

Meta-analysis of some risk factors affecting somatic cell score in dairy cattle

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Mastitis and milk quality in dairy cows are an ongoing concern of great relevance to animal welfare and productivity in modern dairy production. High somatic cell scores (SCS) are an indirect measure of presence of mastitis and low milk quality, they are relatively easy to record and values of heritability are higher than records of mastitis. However, published SCS values are highly variable across studies which makes it impossible to have a reliable reference value. The objectives of this study are to perform a meta-analysis (1) to estimate this reference value and the extent of its variability and (2) to identify whether and how factors of variation (year and country of publication, parity, and breed) influenced this value. Information on SCS was retrieved from 138 papers published between 1979 and 2020 in 40 countries and analyzed with the Metafor package in R software. Standard deviations were estimated from available data or imputed using a Bayesian hierarchical modelling approach. Results of the meta-analysis revealed a significant decrease of 0.04 units in mean SCS with the year of publication, an increase with the number of parities and a significant variability across countries. The reference SCS value was estimated at 3.68 (3.59 - 3.76) and total heterogeneity across studies at 1.24 (1.11-1.38). Further analyses are necessary to verify arguments provided to explain the results.

Abstract

Keywords: SCS, meta-analysis, dairy cattle, risk factors, mastitis.

Ensuring high quality of milk products is of crucial importance as they are part of the official nutritional recommendations in many countries worldwide (Rozenberg *et al.*, 2016). Globally, cow milk represents 80% of total milk production in all regions (Navarro and Emery., 2015) and its consumption has spread around the world in the last forty years (Wiley, Andrea S, 2007). Milk quality depends on many factors, one of which is very important, namely the number of somatic cells (SCC) it contains. Indeed, high milk SCC are an indicator of subclinical infections (Heringstad *et al.*, 2000; Pösö and Mäntysaari, 1996) which is associated with low milk production (Sert *et al.*, 2016), deteriorated flavor quality and shelf life (Sobczuk-Szul *et al.*, 2015), reduced milk processing yield (Najafi *et al.*, 2009) and low protein content (Sharma *et al.*, 2012). Besides infection, many other factors influence directly or indirectly milk SCC. They include cow characteristics (e. g., parity, season of calving, age, stage of lactation, udder conformation), geographical regions (e.g., temperature and humidity) and management

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factors, (e.g., transition to an automatic milking system, herd size (Barkema *et al.* 1998; Feliciano *et al.*, 2020; Oleggini *et al.*, 2001; Van den borne *et al.*, 2021).

It is therefore not surprising that SCC values reported in the literature are variable. However, a part of this variation is also associated with random errors during the measuring process. Several measures (e.g., Q test, I^2 statistics, funnel plots) have been proposed to quantify heterogeneity of results across studies and to determine whether this heterogeneity goes beyond what would be expected by chance (Sedgwick, 2015; Melsen *et al.*, 2014). If it is the case, alternatives exist to study the reasons for this heterogeneity and to generate a pooled SCC value (Cordero and Dans, 2021) such as the meta-regression models (Baker *et al.*, 2009).

The goal of this study is to explore the diversity in SCC values reported in the literature and to determine the level of heterogeneity across studies.

Material and methods

The first step consisted in searching the web with a combination of keywords and subject headings for the following concepts: “Somatic Cell(s) Count(s)”, “Somatic Cell(s) Score(s)”, “Dairy Cattle”, “factors affecting somatic cell(s)”, “parity”, “season”. Globally, articles must have been published between 1970 and 2020 and include information related to a measure of SCC. Measures of SCC included test-day and lactation averages. Reports were mostly written in English, but other languages were allowed. Once an article was selected, all articles referenced within it were consulted. When available, information on breed, country, parity, and year was retrieved in each article. Six authors were contacted personally and provided us information missing in their articles (Knob *et al.*, 2018; Pritchard *et al.*, 2012; Heins *et al.*, 2008; McParland *et al.*, 2013; Koç, 2007, Koç and Kizilkaya, 2009). Finally, records were stored into a Zotero library.

The second step consisted in standardizing the reported values. Indeed, means values were reported as SCC, transformed in logarithm of SCC or in SCS. Herein, SCS were all expressed following the proposition of Wiggans and Shook (1987). When available, information of the variability around the means was retrieved and transformed into SCS standard deviation. When it was not possible to compute these standard deviations from the information available in the article, they were imputed following the procedure of Sung *et al.* (2006), assuming missing variances come from same lognormal distribution.

The last step consisted in evaluating level of SCS heterogeneity across SCS means. We implemented two random-effects models with the function “rma” of the “metafor” R package to obtain REML estimates of the effects included in both models and to create funnel plots (Röver, 2018). Besides the overall mean (fixed intercept), the first model included two random effects both assumed to be normally distributed with zero mean and with between- and within-study variances, respectively. This model allowed us to create the funnel plot and to compute the amount of heterogeneity ($\hat{\delta}^2$) across SCS means. Tests for funnel plot asymmetry (which may be indicative of publication bias) was obtained with function “ranktest.rma”. In addition to these random effects, the second model included the fixed effects of breed and parity of the animals, country of publication and the linear effect of year of publication (covariate). This model allowed us to estimate the pseudo- R^2 value, i.e., the amount of heterogeneity that is accounted for by these fixed effects. The p-value threshold for statistical significance was set at 5%.

Results and discussion

After editing according to the inclusion criteria, we retrieved 637 SCS records from 138 peer-reviewed publications in 40 countries. The number of SCS records used to compute the mean ranged from 4 (Singh N *et al.*,2019) to 13 786 064 (Dezetter *et al.*,2015). The number of mean SCS per study varied from 1 to 22. The predominant breed was Holstein (58.64% studies), followed by Jersey (4.33 %) and Brown Swiss (4.09 %). Most studies were from Europe (46.75 %), Asia (20.60 %) and America (17.75 %).

The SCS mean over all studies is 3.68 (3.59 - 3.76) and \hat{A}^2 is 1.24 (1.11-1.38). The funnel plot (Figure 1) reveals that 95% of the SCS means had standard errors less than 0.24 units which may suggest a bias in favor of studies with a large number of records. Indeed, 65.3% of the studies that reported the number of records used to compute the SCS mean signaled more than 1000 records. No significant difference in the number of studies on each side of the vertical line on the funnel plot was observed, in line with the observation that 57% of the studies reported SCS means lower than 3.68.

Effects included in the second model accounted for 60.87 % of the heterogeneity across the records. Most differences were found across years and countries of publication and across parities. The REML estimates of the effects of country and parity are given in Figures 2 and 3, respectively. In comparison with Austria, estimates were two units higher for countries such as Colombia, Egypt, New Zealand, Poland, South Africa and Turkey. Results from New Zealand may be incorrect as the method used to transform SCC in SCS was unusual (Lembeye *et al.*, 2015 and Lembeye *et al.*, 2016) and this will be corrected in a later report. For the other countries, further analyses are necessary to explain differences. Indeed, studies differed in the nature of the SCS measure (e.g., lactation or test-day, season of measure), in the individual (e.g., health status) and herd characteristics (Khaitisa *et al.*, 1998; Erdem *et al.*, 2010) or weather conditions (Carabaño *et al.*, 2014). Figure 3 reveals that REML estimates increases across parities, being highest for parity higher than 3. Many possible causes could also be suggested to explain this observation. Among others, Sandrucci *et al.* (1992) observed increased amounts of epithelial cells in milk as the number of lactations rises. Breen *et al.* (2009) reported higher risk of clinical mastitis in cows with middle and high parity. A final significant effect was the linear reduction of 0.04 units per increased year.

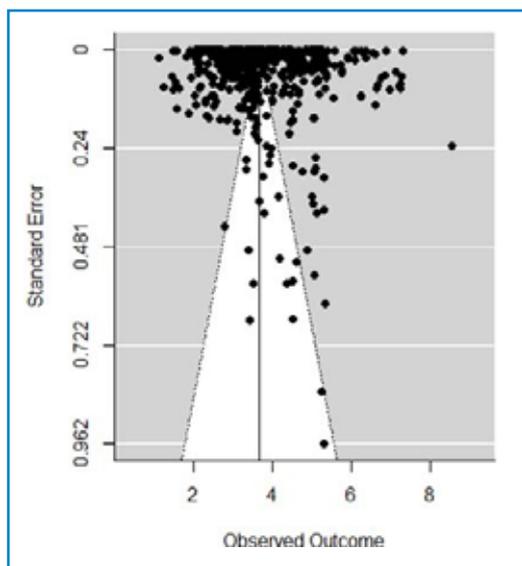


Figure 1. Funnel plot showing the SCS means (observed outcome) and corresponding standard errors for each study

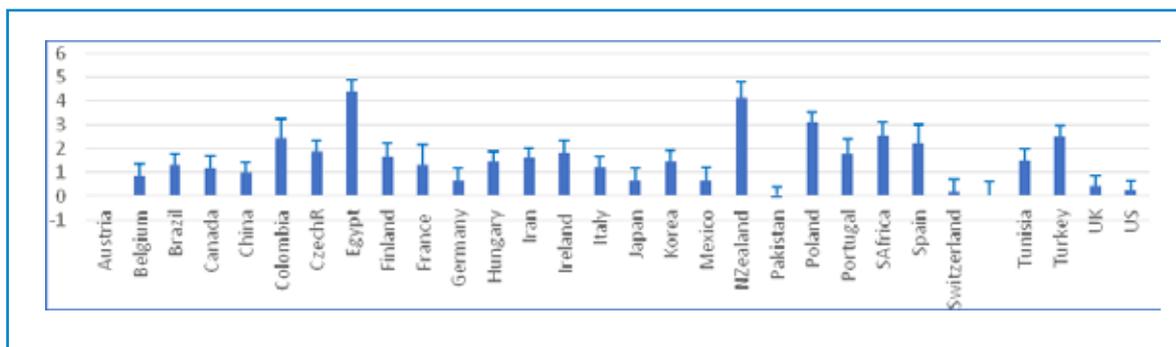


Figure 2. Estimates of the differences in SCS means for Holstein with respect to Austria, adjusted for the effects of parity and year of publication.



Figure 3. Estimates of the differences in SCS means for dairy cows with respect to parity higher than 3, adjusted for the effects of breed, country and year of publication.

Better management techniques (Hiitiö *et al.*, 2017), utilization of robot milking system (Frössling *et al.*, 2017; Johansson *et al.*, 2017) and genetic selection are some of the possible explanations for this trend.

Conclusion

The large number of studies from very different environments have allowed us to highlight significant differences in SCS across studies linked to parity, year, and country of publication. It remains to dissect the results to find clues towards a better understanding of these results.

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