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Cervical mucus symptom and daily fecundability: First results from a new data base

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Keywords: cervical mucus, daily fecundability, fertile period, logit model, Billings ovulation method, fertility awareness, natural family planning

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1. Introduction

Relying on the issues of –say- the past five years of *Studies in Family Planning* and on recent publications of the United Nations (2000, 2002), it is possible to get information about the prevalence of the method of periodic abstinence (in the wording of the DHS of Macro Intentional; rhythm in the UN publications) in natural family planning (or NFP). In the 1998 Cameroon DHS, for instance, this method accounts for more than a half of all contraceptive use. The same happens in a few other developing countries with relatively low contraceptive prevalence (See also Johnson–Hanks 2002). The method is rated first in use in more than a dozen countries. In a few, with very different cultural background (from Poland to Bolivia and Peru, from Mongolia to Ukraine, from Sri-Lanka to the Democratic Republic of Korea), it shows a marked impact.

This method implies the possibility of predicting the fertile phase in a woman's menstrual cycle. For that purpose, the main approaches rely on indicators that can be easily used in the home environment, such as cycle calendar, basal body temperature (BBT) and cervical mucus symptom (CMS). The knowledge of the characteristics of these markers and their relationship with intercourse behaviour allow to identify levels of daily fecundability, defined as the probability of conception for a single day as a result of coitus on that day alone. And it makes also possible to perform bio-statistical research in several directions in the area.

A large data base useful for studying daily fecundability was constructed from a prospective study during 1992-96 with the collaboration of seven European centres providing services on NFP. The data base included also information extracted retrospectively from the records obtained in a prospective study of conceptual cycles performed in 1979-85 in New Zealand (Colombo and Masarotto 2000). The combined data base has been used in an extensive evaluation of the fecundability of healthy non-contracepting sexually active couples in their reproductive years (Rizzi 2000; Dunson,

Sinai and Colombo 2001; Dunson, Colombo and Baird 2002; Dunson and Colombo 2003; Bigelow et al. 2003). For this purpose, appropriate statistical analysis was applied after scaling in time acts of intercourse to a *reference day* uniformly determined in all cycles. This day was conventionally adopted as a surrogate marker of the day of ovulation. Its determination relied on one or the other of the quoted two indicators: BBT and CMS.

A major limitation of this data base arises from the lack of standardization among the centres in the protocol for registration and interpretation of signs qualifying, both in sensation and appearance, observed mucus typologies. An agreed numerical code for different simplified categories of the CMS was employed for data collection and there was an agreed definition of the peak mucus day, for use as a reference day (Colombo and Masarotto 2000; Table 1).

Nevertheless, there was clear centre-to-centre variation in the application of the coding protocol, resulting in detailed and systematic differences among the profile of mucus symptoms recorded. In addition, the days in the menstrual cycle during which mucus records were collected were often too few and variable to permit a systematic study of the relationship between mucus characteristics across the cycle and daily fecundability. These shortcomings produced difficulties and uncertainties in ascertaining the relationship between one important covariate, the CMS, and relevant sexual behaviour and outcomes (see, e.g., Stanford, White and Hatasake 2002). For these reasons, and because previous studies relating mucus information to fecundability (World Health Organization 1983) were limited by underreporting of intercourse (Trussell and Grummer-Strawn 1990), there is a clear need for the establishment of a new more reliable data base. Other studies collecting detailed information on the timing of intercourse relative to a marker of ovulation, either did not collect any information on mucus (Barrett and Marshall 1969, Wilcox et al. 1995) or do not have large enough sample sizes for detailed analysis (Stanford, Smith and Dunson 2003).

This article presents first results from a new data base collected with the collaboration of centres providing instruction on the use of a so-called "ovulation method" of natural family planning: a method which relies only on observations and interpretation of the symptom of cervical mucus. Four Italian centres, all adopting the Billings Ovulation Method (BOM), co-operated in 1993-97 in the collection of the necessary data. In these centres, uniform procedures in teaching, practical applications, and in language and conventions supported homogeneity of record keeping. In addition, couples were prepared to give careful and constant attention to signs of the symptom over the whole cycle, resulting in very few days with missing data and greater homogeneity in trajectories of mucus symptoms across the cycles.

A main aim of this paper is to perform an exploratory analysis of the relation between the cervical mucus symptom and daily fecundability tacking advantage of this new constructed data base.

2. Materials and Methods

2.1. Short preliminary notes to the Billings Ovulation Method

The Billings Ovulation Method (Billings and Westmore 1998) relies on daily observations of the CMS throughout all of the cycle, that is, on the characteristics of the mucus as it appears at the vagina and the assessment of the associated sensation produced at the level of the vulva. In describing her observations a woman makes use of words which seem appropriate to her but which are also understandable to her natural family planning teacher. Her interpretation of the CMS is recorded on a chart usually by use of descriptive adjectives, conventional signs, or coloured stamps and the estimated day of the 'Peak Symptom' (the last day of observations of fertile-type mucus) is marked. In the present study the mucus descriptions have been assigned numerical codes to facilitate the analysis. The observations allow the determination in each cycle of the fertile phase during which intercourse could result in pregnancy and the pre- and post-ovulatory infertile phases. So, the method divides a cycle into sections. The days of the menses are considered potentially fertile since it is not possible to identify the CMS. After the period, a possible infertile preovulatory phase may occur.

The characteristics of the CMS are not, in general, identical for all women. Two so-called *basic infertile patterns* (BIP) occur during the days following the period. The most common is characterised by a sensation of dryness and by absence of mucus. This pattern can usually be identified by the woman already from her first cycle of observation (dry BIP). The second is characterised by damp sensation and/or continuous mucus discharge: it is identified as an unchanging mucus pattern (u.m. BIP). The characteristics of sensation, appearance and consistency of discharge remain in this instance steadily unchanged day after day, cycle after cycle. A suitable number of cycles (generally three) will be necessary to learn to recognise this BIP. Any time the characteristics of the CMS becomes different from those typical for a specific BIP, it is considered that a *fertile phase* is beginning.

The symptom of the *mucus peak* is a crucial indicator for the method. The four centres agreed upon the following conventional definition of the peak mucus day: "The last day of the cycle during which at least one characteristics of high fertility in mucus type has been observed or felt, considering characteristics of high fertility a wet sensation and/or the observation of slippery, transparent, liquid or watery mucus, or of blood trails. Moreover, this day must be preceded by an adequate growth in sensation and appearance of mucus characteristics, which should also show afterwards a clear change to the less fertile". Ovulation is expected within two days after the peak: this can then be used as a reference for

the determination of the end of the fertile phase. When in a cycle no peak is detected, it is not possible to judge if and when ovulation did occur and, therefore, to identify a *postovulatory infertile phase*.

2.2. Study design and population

The investigation was planned as a prospective cohort study and was approved by the Institutional Review Board of Fondazione Lanza (Padua, Italy). The co-ordination of the study was made in the Department of Statistical Sciences of the University of Padua.

With the co-operation of four Italian centres providing services on the Billings ovulation method, during the years 1993-97 were recruited for the exercise 193 women. A few subjects were themselves teachers of the method. They had kept long series of past own observations, going back, in one case, as far as to 1976. So long as it satisfied all the criteria of the programmed protocol, also this little piece of information was utilised in the construction of the data base.

The study entry criteria for the subjects were: the woman was experienced in the use of the Billings Ovulation Method; was married or in a stable relationship; was between 18th and 40th birthday at admission; had at least one menses after cessation of breastfeeding or after delivery (or miscarriage); not taking hormonal medication or drugs affecting fertility. Neither partner could be permanently infertile and both had to be free from any illness that might cause sub-fertility. It was strictly required that couples did not have the habit of mixing unprotected with protected intercourse. Women were excluded if any one of these criteria was not fulfilled.

The participating centres and (in parenthesis) the local Principal Investigator (PI) were: Centro Lombardo Metodo Billings-CLOMB, Milan (Mrs. Medua Boioni); Centro Piemontese Metodo Billings, CEPIMB, Saluzzo (Mrs. Lorella Miretti, RN); Associazione Metodo Billings Emilia-Romagna, AMBER, Parma (Sr. Erika Bucher); Centro Studi e Ricerche Regolazione Naturale della Fertilità, Rome (Mrs. Elena Giacchi, MD). Prof. Bernardo Colombo, Department of Statistical Sciences, University of Padua, was the study coordinator.

2.3. Data collection and study factors

The selection of experienced users of the method and their instruction in view of the purposes of the exercise was in each centre under the responsibility of the local PI. As already noted, some of the admitted participants were teachers of the method themselves. Written consent was required from women selected for participation. Complete subject anonymity and confidentiality was assured identifying each subject only through a study id number. Only the teacher maintained personal relationship with the client: natural trust between the two was essential for obtaining reliable information in a sensitive area encompassing sexual behaviour.

At entry into the study, the following information was collected: month and year of birth of the woman and of her partner; number of previous pregnancies, if any; date of the last delivery (or miscarriage) and of the end of breastfeeding, if relevant; date of last contraceptive pill taken, if relevant; date of marriage and sex of the baby born. In each menstrual cycle, the subject was asked to record on a chart the days of the period and of any disturbances (illness, broken sleep, etc). She was also asked to observe and chart her CMS daily and to record daily every act of intercourse together with specification whether it was unprotected or protected (barrier methods, withdrawal,...). Cycles in which even a single act of protected intercourse or a simple genital contact occurred were excluded from the analysis. The importance of continuing to keep the record chart when subjects were trying to conceive a pregnancy was emphasised.

Charts collected were reviewed in each site. The recorded observations on the mucus symptom typology made by the woman were there codified according to agreed common rules for scoring (Table 1) under responsibility of the PI, who also provided information on the BIP of the cycles. Also the identification of the peak mucus day, if any, was made by the local PI. This peak day was taken as *mucus reference day* and identified as day 0. Periodically, sets of charts were then sent to the co-ordination centre in Padua. Here, after careful checking and possible revisions, all the information received was stored in a computerised data base.

A *menstrual cycle* was defined as the interval from the beginning of one period of vaginal bleeding until the commencement of the next, when day one was the first day of fresh red bleeding, excluding any preceding day with spotting. A *pregnancy* was assumed in the presence of amenorrhoea continuing at 60 days from the onset of the last menses, or when, before that term, a miscarriage was clinically detected.

Table 1: Classification of cervical mucus appearance and/or sensation*

	Sensation	Appearance
0	No information	No information
1	No sensation or dry sensation	No mucus nor loss or insubstantial loss
2	Not any more dry sensation	No mucus nor loss or insubstantial loss
3	Damp sensation	Thick, creamy, whitish, yellowish sticky, stringy mucus
4	Wet, liquid sensation	—
5	Wet-slippery sensation	Transparent, ropy, liquid, watery mucus, blood trails

*If during a day there are different observations of the mucus symptom, the coding is determined by the mucus of the most fertile type

2.4. Statistical analysis

A window of potential fecundability (the fertile period) was first determined. This was defined as a series of days relative to the mucus reference day (taken as a surrogate indicator of ovulation) such that a cycle without intercourse during these days never resulted in a pregnancy. Daily estimates of conception probabilities were then calculated using cycles with only one intercourse act during the said window (a division day by day: number of pregnancies/number of acts of intercourse). In case of multiple intercourse episodes within the window, estimates of daily probability of conception were obtained through application of a model. The model proposed by Schwartz et al. (Schwartz, MacDonald and Heuchel 1980), which extends the pioneering model of Barrett and Marshall (1969), was used for this purpose.

In any study of the relationship between the observed cervical mucus typology on a given day and the probability of conceiving from intercourse taking place on that day only, a major difficulty arises from the large number of parameters to be estimated. Five mucus typologies over a 12 days window means many parameters if one considers possible interaction - day by day - between the observed CMS and the distance from the reference day. Given such a situation, reliable estimates could have been obtained only with a sample size much larger than the one involved in this exercise.

In order to overcome this difficulty, two simplifying approaches have been followed. In the first, the effect of different recorded mucus typology on cycle fecundability was investigated respectively for days at a fixed distance from the reference day. In the second, the assumption of a constant effect on daily fecundability of a given type of mucus over the entire fertile period was made. For each of these two approaches, alternative models were taken into consideration.

Inference was made using the likelihood-based approach: 1) parameter estimates were obtained by maximum likelihood, and 2) likelihood ratio tests were used to test the significance of selected covariates; 3) confidence intervals were then computed for each parameter of interest using the profile log-likelihood (Azzalini 1996, Clayton and Hills 1993).

Descriptive analysis was made using SAS (<http://www.sas.com>). R (<http://www.R-project.org>) was used to fit the Schwartz et al. model to the data. Functions and scripts are available upon request from the authors.

2.4.1. Modelling the relation between CMS and fecundability

a) Keeping fixed the distance from the mucus reference day:

a.1) Let C_j be 1 for a cycle j ($j = 1, \dots, n$: with n = total number of cycles) in which the average score of the mucus recorded over the 5 days window $(-4,0)$ is 4 or more, and 0 otherwise. Let us also define a dichotomous outcome variable $Y_j = 1$ if in a cycle there is a conception, and 0 otherwise. In order to allow for possible effects of mucus typology, one can adapt the Schwartz model through a multiplicative factor β^{C_j} :

$$\Pr(Y_j = 1 | \{X_{ij}\} C_j) = \beta^{C_j} \cdot k \cdot \left[1 - \prod_i (1 - \alpha_i)^{X_{ij}} \right] = \beta^{C_j} \cdot P_j \tag{1}$$

where k is the factor called by Schwartz et al. *cycle viability*, while

$$X_{ij} = \begin{cases} 1 & \text{presence of intercourse in the } i \text{ th day of cycle } j \\ 0 & \text{otherwise} \end{cases}$$

We may take $\log P_j$ as an ‘‘offset’’ in a generalized linear model with a log link and constrain the intercept to be 0. We make so possible to estimate β using any appropriate standard statistical package for generalized linear models. The same approach has been used by Weinberg and Zhou (1997) in another context. We then obtain:

$$\log(\Pr(Y_j = 1 | \{X_{ij}\} C_j)) = C_j \cdot \log \beta + \log P_j$$

and

$$\beta = \Pr(Y_j = 1 | \{X_{ij}\} C_j = 1) / \Pr(Y_j = 1 | \{X_{ij}\} C_j = 0) \quad (2)$$

- a.2) We then take into consideration a specific day in the fertile window (for example, day -2 , -3 , or -4). Let C_h be 1 for a cycle where the mucus score is equal to h ($h = 0, 2, 3, 4$; $h = 4$ including both mucus coded 4 and mucus coded 5), 0 otherwise. The dummy variable representing the mucus code 1 is excluded, because it is the one chosen for the comparison.

The model becomes:

$$\Pr(Y_j = 1 | \{X_{ij}\} C_{hj}) = {}_{(i)}\beta_0^{C_{0j}} \cdot {}_{(i)}\beta_2^{C_{2j}} \cdot {}_{(i)}\beta_3^{C_{3j}} \cdot {}_{(i)}\beta_4^{C_{4j}} \cdot P_j \quad (3)$$

where C_{hj} is the dummy variable indicating the presence of mucus h in the day i of cycle j and ${}_{(i)}\beta_h$ is the parameter that measures the efficacy of the presence of mucus of type h in a given day on the fecundability of the specific day.

b) If we assume the effect of daily cervical mucus typology to be fixed, we can investigate the effect on the fertilization probability either of a specific mucus code or of the simple presence of this symptom.

- b.1) We first model the fertilization probability α_i in the Schwartz model (assumed constant for every cycle and woman) in relation with each type of daily observed mucus. Let Mh be the dummy variable that indicates the presence of mucus code h . Considering a specific day i within a cycle j , we assume a logit relation of the type:

$$\text{logit}(\alpha_i) = \delta_i + \beta_0 M0_{ij} + \beta_2 M2_{ij} + \beta_3 M3_{ij} + \beta_4 M4_{ij} \quad (4)$$

where δ_i is the effect on the probability of fertilization depending on the specific position of day i and β_h ($h = 0, 2, 3, 4$; $h = 4$ including codes 4 and 5) is the effect on the probability of fertilization in the logit scale due to the presence of mucus of code h . This effect means that the odds of fertilization probability on day i , when on that day is present mucus coded h , is increased by $\exp(\beta_h)$ with respect to the instance in which is felt an absent/dry sensation and there is (practical) absence of mucus (code 1 in Table 1).

From the relation (4) we obtain:

$$\alpha_i = \exp(\delta_i + \beta M_{ij}) / (1 + \exp(\delta_i + \beta M_{ij})) \quad (5)$$

where

$$M_{ij} = (M0_{ij}, M2_{ij}, M3_{ij}, M4_{ij})^T \text{ and } \beta = (\beta_0, \beta_2, \beta_3, \beta_4).$$

We get the new model formulation for the fecundability P_j in cycle j :

$$P_j = k \cdot P_{f,j} = k \cdot \left[1 - \prod_i (1 + \exp(\delta_i + \beta M_{ij}))^{-X_{ij}} \right] \quad (6)$$

where $P_{f,j}$ is the probability of fertilization in cycle j of a fertilizable ovule. The parameters estimation can be obtained through standard maximum likelihood procedures.

b.2) Considering the effect on the daily probability of fertilization α_i of the presence of mucus, we model it as:

$$\text{logit}(\alpha_i) = \delta_i + \gamma_0 M0_{ij} + \gamma_1 M2345_{ij} \tag{7}$$

where δ_i is the effect that depends on the day specific position, γ_0 is the effect in the case there is no information about mucus (see 3.1, par. 7) with $M0$ its relative dummy variable, and γ_1 is the effect of observed presence of mucus with $M2345$ its relative dummy variable. As previously mentioned, also in this model the interpretation of the parameters is relative to the mucus with code 1.

The new formulation should plausibly lead to more significant results for the estimate of γ_1 (because of the increased number of cycles available for its estimate), letting the other parameter estimates be similar to the ones of the previous model.

3. Results

3.1. Overview of the sample

A summary of relevant characteristics of the 193 participating couples and of their 2,755 cycles is given in Tables 2 – 5. Among the four centres, there was a marked variation in the level of recruited achieved. The small sample size in two of the centres limits the ability to make comparisons between centres. Consequently, most of our analysis has concentrated on the whole aggregate.

The contact with subjects was made in 1993 – 97, though the documentation collected for a few of them (as clarified in (2.2)) extended over a longer period of time. With these small groups of subjects, the individual characteristics (for instance the reproductive history) may have changed between successive exits and re-entries. Accordingly, their individual contribution to the overall data contained in Table 2 pertain to the situation existing at each entry, ie at re-entry they were classified as new subjects. A rather limited percentage of dropouts (around 14%) was recorded.

Table 2: *Characteristics of women and men participating in the exercise*

Centres	No. of women	No. of entries*	No. of dropouts and end of study † (% of entries)	At any entry*					
				Age of women		Age of men		No. of women with at least one past pregnancy (% of entries)	No. of women with past use of hormonal contraception (% of entries)
				Mean	(S.d)	Mean	(S.d)		
Milan	50	70	24 (34.3)	27.9	(3.34)	31.2	(4.39)	38 (54.3)	3 (4.3)
Parma	98	114	22 (19.3)	27.3	(3.39)	30.0	(4.14)	48 (42.1)	26 (22.8)
Saluzzo	17	22	0 (0.0)	28.9	(4.56)	32.5	(4.69)	17 (77.3)	1 (4.5)
Rome	28	36	12 (33.3)	31.8	(3.22)	34.3	(4.88)	25 (69.4)	9 (25.0)
All	193	242	58 (24.0)	28.3	(3.77)	31.2	(4.58)	128 (52.9)	39 (16.1)

* A woman may reenter in the participation to the study after an interruption.

† Missing information for 7 instances. Out of 58, 34 are dropouts, 24 at end of study.

The average age of women (Table 2) is slightly over 28 years (range: 27.9 - 31.8 yrs). Marked differences between centres are observed in the proportion of women of proven fertility as measured by having at least one past pregnancy (range of percentages: 42.1 - 77.3). While the overall past use of hormonal contraception is relatively small at 16.1%, the centres divide into two groups of differences with this characteristic, less than 5% past-use in one and little more than 20% in the other.

There is much variation in the number of cycles contributed by the various centres, as shown in Table 3. Remarkably high (around 17% on the average) is the proportion of cases in which the peak mucus day was not identified. The difference observed between Rome and the other three centres has resulted because Rome, during the first period of observation, chose to collect preferably cycles with a clear development of the CMS typology towards the peak day.

Later on, this bias in selection was abandoned. The percentage of cycles with missing identification of the peak day is much higher in this study than that obtained (around 6%) in European centres relying on the so-called symptothermal method (STM) of fertility regulation (see Table 3 in Colombo and Masarotto 2000). The difference between the two findings can be explained by the more strict conditions posed in the Italian Billings OM centres with regard to precise identification of the peak mucus day (compare point 2.1 in this paper with point 2.4 in Colombo and Masarotto (2000).

Table 3: Characteristics of cycles and their outcomes.

Centres	No. of cycles	No. of cycles with identification of mucus reference day (% of cycles)	No. of cycles with at least one coition in the window (% of cycles)	No. of detected pregnancies (% of cycles)	No. of miscarriages (% of pregnancies)
Milan	909	739 (81.3)	305 (41.3)	45 (5.0)	3 (6.7)
Parma	1,060	859 (81.0)	328 (38.2)	92 (8.7)	6 (6.5)
Saluzzo	267	222 (83.1)	63 (28.4)	16 (6.0)	2 (12.5)
Rome	519	463 (89.2)	267 (57.7)	24 (4.6)	3 (12.5)
All	2,755	2,283 (82.9)	963 (42.2)	177 (6.4)	14 (7.9)

Of further note, with reference to Table 3 above, the percentage (42.2%) of cycles with at least one coital act in the window of potential fertility (see 2.4) shows that the subjects under observation must have acted for most of the time as pregnancies avoiders. The observed miscarriages, included among the clinically detected pregnancies, refer only -as already noted- to events happening during the first 60 days following the onset of menses.

Table 4: Characteristics of non-conception cycles with identification of reference day

Centres	No. of cycles	Total length of cycles		Duration of phases*			
				Preovulatory		Postovulatory	
		Mean	(S.d)	Mean	(S.d)	Mean	(S.d)
Milan	697	28.6	(3.82)	16.1	(3.71)	12.4	(1.92)
Parma	791	29.5	(4.38)	16.6	(4.32)	12.9	(1.82)
Saluzzo	209	30.6	(7.14)	18.3	(6.67)	12.3	(2.18)
Rome	443	28.7	(3.56)	15.7	(3.29)	13.0	(1.63)
All	2,140	29.1	(4.45)	16.4	(4.29)	12.7	(1.88)

* Conventionally: Preovulatory phase = until the peak mucus day, included;
Postovulatory phase = the remaining part of the cycle

The average duration of cycles without conception of 29.1 (\pm 4.45) days (Table 4) was similar to the 29.0 (\pm 4.25) days observed in the previously reported study of seven European centres (Colombo and Masarotto 2000). The average length of the postovulatory phase, that is the number of days after the peak mucus symptom until the onset of the next menstrual period was the same in both studies at 12.7 days. The consistency among the centres in this finding (range: 12.3 – 13.0 days) and its agreement with that observed in the WHO study of the Billings Ovulation Method (World Health Organization 1983) speak in favour of the reliability, in this respect, of the collected data.

Table 5 presents the results of applying the coding procedure for mucus symptoms according to the classifications provided in Table 1. For normal menstrual cycles, data were taken from the end of menses through to the completion of the cycle. For cycles in which conception occurred, the observation is made through day 29. On average, a specific coding is lacking in a little more than 3 days per cycle. But, in a day following one in which there was an intercourse episode, any observation on the CMS is normally purposely omitted due to the risk of confusion from the presence of residual seminal fluid in the vagina. This underlines the care of the women in recording characteristics of sensation and of mucus appearance. Further specific elaborations were done, restricting the attention to cycles with an identified peak mucus day, and computing for each code similar average numbers of days since the menses up to the peak day included. The computations done distinctly for all cycles and for their subset with dry BIP put in evidence (data not shown) for the last ones versus the whole aggregate a slight increase of instances with code 1 and a decrease of those with codes 2 and 3.

Table 5: Cycles* according to mean[†] number of days in the intermenstrual interval (with standard deviation) for each mucus code

Centres		Mucus code					
		0	1	2	3	4	5
Milan	No. cycles	<i>148</i>	<i>582</i>	<i>623</i>	<i>854</i>	<i>358</i>	<i>870</i>
	Mean days	2.635	9.237	5.864	7.817	2.385	4.722
	Std.dev.	2.478	5.734	4.434	5.346	1.860	2.630
Parma	No. cycles	<i>385</i>	<i>752</i>	<i>644</i>	<i>1,037</i>	<i>346</i>	<i>1,021</i>
	Mean days	3.652	7.806	4.918	9.156	2.561	4.607
	Std.dev.	3.744	5.213	3.746	5.239	2.496	2.682
Saluzzo	No. cycles	<i>46</i>	<i>149</i>	<i>181</i>	<i>266</i>	<i>26</i>	<i>259</i>
	Mean days	4.000	8.094	5.696	9.624	1.846	6.251
	Std.dev.	3.438	5.237	3.187	6.361	0.834	3.309
Rome	No. cycles	<i>135</i>	<i>448</i>	<i>331</i>	<i>508</i>	<i>396</i>	<i>482</i>
	Mean days	2.296	10.603	5.257	6.447	2.371	2.401
	Std.dev.	2.980	5.015	4.409	4.673	1.479	1.218
All	No. cycles	<i>714</i>	<i>1,931</i>	<i>1,779</i>	<i>2,665</i>	<i>1,126</i>	<i>2,631</i>
	Mean days	3.207	8.908	5.391	8.257	2.422	4.404
	Std.dev.	3.406	5.443	4.094	5.403	1.951	2.746

*In conception cycles, data have been taken from only the first 29 days from the onset of the menses. The number in italics indicate the number of cycles in which a specific code is recorded.

[†]The mean is calculated on the cycles in which a specific code is recorded at least once.

A large variability in the use of the various numerical codes was observed among the centres, mostly attributable to interobserver variation. This observation has already been reported and discussed (Bassi, Mion and Colombo 2003). However, this variability only explains in part, as seen for each of the cells in Table 5, the extremely high value of the standard deviation with respect to the pertinent average result. This reflects how much the recorded characteristics of the CMS are subject (and cycle) specific.

Table 6: Average number of acts of intercourse per cycle

Age classes	Intercourse of women				Intercourse of men in			
	Conception cycles *		Non conception cycles		Conception cycles *		Non conception cycles	
	Mean	(S.d.)	Mean	(S.d.)	Mean	(S.d.)	Mean	(S.d.)
18-24	7.21	(3.16)	4.94	(3.23)	7.88	(3.76)	4.30	(2.93)
25-29	5.89	(1.83)	4.17	(2.34)	6.41	(2.38)	4.64	(2.52)
30-34	4.96	(2.35)	3.59	(1.78)	5.47	(2.15)	3.89	(2.31)
35-39	5.20	(1.92)	3.20	(1.60)	4.61	(2.43)	3.39	(1.59)
>=40					5.57	(2.44)	3.13	(1.74)
Total	5.87	(2.45)	3.98	(2.31)				

* In conception cycles, only the first 29 days since the onset of the menses are considered.

Table 7: Direct estimates of fecundability according to the number of acts of intercourse in the window (-8,3) around the mucus reference day

Number of acts of intercourse	Conception cycles (a)	All cycles (b)	Fecundability (a/b)%
0	1	1,321	0.08
1	20	507	3.94
2	34	199	17.09
3	27	122	22.13
4	33	75	44.00
5	16	37	43.24
6 and more	12	22	54.54
Total	143	2,283	6.26
At least one	142	963	14.75
At least two	122	455	26.81

Tables 6 and 7 provide evidence of two aspects of sexual behaviour of the couples. Table 6 shows the relationship between age and frequency of acts of intercourse for males and females respectively. The decline in frequency with age (both sexes) and for the women the lower variability in conception cycles (coefficient of variation: $2.45 / 5.87 = 42\%$ vs. 58%), can be taken as a proof of reliability of collected data. Table 7, presents the distribution of cycles according to the number of intercourse episodes in the fertile window. The decline in number of cycles with increasing incidence of coitus, and the high frequency of cycles with no acts in the window, show again that with regard to pregnancy the subjects must have acted for most of the time as avoiders. Of particular significance is the occurrence of a pregnancy in a cycle with no intercourse in the fertile window. An evaluation of available charts for the couple involved shows that the determination of the peak day in that cycle is consistent with the determinations in previous documented cycles. Two acts of intercourse are registered in the cycle, one ten days before and one five days later than the reference day. Follow-up with the local PI indicated trust in the subject's reliability and truthfulness in keeping records of coitus. Table 7 also contains estimates of fecundability, linked with frequency of intercourse. These estimates relate only to the number and not the location of coitus in the window. The estimate of a conception probability of 17.1% per cycle for two acts of intercourse is definitely higher than the corresponding estimate of 12.9% obtained in the above quoted study of seven European centres (data not shown). The difference might be due to higher fecundability in the population of the Italian Billings centres or to a different timing of intercourse within the fertile window. In cycles with at least two intercourse episodes in the window, the probability is 26.8% in the Billings centres and 18.8% in the European centres. Concerning the latter, two centres in Northern Italy provide two thirds of the study data. In the present study, three of the four centres are also in the northern part of Italy, suggesting that variation in population fecundability does not explain the different findings. Does the explanation lie in selection of the subjects –for instance, in terms of proven fertility- or does this evidence suggest that a careful attention to CMS typology is a good guidance for purposeful location of intercourse? This point deserves further elaboration.

3.2. Direct estimates of daily fecundability

In a first approach to estimating the day by day conception probabilities consideration has been given only to cycles with a single act of intercourse in a defined fertile window. For this purpose, we chose a window of seven days, five before and one after the mucus reference day. For each day the ratio between the number of conception cycles and the total number of cycles gave the wanted specific estimate. However, in order that an intercourse episode on a given day could be identified as the one responsible for conception, an initial selection criterion was applied; all conceptual cycles in which intercourse outside the window could have possibly produced that outcome – though with a small probability – were discarded from the analysis.

In the instance of cycles with coitus on day -5 , and only on that day of the window, were discarded all those showing intercourse on any of the days -8 , -7 and -6 ; for coitus on day -4 were discarded cycles when intercourse had occurred also on day -7 and/or -6 ; for coitus on day -3 were discarded cycles with intercourse also in day -6 . Furthermore, all cycles were discarded in which as well as the single act of coitus within the window there had been intercourse on day

+2. The daily fecundability ratios, (number of pregnancy cycles/number of sexually active cycles), are presented in Table 8.

Table 8: Direct “adjusted” estimates of daily fecundability in the window (-5,1) around the mucus reference day

Cycles	Distribution of single acts of intercourse in the window							Total
	-5	-4	-3	-2	-1	0	1	
Conc. cycles	1	4	2	2	5	5	1	20
All cycles	35	21	13	11	15	12	22	129
Ratio	0.029	0.191	0.154	0.182	0.333	0.417	0.046	0.155

Unfortunately, the small size of the sample does not allow firm conclusions to be drawn owing to possible random errors. But it seems safe to underline how the five days in the centre of the 12 days window are the most relevant for conception probability. The marked drop of fecundability on day +1 seems to give support to the reliability of the peak mucus day as a surrogate marker of ovulation. The higher level of fecundability in the last column of this Table (15.5%), compared with the global figure of Table 7 for cycles with at least one day with intercourse (14.75%), is due to the exclusion here of five outer days of the window, with low conception probabilities.

3.3. Model-based estimates

As stated in (2.4), when there are multiple intercourse episodes in the fertile window, the estimates of daily probability of conception can be obtained applying a convenient model. For this purpose we used the Schwartz et al. model (2.4). This model has been used, for the same reasons, in the paper by Colombo and Masarotto (2000). In Table 9 are presented the findings obtained from 963 cycles and their pertinent 142 pregnancies. These are cycles with identified peak mucus day and at least one intercourse episode in the broader fertile window (-8,3) around the mucus reference day of the indirect marker (see 2.3). The estimates are also presented graphically in Figure 1. The pattern of daily probabilities included in the 12 days window is similar to that found in the quoted larger multinational study (see Table 9).

Table 9 : Daily estimates in cycles with one or more acts of intercourse in the windows around mucus reference day (Schwartz et al. model)

Intercourse day vs reference day	Probability of conception	Lower – Upper 90% Confidence Interval	
		L	U
-8	0.000	0.000	0.008
-7	0.012	0.003	0.032
-6	0.034	0.012	0.070
-5	0.035	0.009	0.085
-4	0.177	0.090	0.286
-3	0.249	0.120	0.402
-2	0.136	0.039	0.285
-1	0.228	0.111	0.367
0	0.429	0.286	1.000
1	0.114	0.025	0.239
2	0.085	0.021	0.183
3	0.033	0.011	0.071
No. of cycles	963		
No. of pregnancies	142		
<i>k</i>	0.444	0.374 – 0.782	

This is put in evidence from various points of view: the location and duration of the fertile period; the general shape of the pattern of the estimates; the confining of the maximum level of conception probabilities to the central 5-6 days of

the window. But there are also marked differences: the maximum value of the probability found on day 0 instead of day -2; the definitely higher sum for daily estimates (1.532 in this study –see Table 9- and 1.028 in the seven European centres of the previous one: see Table 9 of Colombo and Masarotto 2000), but the span of confidence intervals, computed through the profile loglikelihood at the 90% level (Clayton and Hills 1993), appears very wide for all parameters. Particularly, on day 0 the relevant parameter is almost unidentifiable: the value 0.429 falls in a confidence interval (0.286, 1). These peculiarities and shortcomings are due in part to a weakness of the model, which is very sensitive to the size of the sample and to the frequency of days with intercourse (Romualdi 1996).

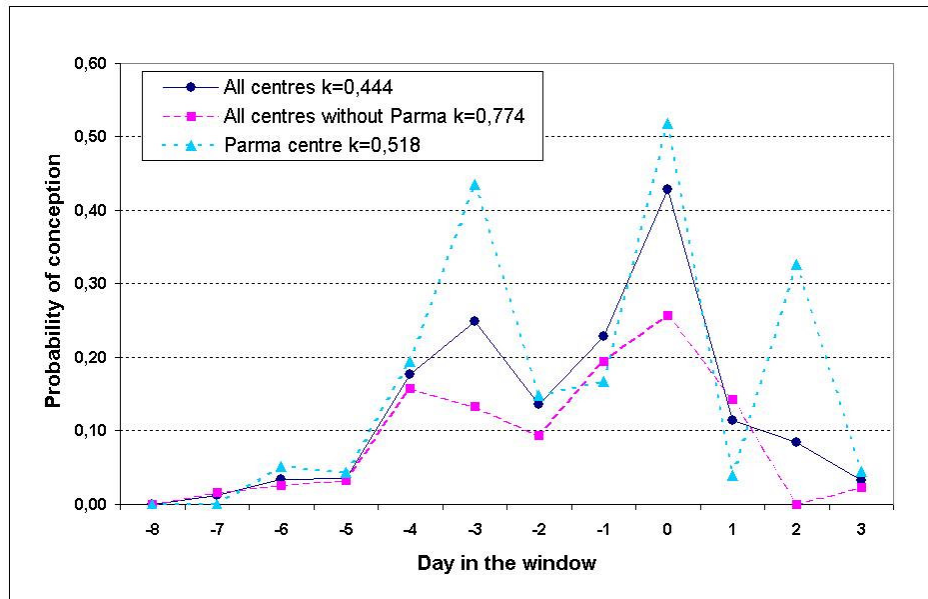


Figure 1: Daily fecundability around the peak mucus reference day. Various groups.

Additionally, the results are influenced in part by the contribution to overall data from one of the four centres: Parma. In Figure 1 it is clearly apparent that the average level of fecundability, and its distinct maximum on day 0, depend heavily on the Parma records. The likelihood ratio test shows that the difference between the results of Parma and the aggregate of those from the other three centres are statistically significant ($p = 0.039$). The data from Parma appear responsible of the quoted marked differences between the sum of the daily conceptions probability over the whole fertile window. We will come back to this point in the Discussion. As to the irregularities in the distribution of the probability values, there is no need to emphasize that they may depend on the small dimension of the subsets.

Owing to the mentioned shortcomings, it is not of value to present details of the results of further calculations of effects of some fixed covariates, considered only one by one in univariate analyses, and furthermore without taking into account heterogeneity among units. In brief, we compared estimated probabilities between appropriate subsets of cycles. Applying the likelihood ratio test, statistical significance at the 90% level was obtained in the following instances: women of age up to the median of 28 years vs. older women; cycles with dry BIP vs. cycles with BIP of the unchanging mucus type; cycles with identified peak mucus day vs. cycles without (here was taken day 14 in the cycle as a reference day). No significant difference was found in the sets of probabilities between women with or without previous pregnancies, nor between women with versus women without previous use of oral contraception.

Some of these results are at variance with what was found in Colombo and Masarotto (2000), but the small dimension of the sample subsets (as low, in two instances, as 18 and 24 conceptions), and the ascertained weakness of the model under such conditions, do not allow firm conclusions on these differences.

3.4. The relation between cervical mucus symptom and daily fecundability

In (2.4.1) we presented four models offering simplified solutions to the problem of investigating the relation between observed type of mucus and fecundability. The results of their application to available data are given in the same order as they were presented. If not differently specified, the models are applied to the entire set of 963 cycles with at least one coition in the window.

Model (a.1) was first applied, disregarding possible interferences of changes in concomitant covariates. The effect on the probability of conception due to the presence of an average mucus score ≥ 4 over the five days window $(-4,0)$, including all days with highest probability of conception, is measured by the parameter $\beta = 1.348$. The relation is positive and statistically significant ($p = 0.026$).

With model (a.2), taking the mucus with score 1 for comparison, particular attention was put on days $-2, -3, -4$, relative to the reference marker of ovulation. For each of the three days all numerical codes were represented, but often in less than 10% of the total in each subset. As an offset, we decided to adopt the pattern of daily conception probabilities around the mucus reference day available from Table 9 of Colombo and Masarotto (2000). That choice was made, in spite of partial discrepancies between the two studies, since it allowed relying on known independent exercise and data. The estimated values of the effects of the different typologies of mucus secretions on daily fecundability are presented in Table 10, with their confidence intervals, for the only relevant parameters β_2, β_3 and β_4 . The large confidence intervals reflect the small size of several subsets. The results are statistically significant, with two exceptions: on day -2 for mucus coded 3, and on day -4 for mucus coded 2. The findings can be taken as a clear indication of the impact that the presence of some types of mucus have on the level of daily fecundability. A comparison of the estimated effects of the various types of mucus secretions, however, reveals some puzzling features. On days -2 and -3 , mucus coded 2 has higher effect than mucus coded 4, and mucus coded 3 the lowest. And the reverse is seen on day -4 . The span of the confidence intervals and their overlapping raises uncertainty in the interpretation of these results. The uncertainty leads to the cautious conclusion that perhaps the quality of the mucus ascertained on a specific day is an insufficient predictor of the probability of conception from intercourse obtaining on that day.

Table 10: *Estimated effect on cycle fecundability of different mucus code registered on day i*

Parameter	Day in the window								
	-2			-3			-4		
	Estim. effect	Lower 90% Confidence Interval	Upper 90% Confidence Interval	Estim. effect	Lower 90% Confidence Interval	Upper 90% Confidence Interval	Estim. Effect	Lower 90% Confidence Interval	Upper 90% Confidence Interval
	L	U		L	U		L	U	
β_2	1.673	1.148	2.587	1.940	1.315	2.598	1.096	0.701	1.896
β_3	1.318	0.968	1.713	1.373	1.085	1.693	1.687	1.411	1.975
β_4	1.527	1.333	1.728	1.593	1.367	1.828	1.471	1.207	1.767

Shifting the attention to models assuming fixed effects of daily CMS typology, we applied model (b.1). Also in this instance, no account was taken of possible influences of concomitant changes in covariates.

The relationship (5) gives the daily probability of fertilization as a function of the presence on a day i of mucus coded h : the constant effect (in the logit scale) for each α_i enters in a non linear manner, leading to an impact of the presence of a definite mucus type varying day by day. The estimates of conception probabilities are presented graphically in Fig. 2. In this Figure is shown with unequivocal evidence, over the entire fertile period, the relevance for daily fecundability of the presence of identifiable mucus (and / or sensation). With surprising results. These are confirmed by the figures in the last column of Table 11, showing the increase of the odds of fertilization probability on day i when mucus h is present relative to the situation of no sensation/dry sensation and of no mucus, nor loss/insubstantial loss. Unexpectedly, the stronger effect is associated with damp sensation and/or thick, sticky mucus (code 3) and not with wet, liquid, wet-slippery sensation and /or transparent, ropy, liquid, watery mucus (codes 4 and 5). Large and overlapping confidence intervals do not allow precise detection of the effects of different typologies of the CMS, but the estimates of all three parameters β_2, β_3 and β_4 —disregarding β_0 as irrelevant—are statistically significant.

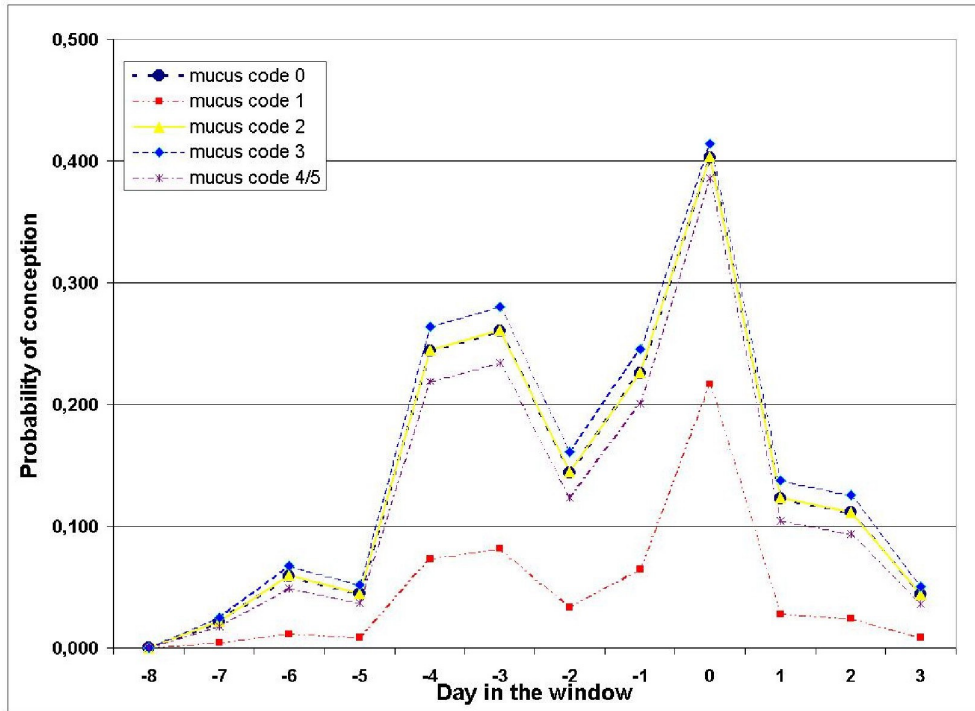


Figure 2: Daily fecundability according to different mucus codes.

In Table 11 we note that practically over the whole window the values of δ_i (the estimate linked to day-specific position relative to mucus code 1) lead to non null probabilities, with extremely large 90% C.I. on days -8 and 0 . The value of k is almost unidentified, with consequences on the reliability of the estimates of daily fecundability.

Table 11: Estimated effect on daily fecundability of specific day-position and different mucus codes.

Parameter	Estimate	Lower – Upper		Parameter	Estimate	Lower – Upper		$\exp\{\beta_h\}$
		90% C.I.*				90% C.I.*		
		L	U			L	U	
δ_{-8}	-26.62	$(-\infty, -4.975)$		δ_1	-2.84	(-4.625, -1.228)		
δ_{-7}	-4.82	(-6.604, -3.434)		δ_2	-2.97	(-4.676, -1.426)		
δ_{-6}	-3.73	(-5.077, -2.574)		δ_3	-4.06	(-5.568, -2.790)		
δ_{-5}	-4.04	(-5.808, -2.571)		k	0.495	(0.378, 1)		
δ_{-4}	-1.75	(-3.318, -0.343)		β_0	1.727	(-1.014, 3.571)		5.624
δ_{-3}	-1.62	(-3.537, 0.927)		β_2	1.733	(0.468, 3.223)		5.658
δ_{-2}	-2.62	(-4.496, -0.731)		β_3	1.885	(0.892, 3.080)		6.586
δ_{-1}	-1.90	(-3.729, 0.507)		β_4	1.517	(0.228, 2.976)		4.559
δ_0	0.25	(-2.797, $+\infty$)						

*C.I. = Confidence Intervals

Model (b.2) should reasonably lead to more meaningful results through the estimate of γ_1 , owing to the higher number of available cycles. The evaluated estimate $\gamma_1 = 1.804$ (CI: 0.850, 2.959) is highly statistically significant ($p = 0.001$) – with a derived substantial effect (= 6.076) on the odds of fertilization –, while $\gamma_0 = 1.680$ (CI: $-1.026, 3.566$) – with effect = 5.364 – is not, owing to its large variability. But, once again, the computed estimate of k (0.469; CI: 0.377, 1) does not allow very firm conclusions.

A similar analysis, limited to the 703 cycles with a dry BIP, provided a rather precise estimate of k (0.441; CI: 0.369, 0.517). As to the other parameters, we obtained $\gamma_0 = 1.792$ (CI: $-0.769, 3.904$) and $\gamma_1 = 2.021$ (CI: 0.913, 3.326), with corresponding effects 6.000 and 7.544, respectively. The relevance of the presence of some mucus signal with more

than a seven time increase in the odds of fertilization is evident. Also the effect of instances with no information appears important, but we know that code 0 is not informative. In fact, only the estimate of γ_1 is highly statistically significant ($p = 0.002$), while that of γ_0 is not, owing to the large variability.

Finally we compared the estimates of fecundability obtained applying the plain Schwartz model (2.4) with those computed using the parameters estimated with model (b.1). In the latter, each daily figure is a weighted average of estimated probabilities for each code h , using as weights the relative frequency of the specific types of mucus observed day by day. The daily probability of fertilization becomes

$$\alpha_i = \sum_{h=0}^4 w_{hi} \cdot \Pr(\text{fertilization} \mid \text{mucus} = h)$$

where $w_{hi} = f_{hi} / \sum_{h=0}^4 f_{hi}$, and f_{hi} is the number of cycles which show mucus h on day i .

Figure 3 shows the patterns over the whole window of daily fecundability computed considering weighted measures from model (b.1) and Schwartz et al. model, respectively. The agreement between the two is substantial.

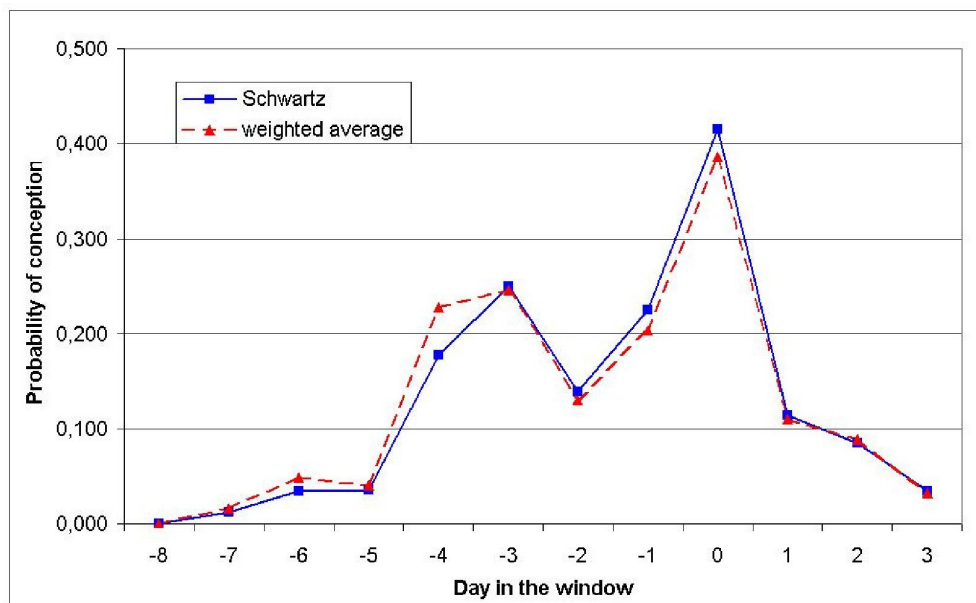


Figure 3: Daily fecundability: Schwartz et al. model and weighted average of estimates for the various codes.

4. Discussion

Before engaging in an evaluation of our results, it seems fitting to draw attention on some critical aspects of the whole exercise.

First of all, concerning the fitness of the cervical mucus marker for identification of ovulation through the peak mucus day. On the subject there is an ample literature. Two recent studies (Guida et al. 1999, Ecohard et al. 2001) checked the performance of that indicator with results obtained through ultrasound detection of ovulation. The answer appears, on the average, satisfactory.

A second questionable point is the choice of the Schwartz et al. model. Certainly, this model rests on simplistic assumptions, the less realistic one being the supposed constancy of daily fecundability over all cycles of all women once the distance from the conventional indicator of ovulation is given (Dunson and Zhou, 2000). The experience from many subsets of data bases of this kind has shown also, since the first steps of analyses on the ongoing previous exercise, that the performance of the model is very sensitive to the size of the sample and the frequency of intercourse in the fertile window. Several analyses done in this study are limited to small samples and to a selected population with a high percentage of so-called “avoiders”. But, in spite of such shortcomings, the model provides fair information on the pattern and level of daily fecundability. As a proof of that, for instance, in this exercise, as in the previously cited, it is possible to see that the results of the direct estimates –without any problem of models- fall within the 90% confidence intervals for the estimates provided by the application of that model. The mentioned caveats are relevant in qualifying the meaning of the computed estimates.

Coming now to the general results of the study, we –first of all- stress important items of agreement with those obtained, with the same marker, in Colombo and Masarotto (2000). They are: the span of the fertile window around the mucus reference day; the higher level of fecundability concentrated in a short central interval and its decline on both sides towards the outer limits (Figure 1) and the average length of the postovulatory phase of non-conception cycles (Table 4). A curious finding, for which it is hard to find a biological explanation, is the marked dip in the pre-ovulatory ascending trend in daily conception probability (Figure 1). In the earlier multinational study a similar depression was found in preliminary analyses using the shift in BBT. But that feature disappeared with increasing sample size. In that study, as in the present one, the dip in the trend was instead a consistent observation when the day of the peak mucus symptom was used as the reference marker (see Table 9 in Colombo and Masarotto 2000).

This study did produce several results which differed from those found previously. Differences can be seen in the percentage of cycles with unidentified peak mucus day (see Table 3), in the maximum value of fecundability observed on the day of the peak symptom, and especially in the higher sum of daily fecundability estimates determined in the present study (see 3.2). These last two features depend heavily on the records contributed by the Parma centre. This centre provided about one half of the total number of pregnancies. A thorough analysis of the records received from Parma and, separately, from the other three centres allowed to make clear one point. During the first period of data collection –say, up to about the middle of 1995- in Parma must have been made a selection of subjects both in current observation and in the use of past records. Precisely, particular attention was given to subjects with past recent history of pregnancies or just looking for a pregnancy.

Concerning the relationship between expressions of the mucus symptom and conception probabilities, the limits of the model used in the calculations need to be taken into account. They surround with uncertainty some of the conclusions. It should be noted also why mucus codes 4 and 5 were aggregated in the various models. At variance with the numerical coding of the previous study, the Principal Investigators decided in this one to make explicit an added feature of the mucus symptom (code 4 in Table 1). This characteristic was found only in about 40% of the cycles, and for a much lower number of days, on the average, than with other code numbers. And it is hardly distinguishable from the characteristics entailing the upper numerical code.

All four applied models underline the association between the presence of mucus and the openness to conception. The results of the application of models (a.1) and (b.2) leave no doubt about that (see 3.4). So does clearly Figure 2, derived from model (b.1). This Figure gives further interesting information. From it –as from a parallel analytical computation (data not shown) – it is possible to see that the increase in the level of fecundability, in the presence of mucus, in contrast to the situation of no sensation and no mucus, is relatively higher at the outer extremes of the curve. It seems that, even far from impending ovulation, the presence of some type of mucus is particularly favourable to a conceptual outcome. The same Figure gives rise to a further suggestion. It appears that the ascending pattern of the δ_i , which features the effect on the specific probability of fertilization depending on the position of day i , englobing also code 1, might be linked with the survival of the spermatozoa. It may then be possible to derive a rough estimate of their average life time. On the other hand, the type of decline in the probability following the reference day could be imputed to errors made in the determination of the day of ovulation through the surrogate marker.

It seems hardly necessary to mention possibilities offered by the present database for the exploration of further issues. For instance, take Table 5: from it we gather that, over the whole aggregate of observed inter-menstrual intervals, code 0 has been recorded at least once in 714 cycles, out of 2,755 (Table 3). On the average, this code has been registered for 3.207 days in the relevant cycles. In "non conception cycles", it was found that the average number per cycle of days with intercourse –almost all in the inter-menstrual periods- was 3.98 (Table 6). Considered together, these figures lead reasonably –though indirectly- to suspect, in practice, some departures in the preovulatory phase from one of the rules contemplated by the Billings ovulation method. Namely, the instruction to confine intercourse in the pre-ovulatory infertile phase to alternate evenings, owing to the risk of confusion between a mucus discharge and the drainage of seminal fluid (see the comment to Table 5). Either the rule was not always complied with, or the subjects were sometimes able to distinguish between the fluid and some type of mucus symptom. A detailed elaboration on the data base would clarify this aspect of behaviour.

Additionally, it will be possible to test for efficiency (in amount of days of abstention) and efficacy (in terms of probability of pregnancy) natural methods of fertility regulation taking advantage of the information provided by the cervical mucus symptom (e. g. Dorairaj K. 1991, Sinai I. et al. 1999).

One final point must be stressed in order to arrive at a more clear understanding of the present results and of possible limits in applications through elaborations performed on this data base. The inter-observer variation in describing through the adopted numerical coding system (Table 1) the different characteristics of the observed mucus secretions must be underlined. An *ad hoc* exercise performed with the collaboration of the same four centres has shown that differences in the interpretations, sometimes even in the determination of the peak mucus day, though small, appear not irrelevant (Bassi, Mion and Colombo 2003). In the present study, the four centres worked independently in coding charts locally collected. This circumstance –that each centre applied the coding to its own charts- assured a more correct evaluation of the records through the advantage of added information on the subjects not available to outsiders. Nevertheless, it is reasonable to suppose that it would also have been appropriate to rely on coding done uniformly on

the whole set of charts by a single experienced investigators. This approach was adopted in the previous study for the determination of the BBT shift.

A revision of the coding by a single reviewer is contemplated, in view of a proposed fusion of this database with a similar one under elaboration. Further improvements could then be added in the extended data base. For example, the determination of the day of the beginning of the increasing development of mucus up to the peak day. This observation, coupled with the relative stability of the pattern of the mucus symptom in succeeding cycles of the same woman (Dunson and Colombo 2003), could improve the chances of reliable forecasts useful for timing intercourse for subjects intending to achieve a conception.

More elaborations through multivariate analysis taking into account heterogeneity in couple's fecundability are planned and will be done once the bigger revised database becomes available.

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