

## Quarter milk somatic cell count in infected dairy cows: a meta-analysis

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**Abstract** – The aim of this paper was to evaluate the effects associated with intramammary infection (IMI) by a bacterium or a group of bacteria (*Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Streptococcus uberis*, coliforms, Staphylococci other than *S. aureus*, and *Corynebacterium bovis*) on the somatic cell count (SCC) in quarter milk of dairy cows. Papers selected for analysis had to provide SCC values associated with the natural infection in quarters by different bacteria. Sampling for measurement of SCC and determination of the infection had to be done on the same day. Only papers published in English or in French after 1971 were considered. Twenty-one papers fulfilled the selection criteria. The animals sampled, the measurement techniques for SCC and the bacteriological identification, as well as the definition of the infection, all differed widely among the selected studies. The meta-analysis method was used to estimate both the mean SCC (arithmetic and geometric) value and the average increase on SCC of each type of infection. The geometric mean SCC in bacteriologically negative quarters was 68 000 c/mL. In case of IMI, the retained SCC was 357 000, 857 000, 547 000, 1 024 000, 1 151 000, 138 000 and 105 000 c/mL in quarters infected by *Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Streptococcus uberis*, coliforms, staphylococci other than *S. aureus* and *Corynebacterium bovis*, respectively. The variation factors that could influence these SCC values and the bacteriological results are discussed.

dairy cow / mastitis / somatic cell count / meta-analysis

**Résumé** – Méta-analyse des effets de l'infection sur la concentration en cellules somatiques du lait de quartier chez la vache laitière. Le présent article a pour objectif d'évaluer l'effet associé à l'infection intra-mammaire (IIM) par une bactérie ou par un groupe de bactéries (*Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Streptococcus uberis*, coliformes,

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Staphylocoques autre que *S. aureus* et par *Corynebacterium bovis*) sur la concentration en cellules somatiques (CCS) du lait de quartier des vaches laitières. Les études rapportant des CCS associées à l'infection naturelle des quartiers par ces différentes bactéries, avec un prélèvement pour détermination de la CCS et de l'infection réalisé le même jour, ont été sélectionnées. Seules les études publiées en anglais ou en français après 1971 ont été prises en compte. Sur la base de ces critères, vingt et une études ont été retenues. Les populations d'étude, les techniques de mesure de la CCS et d'identification bactériologique ainsi que la définition de l'infection différaient considérablement entre les études sélectionnées. Les moyennes arithmétiques et géométriques ainsi que l'augmentation moyenne de la CCS associées à chaque type d'infection ont été estimées par méta-analyse. La moyenne géométrique de la CCS estimée en absence d'IMI était de 68 000 c/mL. En cas d'IMI par *Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Streptococcus uberis*, les coliformes, les staphylocoques autre que *S. aureus* ou par *Corynebacterium bovis*, les CCS retenues étaient de 357 000, 857 000, 547 000, 1 024 000, 1 151 000, 138 000 et 105 000 c/mL respectivement. Les facteurs de variation pouvant influencer ces valeurs de CCS ou les résultats bactériologiques ont été discutés.

## vache laitière / mammite / teneur du lait en cellules somatiques / méta-analyse

### 1. INTRODUCTION

Mastitis is an inflammation of one or several mammary quarters, most often due to a bacterium-related infection. In some cases, this inflammation is accompanied by clinical signs (pronounced signs of mammary inflammation and systemic illness). This is then diagnosed as clinical mastitis. In other cases, the mastitis signs are imperceptible by direct observation. This is then diagnosed as subclinical mastitis, based on the presence of bacteria and on cytological modifications of the milk [22].

Whether accompanied by clinical signs or not, an intramammary infection (IMI) is associated with an increase in the somatic cell counts (SCC) in milk. However, the magnitude of the increase in SCC varies according to the bacteria involved in the IMI [5, 48]. Usually, two types of mastitis pathogens can be distinguished: major pathogens and minor pathogens. The bacteria of the first group (*Staphylococcus aureus*, *Streptococci* (*agalactiae*, *dysgalactiae*, *uberis*) and coliforms, (notably *Escherichia coli* and *Klebsiella* spp.)) are responsible, most of the time, for clinical mastitis. The minor pathogens, on the contrary, are most often associated with a moderate infection rarely associated with clinical signs. These

infections, which are especially frequent, are mainly due to Staphylococci other than *S. aureus* (mostly *S. chromogenes*, *S. hyicus*, *S. epidermidis*, and *S. xylosum*) or to *Corynebacterium bovis* [38].

The SCC is not exclusively influenced by IMI. Other non-infectious factors (animal's age, lactation stage, breed, measurement equipment, fraction of milk sample) might have also a moderate impact [5, 7, 26, 42].

Consequently, the aim of this paper was, after a presentation of the range of reported values of SCC for the main bacteria involved in IMI, to carry out a meta-analysis with the aim to estimate an average effect associated with an IMI by a given bacterium on the SCC. Because of the lack of data on SCC in whole udder milk associated with infection by a specific bacterium, this meta-analysis was restricted to the effects in quarter milk.

### 2. MATERIALS AND METHODS

#### 2.1. Selection of papers

The literature search was carried out to identify the articles reporting SCC associated with a quarter infection by various

bacteria or groups of bacteria. The selection of articles began with research on the Internet using "Medline" after 1966 and "Commonwealth Agricultural Bureau (CAB)" after 1987 databases. The keywords used were "Somatic Cell(s) Count(s), Cell counting, Cow(s), Cattle, Dairy cow, Dairy cattle mastitis, Mammary gland diseases, Intramammary infection, *Staphylococcus*, *Streptococcus*, *Escherichia*, *Corynebacterium*, Coliform". The references quoted in the papers selected at this stage were also consulted. The selected articles had to meet the following criteria:

(1) articles published in English or in French;

(2) papers published after 1971 because since then, new and more specific measuring equipments for SCC as well as more sophisticated bacteriological techniques have appeared;

(3) natural contamination because the infectious dose used in the experiments is, most of the time, higher compared to what is encountered in field conditions;

(4) SCC counting and bacteriological examinations carried out using samples of milk from the same milking.

Moreover, if several studies had been published using the same study sample, only one among them was included in the meta-analysis.

A total of 21 articles were included in the present study (Tab. I). The articles selected were all in English and were generally European or American. Two Israeli, one Australian and one New Zealand studies were also selected.

## **2.1. Data characteristics in selected papers**

### **2.2.1. Samples**

The number of herds involved in these studies varied between 1 [18, 25, 29, 33, 39] and 154 [1, 12]. The number of cows varied

between 3 [29] and 6 215 [23]. The number of quarter milk samples varied between 136 [49] and 28 339 [18] (Tab. I).

With the exception of the study of Erskine et al. [14] in which the milk fraction used was not specified and the study of Ward and Schultz [48] in which SCC was measured on the main flow milk fraction, the bacteriological analysis as well as the measurements of SCC in the remaining studies were carried out on foremilk (Tab. II). Moreover, Woolford et al. [49] focused on the effect of the milk fraction used.

### **2.2.2. Measurement techniques for somatic cell counting**

Three SCC measurement techniques were used in the selected papers (Tab. II). The Coulter Counter counts the number of electric impulses resulting from particles passing between two electrodes [21]. The Fossomatic (Foss-Electric, Hillerød, Denmark) counts the number of cell nuclei which become fluorescent due to ethidium-bromure [21]. Ward and Schultz [48] and Timms and Schultz [45] used a filter-DNA method to measure SCC. This technique consists of filtering a solution of milk mixed with detergent (Triton X-100 EDTA) through a membrane with fine pores. A colorimetric procedure based on the indole reaction with cell DNA is then used to determine the DNA content which is directly related to the number of cells present in the initial sample [4].

### **2.2.3. Bacteriological examinations**

A standard technique for collecting samples and doing bacteriological examinations has been established by the National Mastitis Council [31]. Most of the selected studies refer to this standard technique (Tab. II). It consists of streaking 0.01 mL of milk on a blood agar plate. The streaking plates are then placed in an incubator at 35–37 °C for 24–48 hours. The identification

**Table I.** Source of data, sampling and data collection in selected studies.

Reference	Country	Study period	Herd type <sup>1</sup>	Breed <sup>2</sup>	Number of		Inclusion criteria
					Herds	Cows	
Ward and Schultz [48]	USA	–	–	–	–	225	–
Brooks et al. [6]	Canada	1979	C	–	74	2 381	CM <sup>4</sup> , 723 WCM, 151
Jaartveld et al. [23]	Netherlands	–	C	MRY, H	139	6 215	–
Sheldrake et al. [44]	Australia	–	C, R	H, others	3	160	3 463
Honkanen-Buzalski et al. [20]	UK	–	C	–	15	36	144
Brolund [5]	Switzerland	1976/1977	C	SF, SRB	29	682	25 304
Mattila et al. [29]	Finland	–	R	A	1	3	360
Erskine et al. [14]	USA	–	C	–	LSCC <sup>3</sup> , 16 HSCC, 16	679 690	2 696 2 730
Hogan et al. [17]	USA	–	C	–	16	227	2 975
Timms and Schultz [45]	USA	1983/1984	R	H	2	139	4 488
Hogan et al. [18]	USA	1985/1986	R	H, J	1	160 H, 30 J	28 339
Liljus and Pesonen [27]	Finland	1985/1986	C	A, F	19	132	4 883
Rainard et al. [39]	France	1982/1988	R	H	1	45	1 550
Davidson et al. [10]	Canada	1988/1989	C	–	7	84	1 228
Nickerson and Boddie [33]	USA	–	R	J	1	120	1 747
Arendt [1]	Belgium	1983/1989	C	BBW, BRW	154	3 160	12 640
Schepers et al. [40]	Netherlands	1991/1993	C	–	7	544	22 467
Woolford et al. [49]	New Zealand	–	C	–	4	34	136
Chaffter et al. [8]	Israel	–	C	H	2	24	332
Detilleux et al. [12]	Belgium	1983/1989	C	–	154	2 084	11 453
Leitner et al. [25]	Israel	–	R	H	1	–	143

<sup>1</sup> C: commercial herd; R: research herd.

<sup>2</sup> A: Ayrshire; BBW: Belgian Black and White; BRW: Belgian Red and White; BS: Brown Swiss; F: Friesian; H: Holstein; J: Jersey; MRY: Meuse Rhine Yssel; SF: Swedish Friesian; SRB: Swedish Red and White.

<sup>3</sup> LSCC: herds with a low SCC ( $\leq 150\ 000$  c/mL); HSCC: herds with a high SCC ( $\geq 700\ 000$  c/mL).

<sup>4</sup> CM: quarters with previous treatment for clinical mastitis; WCM: quarters without any previous treatment for clinical mastitis.

–: No information available in the paper.

Herds free of *S. agalactiae* and *C. bovis*  
Cows more than 180 DIM  
Herds with a high prevalence of  
coagulase-negative staphylococci and  
free of *S. agalactiae*; multiparous cows  
Cows with SCC > 300 000 c/mL or  
< 100 000 c/mL.  
Samples free of clinical mastitis  
Primaparous cows  
Samples free of clinical mastitis  
Multiparous cows

**Table II.** Samples preservation and measurement techniques for somatic cells counting and bacteriological examinations in selected studies.

Reference	Preservation	Storage	SCC counting		Bacteriological procedure		Definition of infection
			Material	Fraction <sup>1</sup>	Procedure <sup>2</sup>	Fraction	
Ward and Schultz [48]	-	-	Filter-DNA	MFM	ST-M	F	At least 100 cfu/mL in 2 successive weekly samples
Brooks et al. [6]	Formalin	4 °C	Coulter C.	F	Standard	F	At least 120 cfu/mL in a single sample
Jaartveld et al. [23]	-	-	Coulter C.	F	-	F	-
Sheldrake et al. [44]	-	4 °C	Coulter C.	F	-	F	At least 100 cfu/mL in 2 successive weekly samples out of 3
Honkanen-Buzalski et al. [20]	-	-	Coulter C.	F	ST-V	F	At least 20 cfu/mL in 2 successive weekly samples
Brolund [5]	None	4 °C	Fossomatic	F	Standard	F	-
Mattila et al. [29]	None	None	Coulter C.	F	Standard	F	Several positive samples among a month
Erskine et al. [14]	-	-	Fossomatic	-	ST-D	-	-
Hogan et al. [17]	-	-	Fossomatic	F	ST-D	F	At least 100 cfu/mL in both duplicate samples
Timms and Schultz [45]	-	-	Filter-DNA	F	ST-V	F	At least 20 cfu/mL in 2 successive weekly samples
Hogan et al. [18]	-	-	Coulter C.	F	ST-M	F	At least 100 cfu/mL in 2 successive weekly samples out of 3 or in a sample with clinical mastitis
Lilius and Pesonen [27]	-	-	Fossomatic	F	-	F	-
Rainard et al. [39]	-	-	Coulter C.	F	ST-V	F	At least 240 cfu/mL in 2 successive samples (15 to 20 days interval)
Davidson et al. [10]	-	4 °C	Fossomatic	F	Standard	F	At least 200 cfu/mL in a single sample
Nickerson and Boddie [33]	-	-	Fossomatic	F	ST-T	F	At least 500 cfu/mL in 2 out of 3 triplicate samples, or at least 100 cfu/mL in all the triplicate samples
Arendt [1]	Formalin	4 °C	Fossomatic	F	ST-M-V	F	At least 40 cfu/mL in a single sample
Schepers et al. [40]	-	-	Fossomatic	F	Standard	F	At least 500 cfu/mL in 2 successive samples out of 3 (5 weeks interval), or 100 cfu/mL in 3 successive samples, or 100 cfu/mL in a sample with clinical mastitis
Woolford et al. [49]	-	-	Fossomatic	F, MFM, SM	ST-D	F, MFM, SM	At least 100 cfu/mL in 2 successive samples
Chaffier et al. [8]	-	-	Coulter C.	F	ST-D-M	F	At least 100 cfu/mL in 3 successive daily samples
Detilleux et al. [12]	Formalin	4 °C	Fossomatic	F	ST-M-V	F	At least 40 cfu/mL in a single sample
Leitner et al. [25]	-	-	Coulter C.	F	ST-D-M	F	Chronically infected

<sup>1</sup> F: foremilk; MFM: main flow milk; SM: stripping milk.

<sup>2</sup> Standard: standard procedure (NMC, 1999); ST-D: standard procedure improved with a duplication of samples; ST-M: standard procedure improved using more media; ST-T: standard procedure improved with a triplication of samples; ST-V: standard procedure improved using a larger inoculum volume.

-: No information available in the paper.

of the genera and the species was carried out by taking into account the cultural particularities of the bacteria being developed in the plates. In certain studies, this standard technique was modified at certain stages in order to improve the sensitivity of the bacteriological procedure. Consequently, higher inoculum volumes such as 0.025 mL [1, 39] or 0.05 mL [45] were streaked. Other culture media specific to certain bacteria were also used (Tab. II). Finally, the samples taken could be doubled or tripled during the same

milking in order to decrease the uninterpretable results (Tab. II).

**2.2.4. Definition of the intramammary infection**

The definition of IMI varied among the different studies (Tab. II). Some studies specified the minimal number of colony forming units/mL for a quarter to be declared infected. Infection was determined according to the results (i) of a bacteriological examination of a single sample [1, 6, 10, 12], or

**Table III.** Data provided in selected studies.

Reference	Unit <sup>1</sup>	SCC		Number of samples		Difference <sup>2</sup>	SD <sup>3</sup>	SE <sup>4</sup>
		Positive	Negative	Positive	Negative			
Ward and Schultz [48]	AM	+	+	+	+	-	-	-
Brooks et al. [6]	GM	+	+	+	+	-	+	-
Jaartsveld et al. [23]	GM	-	+	-	-	+	-	-
Sheldrake et al. [44]	L10	+	+	+	+	-	+	-
Honkanen-Buzalski et al. [20]	GM	+	+	+	+	-	-	-
Brolund [5]	L10	+	+	+	+	+	-	-
Mattila et al. [29]	AM	+	+	-	-	-	-	-
Erskine et al. [14]	L10	+	+	+	+	-	-	+
Hogan et al. [17]	L10	+	+	+	+	-	-	-
Timms and Schultz [45]	AM	+	+	+	+	-	-	+
Hogan et al. [18]	L10	+	+	+	+	-	-	-
Lilius and Pesonen [27]	GM	+	+	+	+	-	+	-
Rainard et al. [39]	LN	+	+	+	+	-	+	-
Davidson et al. [10]	LN	+	+	+	+	-	-	-
Nickerson and Boddie [33]	L10	+	+	+	+	-	-	-
Arendt [1]	AM	+	+	+	+	-	+	+
Schepers et al. [40]	LN	+	+	+	+	+	-	-
Woolford et al. [49]	LN	+	+	+	+	-	-	-
Chaffer et al. [8]	GM	+	+	+	+	-	+	-
Detilleux et al. [12]	S	+	+	+	+	-	+	-
Leitner et al. [25]	AM	+	+	+	+	-	-	+

<sup>1</sup> AM: arithmetic mean; GM: geometric mean; L10: logarithm base 10; LN: natural logarithm; S: score of SCC.

<sup>2</sup> Difference between SCC in bacteriologically positive and negative quarters.

<sup>3</sup> SD: standard deviation of SCC values in bacteriologically positive or negative quarters.

<sup>4</sup> SE: standard error of SCC values in bacteriologically positive or negative quarters.

-: Information not available in the paper.

+: Information available in the paper.

(ii) provided by several successive samples at intervals of between 1 day [8, 29] and 35 days [40].

### 2.3. Expression of SCC values

In the selected papers, tables provided means and standard deviations of SCC expressed in different units (crude SCC values, logarithm base 10, natural logarithm or scores of SCC) (Tab. III). According to the parameters of the distributions available in the papers, other parameters were estimated. When the available parameters described the lognormally-distributed crude SCCs, the parameters of natural logarithm of SCCs were estimated as follows [9]:

$$m_Y = \ln \left( \frac{\bar{X}}{\sqrt{\bar{X}^2 + \sigma_X^2}} \right) \quad S_Y^2 = \ln \left( 1 + \frac{\sigma_X^2}{\bar{X}} \right)$$

where:

$m_Y$  = estimated mean of natural logarithm of SCCs,

$S_Y^2$  = estimated variance of natural logarithm of SCCs,

$\bar{X}$  = observed mean of crude SCCs,

$\sigma_X^2$  = observed variance of crude SCCs.

When the available parameters described the normally-distributed logarithm of SCCs, the parameters of crude SCCs were estimated as follows [9]:

$$m_X = \sqrt{e^{\sigma_Y^2 + 2\bar{Y}}} \quad S_X^2 = \left( e^{\sigma_Y^2 + 2\bar{Y}} \right) \times \left( e^{\sigma_Y^2} - 1 \right)$$

where:

$m_X$  = estimated mean of crude SCCs,

$S_X^2$  = estimated variance of crude SCCs,

$\bar{Y}$  = observed mean of natural logarithm of SCCs,

$\sigma_Y^2$  = observed variance of natural logarithm of SCCs.

For each study, arithmetic means obtained either directly ( $\bar{X}$ ) or estimated ( $m_X$ )

from the paper were then quoted as SCC. Similarly, geometric means obtained by the antilog transformation of either observed ( $\bar{Y}$ ) or estimated ( $m_Y$ ) mean of natural logarithm of SCC were quoted as gSCC.

## 2.4. Statistical methods

### 2.4.1. Strategies of analysis

The aim of this paper was to assess a summary effect associated with an IMI by a given bacterium on SCC by meta-analysis on the selected papers. Three different strategies were used. The first two ones (A1 and A2) aimed at estimating the mean SCC value in case of IMI by a given bacterium or group of bacteria, whereas the third one (B) aimed at estimating the increase in mean SCC value in case of IMI, taking as reference that in bacteriologically negative samples. Strategies A1 and A2 differed by the methods of weighting the SCC values issued from each study: based on sample sizes only in strategy A1, and on both standard deviations of SCCs and sample sizes in strategy A2 (see below). Strategies A2 and B were performed according to the general variance-based method described by Petitti [36]. When using this method, data taken into account must be normally distributed. Therefore, the logarithm of the geometric mean of SCC was, in strategies A2 and B, the parameter deemed as relevant.

Whatever the strategy, the effects of the infection by *Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Streptococcus uberis*, *Corynebacterium bovis*, the coliform group and the group of Staphylococci other than *S. aureus* were estimated separately.

### 2.4.2. SCC parameters considered in each strategy

In each study  $i$ , the SCC parameters of interest varied according to the performed strategy.

In strategy A1, the SCC parameters considered were the arithmetic means in positive samples  $p$  for each bacterium or group of bacteria  $b$  ( $aSCC_{pib}$ ). In strategy A2, the SCC parameters considered were the logarithm of the geometric means in positive samples ( $Ln(gSCC_{pib})$ ).

In strategy B, the elementary observed increase ( $\Delta_{ib}$ ) associated with infection by a bacterium or a bacterial group  $b$  was defined as the difference in the logarithm of the geometric mean of SCCs, measured, on the one hand, in the positive samples, and on the other hand, in the bacteriologically negative samples ( $n$ ).

$$\Delta_{ib} = Ln(gSCC_{pib}) - Ln(gSCC_{ni})$$

where:

$\Delta_{ib}$  = elementary observed increase for study  $i$  in bacterial group  $b$ ,

$gSCC_{pib}$  = geometric mean of SCCs in the positive samples for study  $i$  in bacterial group  $b$ ,

$gSCC_{ni}$  = geometric mean of SCCs in the bacteriologically negative samples for study  $i$ .

Consequently, the increase corresponds to the logarithm of the ratio between the geometric mean of SCCs in the two groups. This increase was directly obtained from the study (as an estimate issued from the statistical model) or calculated from the observed data.

**2.4.3. Weight given to each study**

The weight ( $w_{ib}$ ) of a study  $i$  was quantified by its contribution to the calculation of the estimated effect and depends on the strategy.

In strategy A1, we chose to weight each aSCC study  $i$  by the number of positive samples for each bacterium or group of bacteria  $b$  ( $n_{pib}$ ).

In strategies A2 and B, this weight was calculated as the inverse in the variance of

the SCC in positive samples (strategy A2) and both positive and negative samples (strategy B).

$$w_{ib} = \frac{1}{var_{ib}}$$

where:

$w_{ib}$  = weight of the study  $i$  in bacterial group  $b$ ,

$var_{ib}$  = variance of  $\Delta_{ib}$ .

The variance ( $var_{ib}$ ) was estimated in three ways depending on available data (Tab. III).

In case the standard deviations were available, the variance was calculated as:

$$(1) \quad var_{ib} = \left( \frac{\sigma_{pib}^2}{n_{pib}} \right) \quad (\text{strategy A2})$$

$$var_{ib} = \left( \frac{\sigma_{pib}^2}{n_{pib}} + \frac{\sigma_{ni}^2}{n_{ni}} \right) \quad (\text{strategy B})$$

where:

$\sigma_{pib}^2$  = variance of SCC in the positive samples for study  $i$  in bacterial group  $b$ ,

$\sigma_{ni}^2$  = variance of SCC in bacteriologically negative samples for study  $i$ ,

$n_{pib}$  = number of the positive samples for study  $i$  in bacterial group  $b$ ,

$n_{ni}$  = number of bacteriologically negative samples for study  $i$ .

In case the standard errors were available, the variance was calculated as:

$$(2) \quad var_{ib} = SE_{pib}^2 \quad (\text{strategy A2})$$

$$var_{ib} = SE_{pib}^2 + SE_{ni}^2 \quad (\text{strategy B})$$

where:

$SE_{pib}^2$  = standard error of SCC in the positive samples for study  $i$  in bacterial group  $b$ ,

$SE_{ni}^2$  = standard error of SCC in bacteriologically negative samples for study  $i$ .

In case the error mean square of the model was available, the variance was calculated as:

$$(3) \text{var}_{ib} = \text{mse}_i \times \left( \frac{1}{n_{pib}} + \frac{1}{n_{ni}} \right) (\text{strategy B})$$

where:  $\text{mse}_i$  = error mean square of the model in the study  $i$ .

In 9 of 21 selected studies, the data necessary for the calculation of the variance were not available. For these studies, the variance considered for strategies A2 and B was the third quartile of the available variances distribution. Finally, in two selected studies [23, 29] the sample size relative to each type of infection was lacking (Tab. III). Consequently, these two studies were not included in the meta-analysis.

#### 2.4.4. Calculation of the summary estimated effect

Given both the relevant parameters ( $aSCC_{pib}$  or  $\text{Ln}(gSCC_{pib})$  or  $\Delta_{ib}$ ) and weights ( $n_{ib}$  or  $1/\text{var}_{ib}$ ) issued from each study  $i$ , the summary estimated effect ( $E_s$ ) on SCC associated with infection by each group of bacteria as well as its 95%-confidence interval (for strategies A2 and B) were therefore calculated as follows depending on the strategy:

$$E_s = \frac{\sum (w_{ib} \times aSCC_{pib})}{\sum (w_{ib})} \quad (\text{strategy A1})$$

$$E_s = \frac{\sum (w_{ib} \times \text{Ln}(gSCC_{pib}))}{\sum (w_{ib})} \quad \text{and}$$

$$CI_s = E_s \pm 1.96 \times \sqrt{\frac{1}{\sum (w_{ib})}} \quad (\text{strategy A2})$$

$$E_s = \frac{\sum (w_{ib} \times \Delta_{ib})}{\sum (w_{ib})} \quad \text{and}$$

$$CI_s = E_s \pm 1.96 \times \sqrt{\frac{1}{\sum (w_{ib})}} \quad (\text{strategy B})$$

where:

$E_s$  = summary estimated effect associated with infection by bacterial group  $b$ ,

$w_{ib}$  = weight of the study  $i$  in bacterial group  $b$ ,

$aSCC_{pib}$  = arithmetic mean of SCC in the positive samples for study  $i$  in bacterial group  $b$ ,

$gSCC_{pib}$  = geometric mean of SCC in the positive samples for study  $i$  in bacterial group  $b$ ,

$\Delta_{ib}$  = elementary observed increase for study  $i$  in bacterial group  $b$ ,

$CI_s$  = 95%-confidence interval of the  $E_s$ .

#### 2.4.5. Test for homogeneity

The homogeneity of the effects observed in the different studies included in the calculation was tested for strategies A2 and B. The test for homogeneity consisted of calculating for each study a value for parameter  $Q$  [36]:

$$Q = \sum [w_{ib} \times (E_s - \text{Ln}(gSCC_{pib}))^2] \quad (\text{strategy A2})$$

$$Q = \sum [w_{ib} \times (E_s - \Delta_{ib})^2] \quad (\text{strategy B})$$

where:

$E_s$  = summary estimated effect associated with infection by bacterial group  $b$ ,

$w_{ib}$  = weight of the study  $i$  in bacterial group  $b$ ,

$gSCC_{pib}$  = geometric mean of SCCs in the positive samples for study  $i$  in bacterial group  $b$ ,

$\Delta_{ib}$  = elementary observed increase for study  $i$  in bacterial group  $b$ .

This  $Q$  value was referred to the Chi-square distribution with degrees of freedom equal to the number of included studies minus 1. The different reasons for heterogeneity between the studies could have been investigated by comparing the summary estimated increase for different variation factors related to (i) the study design, (ii) the measurement equipment for SCC (Fossomatic versus Coulter Counter) and (iii) the definition of IMI (infection based on a single sample versus several successive

samples) (Tab. II). These effect could not be studied separately given the small number of selected studies and the interrelationships between the putative variation factors. For instance, in the 9 studies using the Coulter Counter, only one study had a definition of the infection based on a single sample, and in the 10 studies using the Fossomatic, only 2 studies had a definition of the infection based on successive samples.

#### 2.4.6. Sensitivity analysis

To investigate the possible impact of very large weight on the summary estimated effect obtained from the meta-analysis, a sensitivity analysis was performed considering as an example the effect of IMI due to *Staphylococcus aureus* on SCC by eliminating the studies with the largest weights one by one for strategies A2 and B.

### 2.5. Expression of the results

In strategy A2, the summary estimated effect associated with an IMI by a given bacterium on SCC was calculated in logarithmic unit. In Table IV, the geometric mean SCC and its 95%-confidence interval were expressed as the antilog of the estimated values. In the strategy B, the summary estimated increase ( $\Delta_s$ ) for each group of bacteria was also expressed in a logarithmic unit. In Table V, this effect was re-expressed in the multiplying factor (the antilog of  $\Delta_s$ ) in case of infection, of the summary mean SCC in the bacteriologically negative samples (calculated in the strategy A2). A simulated SCC value was then calculated by multiplying the summary mean SCC in the bacteriologically negative samples by the multiplying factor.

## 3. RESULTS

### 3.1. SCC values in the bacteriologically negative quarters

In the absence of a diagnosed infection, the geometric mean of milk SCC varied greatly among the different studies (Fig. 1) with extremes of 14 000 [40] and 397 000 c/mL measured on quarters in Meuse Rhine Yssel cows [23]. The 95%-confidence interval of individual values (based on SD) also varied between studies: it was (1 700; 109 000 c/mL) [8], and (7 000; 1 849 000 c/mL) in herds characterised by a high herd SCC ( $\geq 700 000$  c/mL) [14].

The summary estimated SCC value in bacteriologically negative quarters was estimated at 187 000 and 68 000 c/mL from strategies A1 and A2 respectively (Tab. IV).

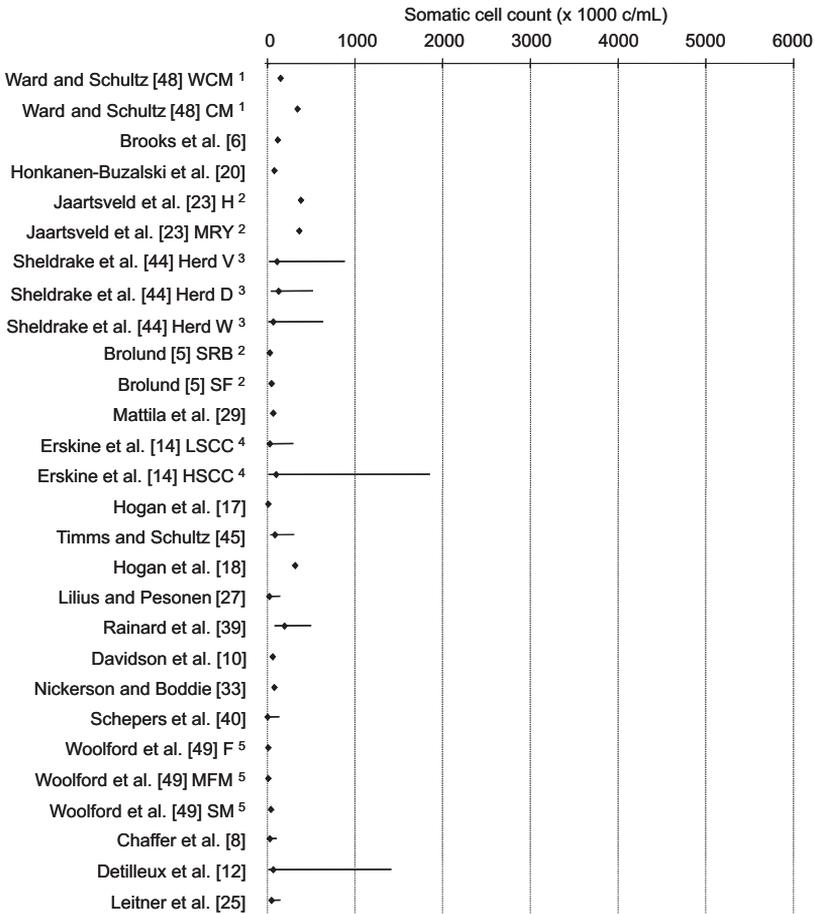
### 3.2. SCC values in the quarters infected by major pathogens

The prevalence (that is the percentage of samples positive to the bacterium among all samples) of IMI due to *Staphylococcus aureus* in the selected studies varied between 0.7% [14] and 16.2% [1]. The geometric mean of SCC in infected quarters varied between 158 000 c/mL [17] and 2 525 000 c/mL [44] (Fig. 2). The summary estimated effect in case of IMI by *Staphylococcus aureus* was a value of 1 426 000 c/mL and 333 000 c/mL from strategies A1 and A2 respectively (Tab. IV) and a multiplying factor of 5.2 which resulted in a simulated SCC value of 357 000 c/mL from strategy B (Tab. V).

The prevalence of IMI due to *Streptococcus agalactiae* varied widely between the selected studies. The extreme values were reported by Erskine et al. [14], in which the prevalence of IMI due to *Streptococcus*

**Table IV.** Summary effects of intramammary infection on quarter somatic cell count ( $\times 1\,000$  c/mL) (strategy A1 and A2).

Bacteriological status	Strategy A1		Strategy A2		Studies (reference numbers)	
	Arithmetic mean	Range <sup>1</sup>	Geometric mean	CI <sup>2</sup>		Q <sup>3</sup>
Negative	187	[27–600]	68	[67–69]		
<i>Staphylococcus aureus</i>	1 426	[191–9 433]	333	[320–348]	824 (s)	[5, 6, 8, 10, 12, 14, 17, 18, 20, 25, 27, 33, 39, 40, 44, 45, 48, 49]
<i>Streptococcus agalactiae</i>	3 792	[561–4 758]	1 129	[1 056–1 206]	492 (s)	[5, 8, 10, 12, 14, 17, 25, 27, 40, 44, 45, 48, 49]
<i>Streptococcus dysgalactiae</i>	1 221	[809–1 944]	547	[492–609]	0.08 (ns)	[12, 14, 17, 48]
<i>Streptococcus uberis</i>	2 065	[851–1 085]	1 024	[880–1 192]	10 (ns)	[1, 25, 40]
Coliforms	5 331	[590–9 009]	4 196	[3 713–4 743]	191 (s)	[40, 45, 48, 49]
Staphylococci other than <i>S. aureus</i>	475	[90–3 040]	155	[152–158]	6 804 (s)	[14, 17, 18, 27, 45]
<i>Corynebacterium bovis</i>	773	[128–1 352]	164	[161–168]	10 859 (s)	[5, 8, 10, 12, 14, 17, 18, 25, 27, 33, 39, 40, 45, 48, 49]
						[1, 6, 14, 17, 18, 20, 40]



**Figure 1.** Geometric mean SCC (◆) and its 95% CI (—) of bacteriologically negative quarters (SCC in × 1 000 c/mL whatever of the measurement equipment used).

<sup>1</sup> CM: quarters with previous treatment for clinical mastitis; WCM: quarters without any previous treatment for clinical mastitis.

<sup>2</sup> H: Holstein; MRY: Meuse Rhine Yssel; SF: Swedish Friesian; SRB: Swedish Red and White.

<sup>3</sup> Results observed in three different herds called V, D and W in the study.

<sup>4</sup> LSCC: herds with a low SCC (≤ 150 000 c/mL); HSCC: herds with a high SCC (≥ 700 000 c/mL).

<sup>5</sup> F: foremilk; MFM: main flow milk; SM: stripping milk.

*agalactiae* was estimated to be less than 0.1% in 16 herds characterised by a herd SCC ≤ 150 000 c/mL, and of 25.7% in 16 other herds characterised by a high herd SCC (≥ 700 000 c/mL). The geometric mean of SCC in infected quarters varied between 366 000 [48] and 2 239 000 c/mL [14] (Fig. 3). The summary estimated effect in

case of IMI by *Streptococcus agalactiae* was a value of 3 792 000 c/mL and 1 129 000 c/mL from strategies A1 and A2 respectively (Tab. IV) and a multiplying factor of 12.6 which resulted in a simulated SCC value of 857 000 c/mL from strategy B (Tab. V).

The prevalence of IMI due to *Streptococcus dysgalactiae* in the selected studies

**Table V.** Summary effects of intramammary infection on quarter somatic cell count (strategy B).

Bacteriological status	Estimated effect <sup>1</sup>	CI <sup>2</sup> 95%	Q <sup>3</sup>	Simulated SCC (× 1 000 c/mL)	Studies (reference numbers)
Negative				68	[5, 6, 8, 10, 12, 14, 17, 18, 20, 25, 27, 33, 39, 40, 44, 45, 48, 49]
<i>Staphylococcus aureus</i>	× 5.2	[5 – 5.5]	508 (s)	357	[5, 8, 10, 12, 14, 17, 25, 27, 40, 44, 45, 48, 49]
<i>Streptococcus agalactiae</i>	× 12.6	[11.6 – 13.6]	359 (s)	857	[12, 14, 17, 48]
<i>Streptococcus dysgalactiae</i>	× 5.7	[5.1 – 6.4]	3 (ns)	388	[1, 25, 40]
<i>Streptococcus uberis</i>	× 9.1	[7.7 – 10.7]	68 (s)	772	[40, 45, 48, 49]
Coliforms	× 16.9	[14.8 – 19.2]	6 (ns)	1 151	[14, 17, 18, 27, 45]
Staphylococci other than <i>S. aureus</i>	× 2.0	[2 – 2.1]	447 (s)	138	[5, 8, 10, 12, 14, 17, 18, 25, 27, 33, 39, 40, 45, 48, 49]
<i>Corynebacterium bovis</i>	× 1.5	[1.5 – 1.6]	481 (s)	105	[1, 6, 14, 17, 18, 20, 40]

<sup>1</sup> Multiplying factor of SCC estimated in bacteriological negative samples.

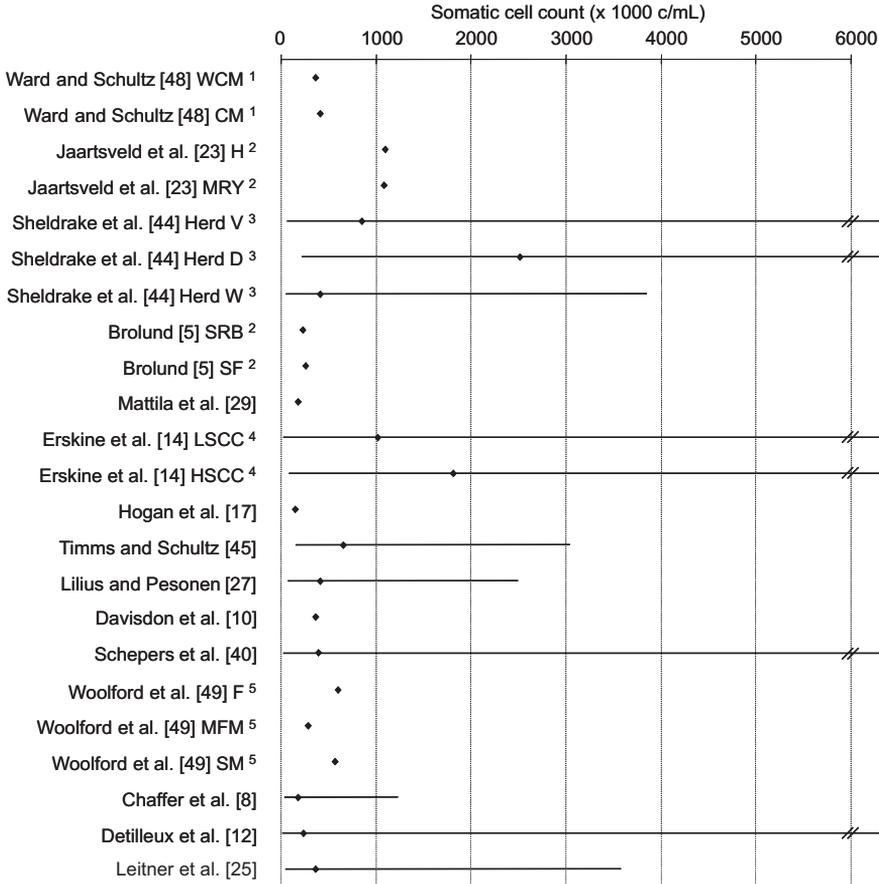
<sup>2</sup> CI: confidence interval of the estimated effect.

<sup>3</sup> Q: test for homogeneity; s: significant; ns: non significant.

varied from 0.03% [1] to 0.4% [40]. When measured by the Coulter Counter, the geometric mean of SCC in infected quarters varied from 420 000 [29] to 1 168 000 c/mL measured on quarters in Holstein cows [23] (Fig. 4). The summary estimated effect in case of IMI by *Streptococcus dysgalactiae* was a value of 1 221 000 c/mL and

547 000 c/mL from strategies A1 and A2 respectively (Tab. IV) and a multiplying factor of 5.7 which resulted in a simulated SCC value of 388 000 c/mL from strategy B (Tab. V).

The prevalence of IMI due to *Streptococcus uberis* in the selected studies varied between 0.5% [40] and 7.9% [48], the latter



**Figure 2.** Geometric mean SCC (◆) and its 95% CI (—) of quarters in cases of infection by *Staphylococcus aureus* (SCC in × 1 000 c/mL whatever of the measurement equipment used).

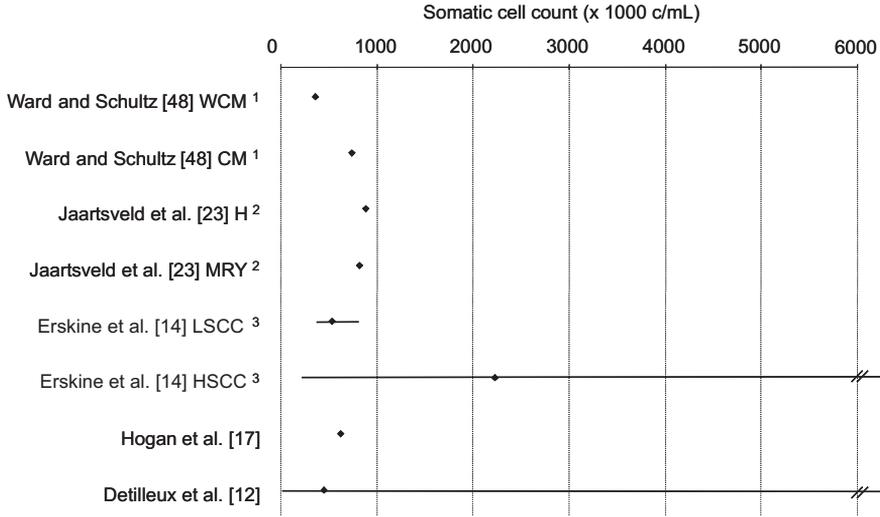
<sup>1</sup> CM: quarters with previous treatment for clinical mastitis; WCM: quarters without any previous treatment for clinical mastitis.

<sup>2</sup> H: Holstein; MRY: Meuse Rhine Yssel; SF: Swedish Friesian; SRB: Swedish Red and White.

<sup>3</sup> Results observed in three different herds called V, D and W in the study.

<sup>4</sup> LSCC: herds with a low SCC (≤ 150 000 c/mL); HSCC: herds with a high (≥ 700 000 c/mL).

<sup>5</sup> F: foremilk; MFM: main flow milk; SM: stripping milk.

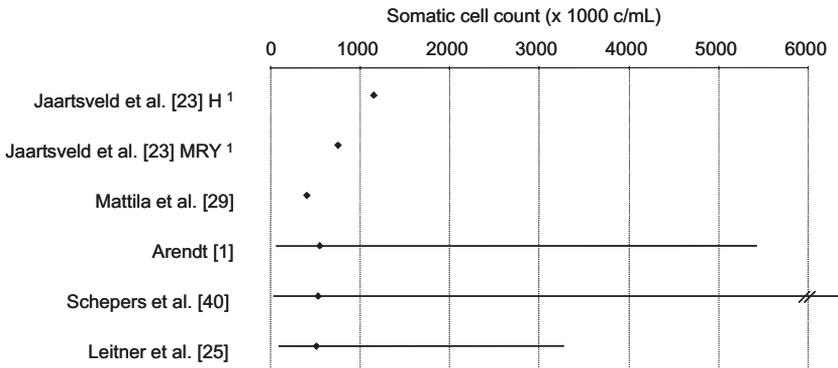


**Figure 3.** Geometric mean SCC (◆) and its 95% CI (—) of quarters in cases of infection by *Streptococcus agalactiae* (SCC in × 1 000 c/mL whatever of the measurement equipment used).

<sup>1</sup> CM: quarters with previous treatment for clinical mastitis; WCM: quarters without any previous treatment for clinical mastitis.

<sup>2</sup> H: Holstein; MRY: Meuse Rhine Yssel; SF: Swedish Friesian; SRB: Swedish Red and White.

<sup>3</sup> LSCC: herds with a low SCC (≤ 150 000 c/mL); HSCC: herds with a high SCC (≥ 700 000 c/mL).

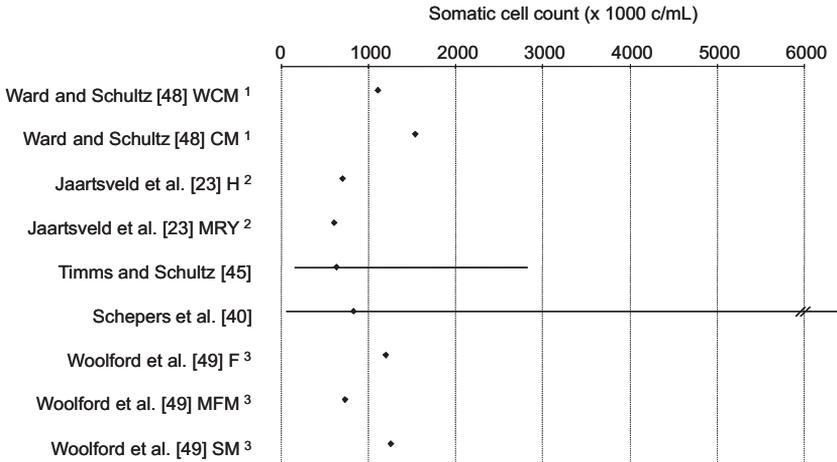


**Figure 4.** Geometric mean SCC (◆) and its 95% CI (—) of quarters in cases of infection by *Streptococcus dysgalactiae* (SCC in × 1 000 c/mL whatever of the measurement equipment used).

<sup>1</sup> H: Holstein; MRY: Meuse Rhine Yssel.

being observed in quarters which had experienced at least one previous treatment for clinical mastitis. The geometric mean of SCC in infected quarters varied between 609 000 [23] and 1 538 000 c/mL [48] (Fig. 5). The summary estimated effect in case

of IMI by *Streptococcus uberis* was a value of 2 065 000 c/mL and 1 024 000 c/mL from strategies A1 and A2 respectively (Tab. IV) and a multiplying factor of 9.1 which resulted in a simulated SCC value of 772 000 c/mL from strategy B (Tab. V).

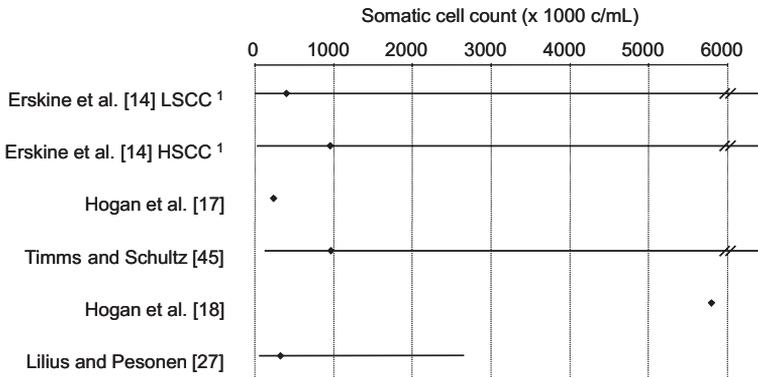


**Figure 5.** Geometric mean SCC (◆) and its 95% CI (—) of quarters in cases of infection by *Streptococcus uberis* (SCC in × 1 000 c/mL whatever of the measurement equipment used).

<sup>1</sup> CM: quarters with previous treatment for clinical mastitis; WCM: quarters without any previous treatment for clinical mastitis.

<sup>2</sup> H: Holstein; MRY: Meuse Rhine Yssel.

<sup>3</sup> F: foremilk; MFM: main flow milk; SM: stripping milk.



**Figure 6.** Geometric mean SCC (◆) and its 95% CI (—) of quarters in cases of infection by Coliforms (SCC in × 1 000 c/mL whatever of the measurement equipment used).

<sup>1</sup> LSCC: herds with a low SCC (≤ 150 000 c/mL); HSCC: herds with a high SCC (≥ 700 000 c/mL).

The prevalence of IMI due to coliforms in the selected studies varied between 0.02% [27] and 3.4% [17]. The geometric mean of SCC in infected quarters varied between 251 000 [17] and 5 816 000 c/mL [18] (Fig. 6). The summary estimated effect

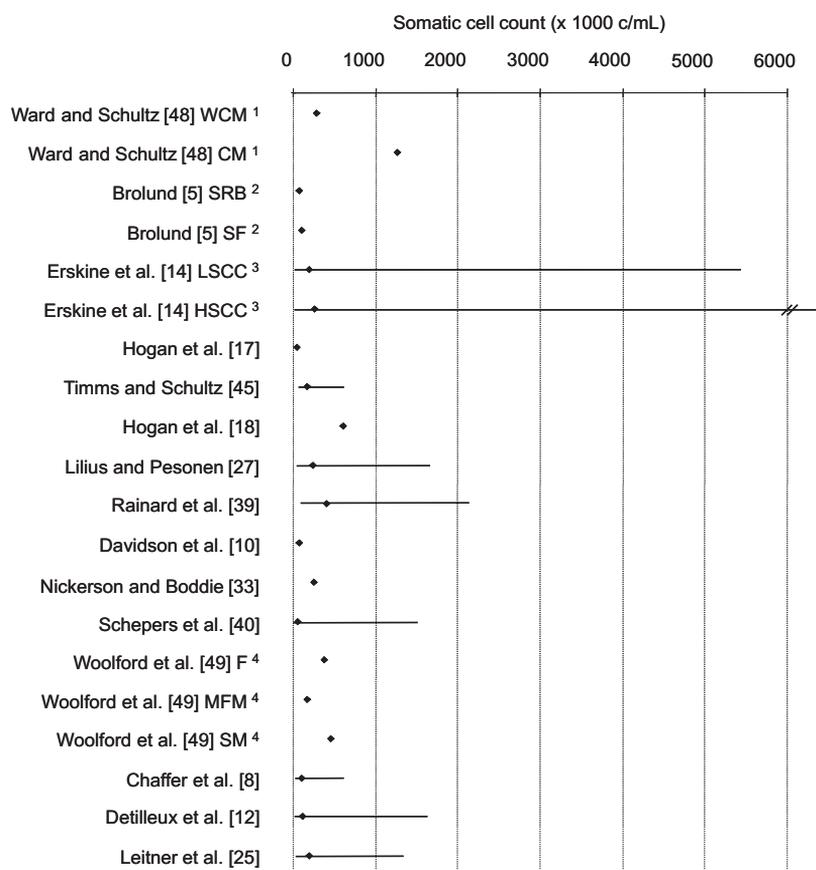
in case of IMI by coliforms was a value of 5 331 000 c/mL and 4 196 000 c/mL from strategies A1 and A2 respectively (Tab. IV) and a multiplying factor of 16.9 which resulted in a simulated SCC value of 1 151 000 c/mL from strategy B (Tab. V).

### 3.3. SCC values for quarters infected by minor pathogens

The prevalence of IMI due to staphylococci other than *S. aureus* in the selected studies varied between 5.5% [48] and 27.1% [8]. The geometric mean of SCC in infected quarters varied between 63 000 [17] and 1 277 000 c/mL measured on quarter with previous treatment for clinical mastitis [48] (Fig. 7). The summary estimated effect in case of IMI by staphylo-

cocci other than *S. aureus* was a value of 475 000 c/mL and 155 000 c/mL from strategies A1 and A2 respectively (Tab. IV) and a multiplying factor of 2 which resulted in a simulated SCC value of 138 000 c/mL from strategy B (Tab. V).

The prevalence of IMI due to *Corynebacterium bovis* in the selected studies was from 5% [17] to 41% [40]. The geometric mean of SCC in infected quarters varied between 40 000 [17] and 421 000 c/mL [18] (Fig. 8). The summary



**Figure 7.** Geometric mean SCC (◆) and its 95% CI (—) of quarters in cases of infection by staphylococci other than *S. aureus* (SCC in  $\times 1\,000$  c/mL whatever of the measurement equipment used).

<sup>1</sup> CM: quarters with previous treatment for clinical mastitis; WCM: quarters without any previous treatment for clinical mastitis.

<sup>2</sup> SF: Swedish Friesian; SRB: Swedish Red and White.

<sup>3</sup> LSCC: herds with a low SCC ( $\leq 150\,000$  c/mL); HSCC: herds with a high SCC ( $\geq 700\,000$  c/mL).

<sup>4</sup> F: foremilk; MFM: main flow milk; SM: stripping milk.

estimated effect in case of IMI by *Corynebacterium bovis* was a value of 773 000 c/mL and 164 000 c/mL from strategies A1 and A2 respectively (Tab. IV) and a multiplying factor of 1.5 which resulted in a simulated SCC value of 105 000 c/mL from strategy B (Tab. V).

**3.4. Sensitivity analysis**

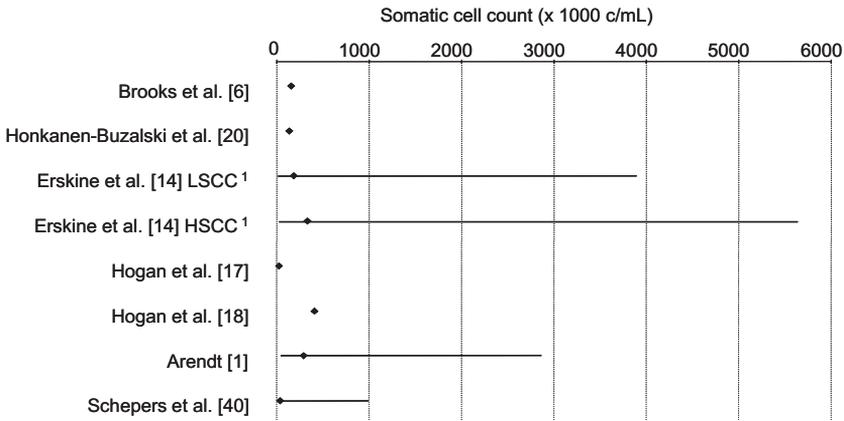
The recalculation of the summary mean SCC in case of IMI by *Staphylococcus aureus* when studies with large weights were eliminated one by one showed that the estimated effect varied from 287 000 to 414 000 c/mL, when using strategy A2. From strategy B, the multiplying factor varied from 5.0 to 6.3 (Tab. VI).

**4. DISCUSSION**

A meta-analysis is a quantitative approach used to provide a summary estimate of the effect associated with a given factor, by combining the results of several studies. In the present paper, this method was applied to assess a summary effect associated with an IMI by a given bacterium on SCC at

quarter level. To our knowledge, no previous meta-analysis has been carried out on this topic.

Three strategies were performed to reach this goal. The first one (strategy A1) used crude SCC values, and provided a summary estimate based on arithmetic means of SCC, weighted by study-sample sizes. However, crude SCC values are known to be lognormally-distributed. Consequently, arithmetic means of crude SCC are heavily influenced by high SCC values (which are rather rare), and therefore may not be the relevant parameters to get a summary effect. The two other ones (strategies A2 and B) used SCC values after logarithmic transformation, and provided a summary estimate based on geometric means of SCC, which are known to be close to the median value of crude SCC distribution. Furthermore, when choosing these two latter strategies, the calculation based on the general based method described by Petitti [36] was made possible. This method allows us to improve the weighting by taking into account both the sample size in each study and the within-study SCC variability (standard deviation of the logarithm of SCC). To our opinion, the summary effects



**Figure 8.** Geometric mean SCC (◆) and its 95% CI (—) of quarters in cases of infection by *Corynebacterium bovis* (SCC in × 1 000 c/mL whatever of the measurement equipment used).

<sup>1</sup> LSCC: herds with a low SCC (≤ 150 000 c/mL); HSCC: herds with a high SCC (≥ 700 000 c/mL).

**Table VI.** Consequences of the exclusion of the studies characterised by large weight on the results of the meta-analysis in cases of infection by *Staphylococcus aureus*.

	Strategy A2		Strategy B	
	Estimated effect <sup>1</sup>	Study weight	Estimated effect <sup>2</sup>	Study weight
Inclusion of all the studies	333	–	5.2	–
Elimination of Sheldrake et al. [44]	287	108	5.1	57
Elimination of Brolund [5]	414	506	5.5	472
Elimination of Erskine et al. [14]	313	75	5.0	65
Elimination of Lilius et Pesonen [27]	331	68	5.1	59
Elimination of Schepers et al. [40]	328	169	4.9	195
Elimination of Detilleux et al. [12]	371	574	6.3	486
Elimination of these 6 previous studies	298	–	5.4	–

<sup>1</sup> Geometric mean ( $\times 1\,000$  c/mL).

<sup>2</sup> Multiplying factor of SCC estimated in bacteriological negative samples.

estimated from strategies A2 and B were deemed more convenient.

Strategies A2 and B differed by the fact that the former aimed at estimating the summary effect of each type of IMI from the SCC value in positive samples, and the latter from the increase in SCC value associated with infection, taking as reference that observed in bacteriologically negative samples. The summary SCC values estimated from the two strategies were quite different (Tabs. IV and V). However the Q-test values calculated for a given bacterium or group of bacteria in the two strategies can be compared (because they follow a chi-square distribution with the same degrees of freedom). The idea was that the smaller the Q-test value was, the more convenient the summary estimate. In case of infection by *Staphylococcus aureus*, *Streptococcus agalactiae*, coliforms or minor pathogens, the summary effect of IMI calculated on the basis of the increase in SCC (Tab. V) seemed to give a better estimation than that based on SCC values in positive samples.

On the contrary, in case of infection by *Streptococcus dysgalactiae* or *Streptococcus uberis*, the summary effect of IMI calculated on the basis of SCC values in positive samples were preferred (Tab. IV). The mean SCC in bacteriologically negative quarters was 68 000 c/mL. In case of IMI by major pathogens, the retained mean SCC was 357 000, 857 000, 547 000, 1 024 000 and 1 151 000 c/mL in quarters infected by *Staphylococcus aureus*, *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, *Streptococcus uberis*, coliforms respectively. In case of IMI by minor pathogens, the retained mean SCC was 138 000 and 105 000 c/mL in quarters infected by staphylococci other than *S. aureus* and *Corynebacterium bovis*, respectively.

The estimations presented above depend on the weight given to each study. A sensitivity analysis was performed in order to evaluate the impact of the study weight on the summary estimated effect associated with infection by *Staphylococcus aureus*.

Whatever the strategy performed (A2 or B), little variation in SCC depending on the studies taken into account was observed (Tab. VI), suggesting that heterogeneity between studies had, in this case, a little impact on summary estimates.

Papers were selected based on a list of criteria to limit the main sources of heterogeneity that may have biased the results. This preliminary step improves a priori the reliability of estimates obtained by the meta-analysis. In this study, selected papers were recent, the IMIs were natural and the measure of SCC and the bacteriological examinations were performed from samples collected on the same milking. Other variation factors may, however, remain (in relation to country, year, farming practices, prevalence of infection, the nature of the main bacteria involved and SCC measurement equipment). The meta-analysis performed on data stratified according to the main putative variation factors (for instance, measurement equipment, definition of IMI, country) could be done in order to quantify the effect of each variation factor. Such analysis was not performed in the present study given the small number of selected studies and the interrelationships between the putative variation factors. Furthermore, in some selected papers, such information was lacking.

Some variation factors are related to the sampling and storage conditions of milk. The way of preserving milk samples has an effect on SCC: samples which were kept using potassium-bichromate had SCC (450 000 c/mL) higher than the same samples not preserved (400 000 c/mL) [28]. The temperature and duration of storage may also influence both SCC [3, 16] and bacteriological results [15, 41, 47]. Samples had SCC slightly lower (minus 25 000 c/mL) when stored for 10 days at 4 °C than when stored at room temperature [16]. Freezing at -20 °C was associated with a slight decrease in SCC [3], and with a reduction in the number of positive samples

to *E. coli* and *Corynebacterium pyogenes* and an increase in the number of positive samples to Staphylococci [41].

The SCC measurement equipment used (Fossomatic, Coulter Counter or filter DNA) was reported to affect the SCC values. For instance, Miller et al. [30] reported that the geometric mean of SCC was increased by 12 000 c/mL in foremilk and by 130 000 c/mL in the stripping milk when SCC was measured by the Coulter Counter compared to that measured by the Fossomatic. Contrary to the Fossomatic, the Coulter Counter is not DNA specific. The increase in SCC observed with the Coulter Counter is probably related to the counting of cellular fragments, protein aggregates, and various artefacts [30].

The reported variability between studies may also be related to the bacteriological procedures implemented. If the quantity of bacteria present in the milk is large, streaking a small volume of milk could be enough to detect the IMI [7]. On the contrary, if the quantity of bacteria present in the milk is small, a false negative diagnosis is probable if the volume of the inoculation is small. Streaking 0.1 or 0.05 mL instead of 0.01 mL (recommended by the standard technique) greatly improved the sensitivity of identifying *Staphylococcus aureus* [7, 24]. The sensitivity of detection of a bacteriologically positive result was found to be 77%, 85%, and 90% in cases of 0.01, 0.05, and 0.1 mL streaking of udder milk respectively [24].

In some selected papers, the infectious status of the quarter was defined on the basis of a single bacteriological result, whereas others accounted for at least two successive samples (daily, weekly or monthly). The determination of the IMI based on a single result is most of the time not very accurate [37]. Some chronically infected quarters eliminate bacteria in milk sporadically, leading to possible false negative results [7, 29, 43]. Taking repeated samples limits the number of false-negative samples. The sensitivity of the bacteriological

examination to detect infected quarters by *Staphylococcus aureus* goes from 60% if the bacteriological examination is done with single samples to 91% if the samples were taken for 3 successive days [7]. In this context, the IMI may also be defined considering the dynamics of the infectious process during the whole lactation, and not as if each bacteriological result was independent (as in most studies selected here). Brolund [5] reported that for Swedish red and white breed, the SCC of quarters with a low occurrence of bacteriologically negative findings (less than 20% of lactation) was on average 3.2 time higher than SCC of quarters with a high occurrence of bacteriologically negative findings (84 to 100% of lactation) (123 000 vs. 39 000 cell/mL). The corresponding deviation in Swedish Friesian breed was on average 2.8 time (119 000 vs. 42 000 cell/mL). Furthermore SCC measured in a bacteriologically negative quarters may vary whether or not a previous IMI occurred. After a cured IMI, SCC may remain high for several days [11, 13, 32, 48].

Anyway, the effect associated with all these putative factors appears to be small in comparison to that associated with infection.

The selected studies reported SCC values measured in quarters in the absence or presence of IMI by a specific bacterium. Because of the insufficient number of studies reporting the same type of data in milk from the whole mammary gland, no meta-analysis was carried out at this level of measurement. As a general rule, the increase in SCC during IMI is less pronounced if it is measured at the udder level than if it is measured at the quarter level [6, 46]. For instance, Timms et al. [46] reported that infections caused by major pathogens, SCC was 679 000 c/mL for udder milk and 1 251 000 c/mL for quarter milk. The relation between SCC measured on udder milk and IMI must be interpreted with caution. Firstly, a mammary gland is often considered as infected when at least

one quarter is infected [23, 46]. An increase in SCC value associated with an IMI in one quarter may be reduced by a 'dilution' effect if all other quarters are found to be bacteriologically negative. On the contrary, in the case of IMI in a quarter, an inflammatory reaction (associated with an increase in SCC of at least 250 000 c/mL) may occur in an adjacent bacteriologically negative quarter [2]. However, the SCC measured at the mammary gland level was reported to increase with an increased number of infected quarters [23, 32]. Secondly, controlling for all other variation factors, SCC may also depend upon the fraction of milk sampled [19, 34, 35, 49]. The SCC at the quarter level is measured, most often, on only foremilk whereas SCC at the udder level is measured on the milk from the entire milking.

Using the meta-analysis method, this paper aimed at combining the results of several studies to estimate the average quarter SCC value for a quarter infected by a given bacterium. The method allowed the estimation of average values from very large and diverse populations. The average SCC in bacteriologically negative quarters was about 70 000 c/mL, quarters infected by minor pathogens had an average SCC between 110 000 and 150 000 c/mL, and quarters infected by major pathogens had an average SCC higher than 350 000 c/mL.

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