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# Decision making on dry cow therapy: Economic evaluation using field data under Argentinian production conditions

## Tomada de decisão sobre terapia de vaca seca: Avaliação econômica usando dados de campo sob condições de produção argentinas

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### ABSTRACT

The cow somatic cell count (CSCC) is an indicator of intramammary infection (IMI), and it has been used to make decisions at dry-off about selective dry cow therapy (SDCT). This study assessed ex-ante the economic impact of implementing SDCT under milk production conditions in Argentina, using CSCC to identify cows with IMI at dry-off. Eighty six cows were sampled at dry-off and considered being infected if at least one quarter was infected with major mastitis pathogens. The CSCC sensitivity and specificity were estimated using the CSCC recorded from the test-day prior to dry-off. A simulation model was then developed to look into the economic benefits of applying SDCT under two herd level IMI prevalence (low: 5-15%, and high: 16-25%) at dry-off. The input variables were obtained from the field study, scientific literature, and real-world prices. The output was the net economic difference (NED) between SDCT and blanket dry cow therapy at the herd level. The sensitivity and specificity estimated for identifying cows infected with major pathogens for a CSCC threshold of 200,000 cells/mL were 31.4 (95% CI, 14.6-48.2) and 64.7 (95% CI, 50.6-78.8), respectively; the value for NED was maximized to -634 US$ and -455 US$ in the low and high IMI prevalence, respectively. In general, CSCC specificity was the variable with the most impact on NED and, in high IMI prevalence, milk price had a similar relevance. Thus, SDCT based on CSCC is a cost-effective option, under the milk production conditions in Argentina.

**Index terms**: Antibiotics; intramammary infection; net economic difference; selective dry cow therapy; somatic cell count.

### RESUMO

A contagem das células somáticas por vaca (CCSV) é um indicador da infecção intramamária (IIM). A CCSV tem sido usada para decidir o tratamento com antibiótico no esquema de terapia seletiva de vacas secas (TSVS). O estudo avaliou ex-ante o impacto econômico da implementação do TSVS nas condições de produção da Argentina, usando a CCSV para identificar IIM na secagem. Foram coletadas amostras do leite de 86 vacas no momento da secagem para determinar IIM com os principais patógenos associados à mastite. A sensibilidade e especificidade da CCSV foram estimadas através dos dados obtidos no controle do leite antes da secagem. Foi desenvolvido um modelo de simulação para determinar os benefícios econômicos da aplicação do TSVS em dois cenários de prevalência de IIM (baixo: 5–15%; alto: 16–25%). O resultado do modelo foi a diferença econômica liquida (DEL) entre TSVS e a terapia em massa no nível do rebanho. A sensibilidade e especificidade estimadas para identificar vacas infectadas com os principais patógenos para um valor limite de 200.000 células/mL na CCSV foram de 31,4 (95% IC, 14,6-48,2) y 64,7 (95% IC, 50,6-78,8), respectivamente. O DEL máximo foi de US$ -635 e US$ 455 nos cenários de prevalência baixa e alta, respectivamente. Em forma geral, a especificidade da CSCC foi a variável de maior impacto sobre o DEL e no cenário de alta prevalência de IIM o preço do leite teve relevância semelhante. Portanto, o TSVS baseado em CCSV é uma opção econômica nas condições de produção na Argentina.

**Termos para indexação**: Antibiótico; infecção intramamária; diferença econômica líquida; terapia seletiva de vacas secas; contagem de células somáticas.

## INTRODUCTION

Dry cow therapy (DCT) is an antibiotic-based treatment applied in dairy herds at dry-off, to cure existing intramammary infections (IMI) and preventing new ones during the dry period (Halasa et al., 2009; Halasa et al., 2009b). In the last decade, antibiotic resistance is regarded as a serious global public health threat (World Health Organization - WHO, 2015), which has led to introducing selective DCT instead of blanket DCT (McCubbin et al., 2022).

Selective DCT has been found to be more economically beneficial when carried out in herds with low IMI prevalence (Scherpenzeel et al., 2016). Additionally, its implementation should not be considered alone but as part of a comprehensive udder health management program, including practices such as post-dipping and proper treatment of clinical mastitis cases (Ruegg, 2017). Adoption of DCT is variable among South American countries, and some concerns have been raised about the erratic adoption of comprehensive udder health programs (Vissio et al., 2013; Vissio; Bouman; Larriestra, 2018). In a recent national survey about the production conditions in Argentina showed that between 101 and 200 ha is the area with the highest frequency among the dairy farms (43%); the stratum with 101 to 250 dairy cows is the largest (44.1%) with an average of 141 lactating cows per farm; and approximately the 80% of the farms were pasture-based systems (Engler et al., 2022). Although the most producers applied DCT in a survey that included producers from this herd size stratum (Vissio et al., 2013), to the best of our knowledge, there are no reports in Argentina on the degree of implementation of selective DCT.

As a management tool, the economic evaluation of adoption of selective DCT depends on how much it may reduce the costs associated with the total amount of antibiotics used. The cost of leaving cows untreated at dry-off and thus of facing further udder health issues in the next lactation is also a decisive factor. Once these two cost components have been taken into consideration, the final economic result will be influenced mainly by control expenditures and the accuracy with which cows are individually chosen to be treated at dry-off.

Diagnostic tests based on microbiological cultures (Vasquez et al., 2018), somatic cell counts (SCC) (Lipkens et al., 2019) and enzymes (Rowe et al., 2020), among others, can be used at dry-off to screen candidates for antibiotic treatment. The SCC is a practical and often easily accessible parameter to assess udder health (Schukken et al., 2003). Although the monthly reports of test-day SCC values can lead to the following screening errors: 1) a cow with mastitis might be classified as healthy (false negative) and therefore not be treated, and 2) a cow without mastitis (healthy) might be classified as mastitic (false positive) and therefore be unnecessarily treated. This means that, at the herd level, decision-making regarding DCT should consider the cost of diagnostic misclassification in selective DCT and the antibiotic expenditures for blanket DCT. The biological and economic implications of such decisions can be assessed through simulation models: these are not only adjusted to herd-specific parameters but can also take in aspects such as the sensitivity (Se) and specificity (Sp) of the diagnostic tools and the effectiveness of antibiotics (Halasa et al., 2010). The expected outcomes provided by these models considering different herd situations and other relevant information can support the decision-making process about whether or not to implement selective DCT. Moreover, the results of this model could be used as prior information for the development of clinical trials to evaluate DCT efficacy.

The objective of this study was to evaluate *ex-ante* the economic impact of implementing selective DCT under the current milk production conditions in Argentina, using cow SCC (CSCC) to identify cows with IMI at dry-off. Our hypothesis was that the selective DCT is a cost-effective practice in relation to blanket DCT under simulated production conditions based on Argentinan data.

## MATERIAL AND METHODS

### Field data about the validation of CSCC as a diagnostic test

In a convenience sampling, 86 Holstein dairy cows were enrolled for the study at dry-off over a two-month period, from a herd in Arroyo Cabral, Córdoba (Argentina). The herd had a total of 375 lactating cows managed in a pasture-based system and applying a comprehensive mastitis control plan that included blanket DCT. Single quarter milk samples were aseptically collected for culturing on dry-off day, before the last milking and after discarding the first streams of milk. All animals involved in this investigation were cared for in accordance with the International Guiding Principles for Biomedical Research Involving Animals (CIOMS-ICLAS, 2012).

The samples were transported and stored at 4 °C, and microbiological cultures were performed within the first 24 h after collection. More specifically, 0.01 mL from each sample was cultured on trypticase soy agar plates (BBL, Cockeysville, MD, USA) containing 5% sheep blood. The plates were incubated at 37 ± 1 °C for 48 h, and during this time they were observed for bacterial growth after 24 h and after 48 h, i.e. at the end of the incubation. After observing colony morphology and haemolytic patterns, further examinations were carried out by Gram staining, catalase and oxidase testing, and additional biochemical and metabolic tests for major pathogens and minor pathogens. A sample was considered positive when the growth of a particular organism was ≥3 CFU/mL and when <3 colony types were detected on the plate. For *Staphylococcus* spp., a minimum of 1 CFU was required. Samples yielding ≥3 colony types were considered to be contaminated and excluded from the analysis. Streptococci, enterococci and enterobacteria were identified using methodology based on standards by the National Mastitis Council (2004). Colonies with typical zones of complete and incomplete hemolysis and nonhemolytic colonies that had a positive tube test for free coagulase, aerobic acid production from maltose, positive Voges Proskauer reaction, and growth at 45 ºC were classified as *Staphylococcus aureus*; the strains that were negative coagulase test and susceptible to the furazolidone test were identified as non-aureus staphylococci (NAS). The microbiological analysis was performed in the same way as in the study from Vissio et al. (2014). All bacteriological analyses were done by the same person, who was blinded with respect to cow SCC test results.

Bacteriological causes of infection were categorized as either major pathogens (*Escherichia coli*, *Klebsiella* spp., environmental or non-agalactiae streptococci, *Staphylococcus aureus*, *Streptococcus agalactiae*, and others as *Pseudomonas aeruginosa* and *Arcanobacterium pyogenes*, or minor pathogens (NAS and *Corynebacterium bovis*). A quarter was deemed infected when at least one major pathogen was isolated from it, regardless of the presence of minor pathogens. A cow (the unit of analysis) was defined as infected if at least one quarter was infected (parallel interpretation), while negative cultures in all quarters defined an uninfected cow. Cows with at least one quarters considered to be contaminated for culture were excluded from the study.

To assess the diagnostic properties of CSCC, we only used the records of the last milk test-day collected at an average of 20 days (SD=4.6) before drying off. Sensitivity (Se), specificity (Sp), positive predictive values (PPV) and negative predictive values (NPV) were calculated for CSCC, to differentiate between major pathogen-infected cows and cows that were either uninfected or infected with minor pathogens at dry-off. Culture results at dry-off were the gold standard for the cow's IMI status, and different CSCC thresholds (above which the test was considered positive) were tested in 2×2 tables (Dohoo; Martin; Stryhn, 2003).

### Simulation model outline

A model was designed to understand whether implementing selective DCT is a sound decision to reduce the use of antibiotics without negatively affecting the udder health of the herd. The model perspective looks for the prescription of a selective DCT defining cows at risk of being infected using 4 CSCC thresholds (≥100,000; ≥150,000; ≥200,000; and ≥250,000 cells/mL) as a diagnostic test, and under two scenarios of IMI prevalence at dry-off in the herd: low (between 5 and 15%) and high (16-25%) for all pathogens. In total, then, 8 possible scenarios were analyzed. The model output was defined as the net economic difference (NED) at herd level between selective and blanket DCT (Figure 1), following the format of a partial budget (Rowe et al., 2021). In selective DCT, the model essentially considered the trade-off between the total cost due to antibiotics and the economic consequences of post-partum infections experienced between the two groups of cows: one which tested positive on the last day of CSCC monitoring and was subsequently treated with antibiotics, and another one which tested negative and was left untreated at dry-off (Figure 1).

In both DCT strategies, the cost of antibiotic treatment included the price cost of antibiotic and the labor cost corresponding to the farmer (Table 1), and in selective DCT included fees charged by the veterinarian who advised in the implementation of this strategy (Table 1). Internal teat sealants were assumed to be used in all quarters for both blanket and selective DCT and equal among all aspects of the partial budget, thus, not explicitly calculated. The monetary losses derived from the clinical mastitis (CM) episode at postpartum were estimated considering the discharged milk, treatment, and the lower milk production along the lactation curve (Table 1) (Richardet et al., 2016). The cost of milk production losses ascribed to subclinical mastitis (SM) for IMI at postpartum were based on Vissio et al. (2015), assuming that the average duration of a subclinical case was 30 days. The cost of premature culling considered the depreciation at the time of removal of the cow, as well as the costs of replacement and salvage adjusted for DIM and parity, as described by Pinzón-Sánchez, Cabrera and Ruegg (2011). Then, this cost was multiplied by the culling risk attributable to mastitis in a pasture-based dairy system based on Kerslake et al. (2018; Table 1).

All the costs were estimated considering US dollars for December 2020.

The Equation 1 to calculate NED was as follows:

$$NED_{1-2} = (TR_1 + LAB_1 + ML_1 + CC_1 + DCT_1) - (TR_2 + LAB_2 + ML_2 + CC_2 + DCT_2) \quad (1)$$

where NED = net economic difference between selective DCT (1) and blanket DCT (2), TR = CM treatment cost, LAB = labor costs, ML = CM and SM milk losses, CC = culling cost, and DCT = dry cow therapy cost.

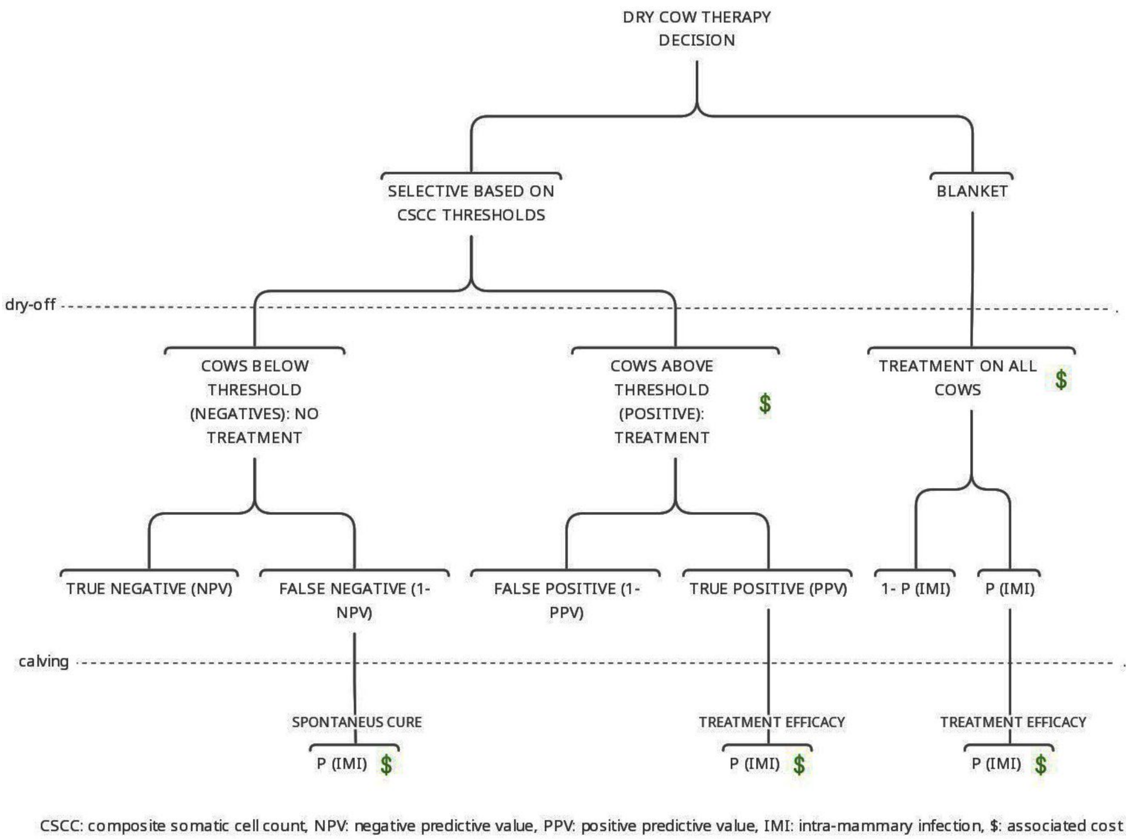


**Figure 1**: Dry cow therapy decision making conceptual model.

**Table 1**: Simulation model input about biological and economic variables.

| Inputs variables | Values | Distribution | Source |
|---|---|---|---|
| Dry cow therapy efficacy (%)[1] | 78 | 71-85 | (Halasa et al., 2009b) |
| Spontaneous cure of IMI (%)[1] | 46 | 37-56 | (Halasa et al., 2009b) |
| Proportion of IMI that develop CM at postpartu1 | 0.273 | 0.21-0.39 | (Halasa et al., 2009b) |
| Culling risk due to clinical mastitis (%)[2] | 12 | | (Kerslake et al., 2018) |
| Milk losses due to subclinical mastitis (liters/cow/day)[2] | 2.8 | | (Vissio et al., 2015) |
| Milk losses due to clinical mastitis (liters/case)[2] | 321 | | (Richardet et al., 2016) |
| Milk price (US$/liter)[2] | 0.289 | 0.164-0.379 | (Observatorio de la Cadena Lactea Argentina - OCLA, 2021) |
| Antibiotic dry cow therapy cost (US$/cow)[2] | 12 | | |
| Antibiotics cost to treat clinical mastitis for 3 days (US$/quarter/day)[2] | 3 | | |
| Labor cost (US$/cow)[2] | 0.63 | | (Unión de Trabajadores Rurales y Estibadores -UATRE, 2021) |
| Veterinary fees charges (US$/cow)[2] | 2.72 | | (Colegio Médico Veterinario de la Provincia de Córdoba - COVET, 2020) |

IMI: Intramammary infection. [1] triangular, [2] uniform.

In all cases, the economic benefit of selective DCT was simulated for a Holstein dairy herd that dried off 150 cows/year based on biological and economic parameters obtained from literature and prices for Argentinian conditions.

The model was created using the Monte Carlo simulation framework in Microsoft Excel 2007 with the add-on package Model@Risk (version 4.05, Palisade Corporation, New York, USA). Model simulations were run using 50,000 iterations and latin hypercube sampling. The model had several sources of uncertainty, such as the efficacy of the antibiotic treatment, the rate of spontaneous cure, the proportion of IMI that develop CM at postpartum, and the milk price. All input variables in the model and its distribution were displayed in Table 1. In addition, triangular distribution for herd IMI prevalence, and CSCC Se and Sp was used in the model. At a low level of IMI prevalence at dry-off, the min, max and most likely values were 5, 15 and 10%, respectively, whereas at a high level at dry-off these values were 16, 25 and 21.4% (Dieser et al., 2014), respectively. In the same way, confidence intervals and estimates for CSCC Se and Sp obtained from validation study were also used as parameters of triangular distribution.

The ranking of variable (CSCC Se and Sp, treatment efficacy, spontaneous cure, milk price, and IMI herd prevalence) according to their contribution to the variance of NED was evaluated using the tornado plot, within each diagnostic threshold level (between 100,000 to 250,000 cells/mL) and prevalence level (low and high) at dry-off. Also the distribution of the NED was evaluated to explore which were the diagnostic threshold that improved the NED in favor of SDCT under each herd IMI prevalence scenario.

## RESULTS AND DISCUSSION

Out of the 86 cows in the field study, 29.1% and 23.2% and 47.7% were ending their first, second and third or more lactation, respectively. The median value for days in milk (DIM) was 398 (interquartile range between 335 and 585). At dry-off, 40.7% of the cows were classified as infected with a major pathogen, 4.7% as infected with a minor pathogen, and 54.7% as uninfected. Fifty-nine milk quarter samples were positive to some pathogen: *Staphylococcus aureus* (28.8%), NAS (30.5%), *Streptococcus agalactiae* (11.9%), *Streptococcus dysgalactiae* (10.2%), *Enterobacter* spp. (6.8%), *Escherichia coli* (5.1%), *Corynebacterium bovis* (3.4%) and *Pseudomonas* spp. (3.4%). According to the records for the last milk test day before dry-off, the geometric median for SCC was 140,177 cells/mL (interquartile range between 75,000 and 335,000 cells/mL). In 33.7% of the cows the SCC was ≥200,000 cells/mL. Table 2 shows the accuracy and predictive values for CSCC on the last milk test day to detect IMI caused by major pathogens.

Lipkens et al. (2019) estimated the accuracy of CSCC to detect IMI at the end of lactation and reported slightly higher values for Se and Sp than the ones in our study when it came to detecting major pathogens. Taking into account that our estimations could have a low precision, previous report (Lipkens et al., 2019) were also considered to define an operational threshold 200,000 cells/mL as a practical value to select infected cows in a framework of selective DCT. The differences in PPV and NPV could be attributed to the fact that prevalence at herd level in our study was twice the mean prevalence in the herds that they studied, although we observed that CSCC was slightly better able to predict infection than they did, our NPV values (almost 60%) were lower than theirs (85%). In herds where udder infection is under control, with low IMI prevalence, it is to be expected high NPV. Thus, the selective DCT based on CSCC could be considered as a strategy to implement in these diary herds, because the risk of not treating an infected cow with antimicrobials should be low (1-NPV; Lipkens et al., 2019).

The NED distribution for each threshold and both levels of prevalence are shown in Table 3. The NED had consistently negative values across almost all 8 scenarios combining the different CSCC thresholds and levels of prevalence (Table 3), which means that selective DCT would be more cost-effective under the conditions given in the model.

A recent meta-analysis of trials comparing selective and blanket treatment showed that the frequency of IMI at calving in cows assigned to the selective DCT protocol was higher than that of cows in the blanket therapy groups (RR = 1.34; 95% CI = 1.13, 1.59) (Winder et al., 2019). Nevertheless, selective DCT could be an economically efficient alternative to reduce antibiotic use. In this sense, the costs associated to selective DCT were found to be lower than those of blanket DCT under European conditions (Huijps; Hogeveen, 2007; Scherpenzeel et al., 2017), and Rowe et al. (2021) reported that selective DCT may be cost-effective for US herds as well, if implemented appropriately. In the two prevalence scenarios evaluated in our study, NED was in favor of selective DCT, especially at a threshold of 200,000 cells/mL. Rowe et al. (2021) using a partial budget analysis reported that implementing selective DCT on the basis of an algorithm guide with the same CSCC thresholds as in our study made it possible to save roughly US$7.85 (between US$3.39 and US$12.90) per cow at dry-off, with respect to the cost of blanket DCT. Our model rendered savings of US$2.89 (between US$1.16 and US$4.39) and US$4.16 (between US$2.85 and US$5.51) per cow at dry-off at high and low prevalence levels, respectively. These lower values could be mainly explained by the fact that the other study did not consider differences in post calving udder health between selective and blanket DCT, and thus costs attributable to CM and SM due to leaving cows untreated did not enter their analysis either.

The 200,000 cells/mL threshold maximized NED at both levels of prevalence at dry-off, with the median being -634 US$ (percentiles 5, -435.6; 95%, -827.4) for low prevalence and -455 US$ (percentiles 5, -202.9; 95%, -675.4) for high prevalence. The magnitude of the changes did not follow any linear trends across thresholds: in fact, NED changed more remarkably between 200,000 and 100,000 cells/mL than between 200,000 cells/mL and 250,000 cells/mL. The value of NED dropped to about a third when the CSCC threshold changed from 200,000 to 100,000 cells/mL, at both high and low prevalence at dry-off. This may respond to an increase in the number of cows treated at dry-off when CSCC is lower, a cost that may not be compensated despite the decrease in the number of cows treated for post-partum mastitis. The cost of operation management (labor cost and veterinary fee charges) was lower in blanket than in selective DCT because in the last the veterinary advice was included; no relevant differences were observed between thresholds for this aspect.

**Table 2**: Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) of cow somatic cells count (CSCC) from the last milk test day records before drying off to detect intramammary infection caused by major pathogens in the field study.

| CSCC (cells/mL) | % Se (CI 95%) | % Sp (CI 95%) | % PPV (CI 95%) | % NPV (CI 95%) |
|---|---|---|---|---|
| 100,000 | 62.9 (45.4-80.3) | 39.2 (24.8-53.6) | 41.5 (27.3-55.7) | 60.6 (42.4-78.8) |
| 150,000 | 40 (22.3-57.7) | 60.8 (46.4-75.2) | 41.2 (23.2-59.2) | 59.6 (45.3-73.9) |
| 200,000 | 31.4 (14.6-48.2) | 64.7 (50.6-78.8) | 37.9 (18.6-57.3) | 57.9 (44.2-71.6) |
| 250,000 | 22.9 (7.5-38.2) | 64.7 (50.6-78.8) | 30.8 (11.1-50.4) | 55 (41.6-68.4) |

CI: confidence interval.

**Table 3**: Simulation model output: net economic difference (NED; US$) distributions across cow somatic cell count (CSCC) thresholds under both low and high intramammary infection (IMI) prevalence at dry-off scenarios.

| IMI prevalence at dry-off scenario | CSCC (cells/mL) | Percentile | | | | |
|---|---|---|---|---|---|---|
| | | 5% | 25% | 50% | 75% | 95% |
| Low: mean 10% (range: 5-15) | 100,000 | -405.0 | -302.9 | -226.9 | -149.7 | -49.3 |
| | 150,000 | -765.5 | -655.6 | -574.6 | -491.8 | -382.3 |
| | 200,000 | -824.0 | -716.5 | -634.4 | -550.2 | -433.4 |
| | 250,000 | -824.0 | -711.7 | -627.8 | -541.5 | -419.8 |
| High: mean 21.4% (range: 16-25) | 100,000 | -298.8 | -198.0 | -122.4 | -44.7 | 63.1 |
| | 150,000 | -617.8 | -500.4 | -410.9 | -316.5 | -174.5 |
| | 200,000 | -673.8 | -550.9 | -455.7 | -352.5 | -201.8 |
| | 250,000 | -674.6 | -545.2 | -441.5 | -332.7 | -170.8 |

A similar pattern across CSCC thresholds for the relative importance of the variables evaluated at each level of prevalence at dry-off was found. In a low prevalence scenario, CSCC specificity was the most important variable influencing NED and thus contributed the most to making selective DCT economically efficient: as Sp went up, NED went down (Figure 2a). With high prevalence, milk price was slightly more important than specificity (Figure 2b), followed by spontaneous cure rate. At low-level prevalence, our model was mainly sensitive to changes in CSCC specificity. The PPV value is known to be low when prevalence is low, so in this case the treatment of false positive cows at dry-off increased the cost of selective DCT and reduced its economic advantage. On the other hand, milk price became very relevant as well when prevalence was higher (20%). This could be because NPV was lower, so cows with mastitis were left untreated at dry-off and were more likely to develop IMI post-partum, with the consequent loss of milk. In this case, it was an increase in milk price which lowered the economic benefit of selective DCT. Similarly, the spontaneous cure rate became relevant because upon its increase, infections and associated milk losses decreased in the next lactation.

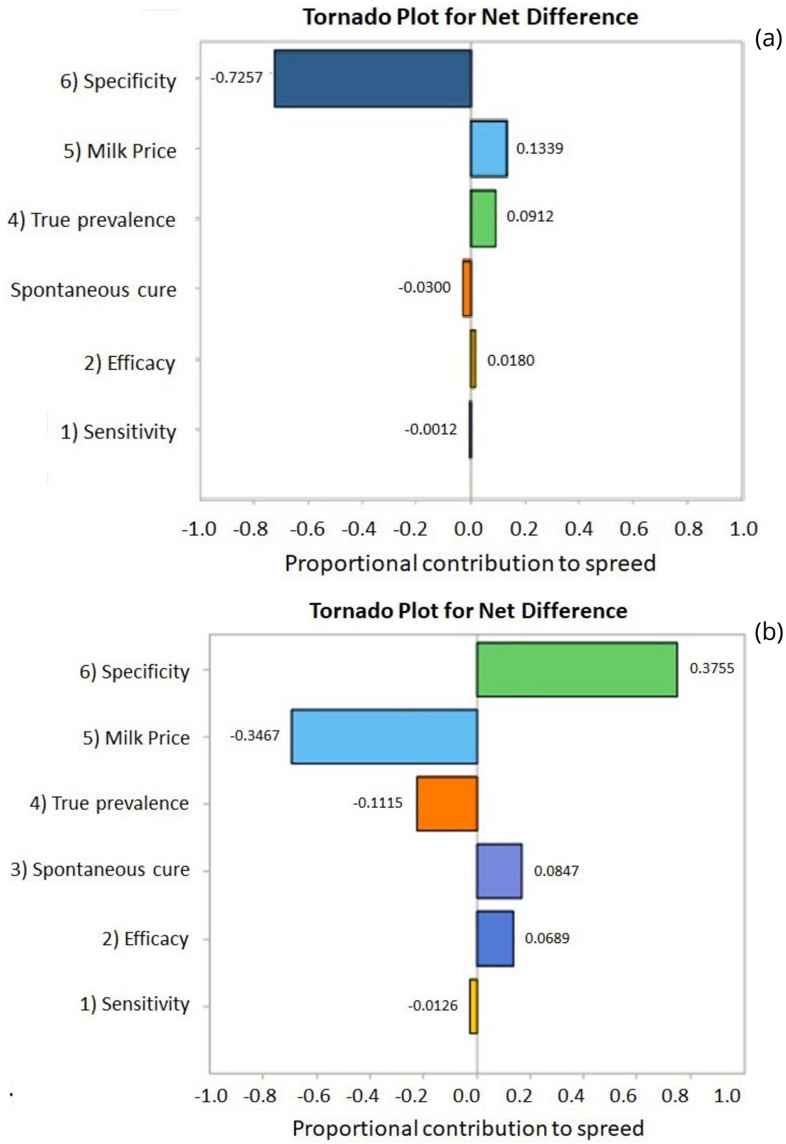


**Figure 2**: Relative importance of factors over net economic difference (NED) between selective and blanket dry cow therapy at 200,000 cells/mL cow somatic cell count threshold in low (a) and high (b) intramammary infection prevalence at dry-off.

The imprecise Se and Sp estimates due to small sample size of this field could be affect NED. However, similar values were reported previously (Lipkens et al., 2019) and therefore we believe that these estimates could be used in the simulation model as input. Furthermore, the NED between selective and blanket DCT showed that selective DCT should be a cost-effective option in almost evaluated scenarios even considering the large variations in Se and Sp. Generalization of these results must be made with caution and taking into account the assumptions of the model because changes in market and milk production conditions could affect the estimates reported in this study. The CSCC is used as a simple, inexpensive and reliable tool to detect IMI and it is accessible for farmers in our country and this could favor the implementation of selective DCT. Finally, the use of AM without it being necessary is not desirable and there also seems to be no economic reason to do so. Other aspects that could justify the use of selective DCT are given by the potential effect of antimicrobial resistance, the public opinion, political issues, and animal welfare.

## CONCLUSIONS

Selective DCT was found to be a cost-effective option in a simulated herd under production condition of Argentina when applied on the basis of test-day CSCC values and assuming overall good udder health management. Its adoption seems to be economically efficient regardless of the IMI prevalence scenario and at different CSCC thresholds, although the NED tends to be maximized at low prevalence, 5-15% at herd level, using the 200,000 cells/mL threshold to decide which cows should be treated at dry-off.

## AUTHOR CONTRIBUTION

Conceptual idea: Vissio, C.; Larriestra, A.J.; Methodology design: Vissio, C.; Richardet, M.; Issaly, L.C.; Larriestra, A.J.; Data collection: Vissio, C.; Richardet, M.; Data analysis and interpretation: Vissio, C.; Richardet, M.; Issaly, L.C.; Larriestra, A.J., and Writing and editing: Vissio, C.; Richardet, M.; Issaly, L.C.; Larriestra, A.J.

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