. Sorting the existing dairy herd can be a suitable solution, relying on the future income and cost of production in estimating the expected net present value. This method means that each cow should be kept or replaced with a heifer. If replacement is done later or earlier than the due date, without paying special attention to their present and future value, it will reduce the overall benefit of the dairy herd (Figure 3).

Sensitivity analysis is an essential component of the economic evaluation of breeding programs and livestock decision-support models, as it assesses the extent to

which model outcomes are affected by changes in economic and non-economic parameters. In this approach, each parameter is varied individually while all other model parameters are held constant, allowing its independent effect on the output variables to be evaluated. The results are typically expressed as the percentage change in model outputs relative to the percentage change in input parameters, enabling the relative importance of individual parameters to be identified and ranked. The primary objective of sensitivity analysis is to evaluate the robustness of the optimal solution under potential changes in model parameters and to identify those variables that exert the greatest influence on model outcomes. Identifying such sensitive parameters not only improves the accuracy of parameter estimation but also facilitates the selection of solutions that remain reliable under varying economic conditions. In the present study, sensitivity analysis was conducted to evaluate the response of the model to changes in key economic variables. Specifically, the effects of a 10% increase and decrease in milk price, replacement heifer

price, and discount rate on the optimal average herd

herd life and replacement rate were assessed.

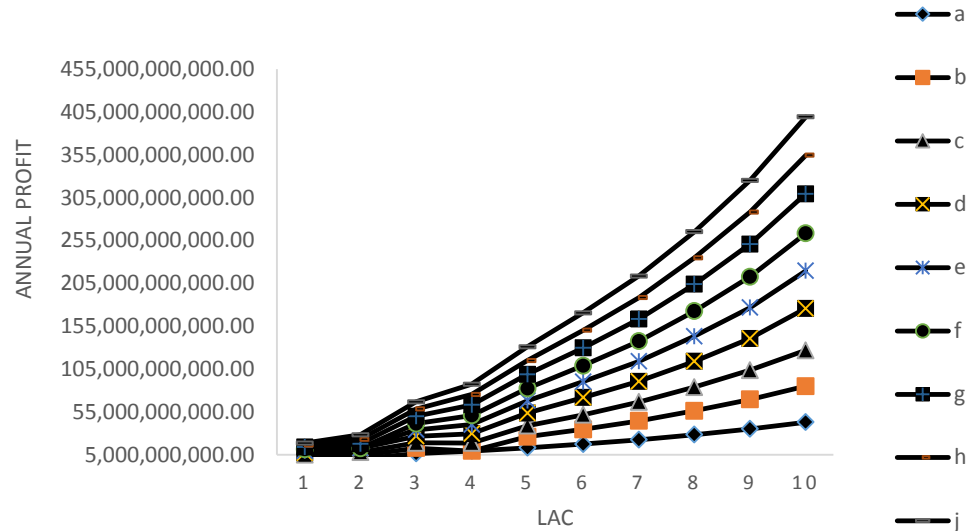


Figure 3. Annual profit per lactation period for different production and lameness statuses in different lactation periods (million Rials) a = Low milk production + Normal; b = Low milk production + Subclinical lameness; c = Low milk production + Clinical lameness; d = Moderate milk production + Normal; e = Moderate milk production + Subclinical lameness; f = Moderate milk production + Clinical lameness; g = High milk production + Normal; h = High milk production + Subclinical lameness; j = High milk production + Clinical lameness

The average optimal herd herd life is the time interval between first calving and culling. The difference in the values of the optimal herd herd life is due to the difference in market conditions at the time of each of these studies. The annual replacement rate is obtained by reversing the optimal herd herd life, which is equal to the sum of the mandatory and voluntary culling rates. As a result, the relationship between the optimal herd life and the replacement rate is an inverse relationship, and as the optimal herd life increases, the replacement rate decreases. Because costs and revenues occur at different points in time, their values cannot be directly compared without accounting for the time value of money. Therefore, a discount rate was applied to convert all future cash flows into their present values. In the present model, changes in the discount rate affected economic outcomes through the discount factor, which determines the present value assigned to future revenues and costs. The process of converting future cash flows into equivalent current values is known as discounting, and the interest rate used for this purpose is referred to as the discount rate. The discount factor serves as a weighting coefficient that translates future benefits and expenses into present values. Consequently, a higher discount rate reduces the present value of future cash flows, whereas a lower discount rate increases the relative importance of future revenues and costs in economic decision-making. Factors such as heifer price, discount factor, and milk price cause changes in the optimal herd herd life. It should be noted that the discount rate is inversely related to the discount factor. Fluctuations in milk price and the

cost of replacement have an overall impact on the decision to replace optimally.

According to Table 5, with an increase in the discount factor (decrease in the discount rate), the optimal herd life decreases, causing older cows to be culled more than younger cows and the percentage of cull cow's increases. As the discount rate decreased (and consequently the discount factor increased), the optimal herd life decreased.

It should be noted that reducing the discount rate requires creating stability in the overall structure of the economy of each country. There is an inverse relationship between the price of milk and the optimal herd life of the herd. Since the objective of the model is to maximize the profit generated by dairy cows over their economic lifetime, the net present value (NPV) of a cow remaining in the herd is compared with that of a replacement heifer at the end of each period Owusu-Sekyere et al. (2024). When milk price decreases, the expected future revenues from milk production decline, resulting in a lower net present value of the cow in the herd. Under such circumstances, it becomes more difficult to recover the cost of replacement because the cost of purchasing or raising a replacement heifer represents a larger share relative to the expected economic returns from either retaining or replacing the cow. Consequently, changes in milk price can influence replacement decisions and ultimately affect the optimal economic herd life of dairy cows within the herd., which is consistent with the results of Kalantari et al. (2010). While with an increase in the price of heifers, the optimal herd life also increases because fewer cows are culled,

indicating a direct relationship between these two factors. According to the research of Han et al. (2024),

the optimal herd life also decreased with a decrease in the price of heifers.

Table 5. Effects of 10% changes in parameters affecting the percentage of removal on the optimal herd life and replacement rate in lameness

Parameters	Percentage of changes	Optimal herd life (years)	Replacement rate (%)
Baseline scenario		4.69	21.32
Heifer price	+10	4.83	20.70
	-10	4.33	23.09
Milk price	+10	4.33	23.09
	-10	4.69	21.32
Discount rate	+10	4.80	20.83
	-10	4.31	23.20

Conclusion

Early detection and prevention of lameness should be prioritized, as lameness significantly reduces milk production and overall herd profitability. Culling and replacement decisions should consider both production level and expected future economic value rather than relying solely on current milk yield. High-producing cows may remain economically profitable for a longer period despite a higher prevalence of lameness; therefore, management decisions should be based on comprehensive economic evaluations. Maintaining an appropriate replacement strategy can improve herd profitability by balancing replacement costs and future production returns. Changes in milk prices, replacement heifer prices, and discount rates can substantially influence optimal herd life; therefore, replacement policies should be periodically reviewed under changing market conditions. Bio economic models can serve as useful decision-support tools for optimizing herd life, replacement rates, and overall economic performance in dairy farms.

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Ethical Statement

This article was extracted and analyzed from data on animal breeding and genetic management. It did not require obtaining a code of ethics or working directly with animals.

Declaration of Generative Artificial Intelligence (AI)

The article and tables and figures were not written/created by AI and AI assisted technologies.

Conflict of Interest

The authors declare that when conducting their search, there was no business or financial relationships that may be interpreted as constituting a conflict of interest.

Data Availability Statement

All data and materials are available.

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