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Probability of conception on different days of the menstrual cycle: an ongoing exercise

G. MASAROTTO and C. ROMUALDI

Dipartimento di Scienze Statistiche, Università di Padova, via San Francesco 33, 35121 Padova, Italy

Abstract

The design of the European Multicenter Study on the probabilities of conception in different days of the menstrual cycle is reviewed. Some results, based on part of the data, are presented. These can be summarized as follows:

a) Estimates of the probabilities of conception are lower than the ones previously reported in the literature;

b) A strong effect of the man's age on fecundability was found. No evidence of a similar impact of the woman's age was demonstrated;

c) The number of days with 'most fertile' mucus and parity affect fecundability.

Introduction

Knowledge of the extent and location of the so-called 'fertile window' – that is, the set of consecutive days around ovulation in which the conception probabilities differ from zero – is useful for several applications in the field of natural regulation of fertility. Also useful is the knowledge of the pattern of these probabilities of conception within the fertile phase for the purpose of either avoiding or achieving pregnancy. In addition, it is important to determine the characteristics of the partners and of the cycles because they affect these probabilities. Among the applications of this knowledge are the following:

1. To compare the reliability of different rules for the determination of the so-called 'unsafe period' on the basis of objective evidence free from the confounding factor of differential behavioral components;

2. To compare the same rules in terms of duration of the required period of abstinence at the same rate of possible failure;

3. To find new methods with shorter intervals of abstinence linked to control of uncertainty deriving from biological variability;

4. To provide indirect estimates of the reliability of physical and biochemical devices for fertility detection;

5. To elaborate and test new algorithms making reference to the more usual 'clinical' indicators, basal body temperature (BBT) and mucus, separately or jointly;

6. To verify the probability of conception associated with different types of mucus;

7. To evaluate the sensitivity of the calculated parameters by comparison of results drawn from evidence collected in different sites or obtained through different models;

8. To provide estimates of these parameters for distinct categories of subjects;

9. In infertility management to suggest the optimal days to achieve pregnancy.

This paper describes an ongoing study to obtain new estimates of the chance of conceiving on a given day of the cycle conditional to 'unprotected' intercourse taking place only on that specific day. The objective of the study is to obtain more precise and informative estimates of the time of fecundability than the few already available in the literature [1–7].

Fecundability, defined as the likelihood of conception in a cycle under a regimen of natural fertility, is usually qualified as total (counting each union of two gametes); apparent (counting all detected pregnancies, usually early in gestation); and effective (counting only conceptions leading to a live birth). In the following, we limit our attention to pregnancies ascertained through a positive test.

The European Multicenter Study on the probabilities of conception on different days of the menstrual cycle

This paper reviews the basic characteristics of the study; describes some models that can be used to analyze the type of data we are collecting; and presents some preliminary results, based on a part of our data.

Information was gathered for several hundred pregnancies. Taking into account the precision of the previously obtained estimates, in particular those computed using the Barrett and Marshall data, the aim of reducing the statistical error, the time required for gathering adequate information and the available resources, a target of some 500 pregnancies was planned. It was clear that recourse should have to be made to the cooperation of a few natural family planning centers operating in Europe and structured enough to carry out this kind of work. The main problem was to ensure the collection of good data in a delicate field involving sexual behavior. A good relationship and reciprocal trust between subject and instructors were considered essential for the success of the study.

After a few random pilot studies, a plan was made to recruit seven European centers, located in Verona, Milan, Lugano, Paris, Lyon, Düsseldorf, Brussels and London. A central coordinating center was established in Padua. All centers used the so-called 'sympto-thermal method' for natural fertility regulation. It was possible to obtain for each cycle daily information of BBT, characteristics of mucus, intercourse episodes, menstruation, and episodes of stress or illness. Cycles and couples strictly adhering to the practice of only unprotected intercourse were taken into consideration. Data were collected about partners: age and number of previous pregnancies. Only couples who were married or in a stable relationship entered the sample, which included women from 18 to 40 years old at the time of contact with the center. Procedures for eliciting informed consent and ensuring absolute anonymity were rigorously followed. The prospective study started four years ago and up to now a total of 468 pregnancies and 6434 cycle charts from 767 women have been collected for electronic processing. Further documentation is still incoming to Padua and some more work remains to evaluate the entire set of data. In the meantime, though the courtesy of Professor Trussell, it has been possible to include the data collected by John Marshall. Professor France also made available the documentation gathered in a previous prospective study with other purposes. These additions enrich the possibilities of analysis and can lead to further conclusions.

In the Results section, only the experience of the INER center, Italy (Verona) was considered. INER, Italy operates mainly in the Venetian region but also in some provinces of the nearby region of Emilia-Romagna.

The Schwartz–Barrett–Marshall model

The basic framework for the analysis of the collected data has been described by Barrett and Marshall [1]. For each cycle, the observed outcome (conceive or not conceive) can be viewed as a Bernoulli random variable with parameter (the probability of conception in that cycle) that depends on the number and the timing of intercourse events.

Barrett and Marshall [1] assumed that (i) different intercourse events have independent effects on the outcome and (ii) the probability of conception following intercourse only on day j, π_j, say, is constant between couples and cycles. The probability of conception in cycle i is:

$$\alpha_\iota = 1 - \prod_j (1 - \pi_j)^{x_{ij}} \quad (1)$$

where $x_{ij} = 1$ if there was intercourse in day j of the cycle i and $x_{ij} = 0$ otherwise. Estimates of the parameters can be obtained through standard likelihood calculations.

Schwartz *et al.* [5] observed that not all cycles may be 'viable'. For example, it may happen that the embryo does not survive long enough for the conception to be recognized. If k is denoted as the probability of 'viability', then the probability of conception becomes $k\alpha_i$. (The Schwartz–Barrett–Marshall (SBM) model). Observe that we can let k and/or the π_j's depend on some covariates, e.g. the age of the woman or the type of mucus. In this way the effects of these factors on fecundity can be studied. In the next section only k varies. In particular, a logistic regression type relation between k and the covariates is assumed. Formally, it is supposed that

$$\log \left[\frac{k}{1-k}\right] = z_i{}' \gamma \tag{2}$$

where z_i denotes the vector of covariates for the i-th cycle and γ are regression parameters. Significance of these parameters can be checked using likelihood ratio tests.

For other extensions of this model see Royston [9] and Zhou *et al.* [10].

Results

Description of the data set

The data used in this paper were collected in the Verona center. From the start of the study to mid-January 1997, 1111 charts collected by 169 couples were sent by this center to Padua. Table 1 shows the couples classified according to the age of the woman, the age of the man, and the number of children. Table 2 presents the cycles

Table 1. Couples classified by age and number of children

	Women	*Men*
Age		
<25	17	5
25–29	81	69
30–34	53	63
35–39	18	25
⩾40	–	8
Children	*Couples*	
0	116	
1	42	
2	14	
3	4	
4	1	

Table 2. Cycles classified by number of intercourse events

Intercourse events	1	2	3	4	5	6	7	8	9	10	11	⩾12
Cycles	57	111	136	197	162	129	84	51	37	28	18	49

Table 3. Estimates of the probability of conception. No heterogeneity

Day of intercourse	*Day 0 is the first day with high temperature*	*Day 0 is the first day with high temperature*	*Day 0 is the peak day of the mucus*
–9	0.04		
–8	0.09		
–7	0.02		
–6	0.03		
–5	0.08	0.10	0.11
–4	0.08	0.09	0.15
–3	0.24	0.24	0.09
–2	0.25	0.24	0.14
–1	0.03	0.07	0.15
0	0.00	0.00	0.14
+1	0.04	0.05	0.05
+2			0.00
+3			0.14
k	0.25	0.25	0.26

Table 4. Estimates of the probability of conception. SBM model with covariates

Day of intercourse	*Probability*	*Covariates*	
–9	0.03	Constant	2.34
–8	0.10	Age of man	–0.13 ($p < 0.001$)
–7	0.02	Number of children	0.56 ($p = 0.002$)
–6	0.04	Day of fertile mucus	0.12 ($p = 0.018$)
–5	0.11		
–4	0.09		
–3	0.24		
–2	0.24		
–1	0.04		
0	0.00		
+1	0.04		

The probabilities of conception have been computed establishing age of the man = 30; number of children = 0; day of fertile mucus = 3

Table 5. Values of *k*

Day of fertile mucus	*Age of the man* 20	*30*	*40*	*50*
No child				
1	0.47	0.19	0.06	0.02
5	0.58	0.28	0.09	0.03
10	0.72	0.41	0.16	0.05
Two children				
1	0.73	0.42	0.17	0.05
5	0.81	0.54	0.24	0.08
10	0.89	0.68	0.37	0.14

classified on the basis of the number of intercourse events. It should be observed that the sample includes mainly young couples (the average age is 28.5 years for the woman and 31 years for the men) and that more than 2/3 of the couples have no children.

The day of the rise in temperature was determined using the '3 over 6' rule suitably adapted to take into account episodes of illness or special events. Because it was not possible to determine the day of the rise in 169 cycles, these were excluded. The number of conceptions detected by a chemical test in the remaining cycles was 110.

The peak of the mucus was used as a reference point as well. This information was missing for 68 cycles resulting in a reduced sample of 1042 cycles with 125 conceptions.

Estimation of the probability of conception: no heterogeneity

Table 3 shows the estimates of the probability of conception obtained fitting the SBM model without any covariate. Three sets of estimates, obtained for different choices of reference point (BBT rise or peak of the mucus) and of length of the fertile window, are given.

Estimation of the probability of conception: evaluation of the effect of some possible covariates

For this exercise, we used a fertile window lasting from day –9 to day +1 of the BBT rise. We considered four possible covariates: (i) the age of the woman; (ii) the age of the man; (iii) the number of children; (iv) the number of days with 'most fertile' mucus during the fertile window. The study protocol defines as 'most fertile' mucus with appearance 'transparent, like raw egg white, stretchy/elastic, liquid, watery, reddish'

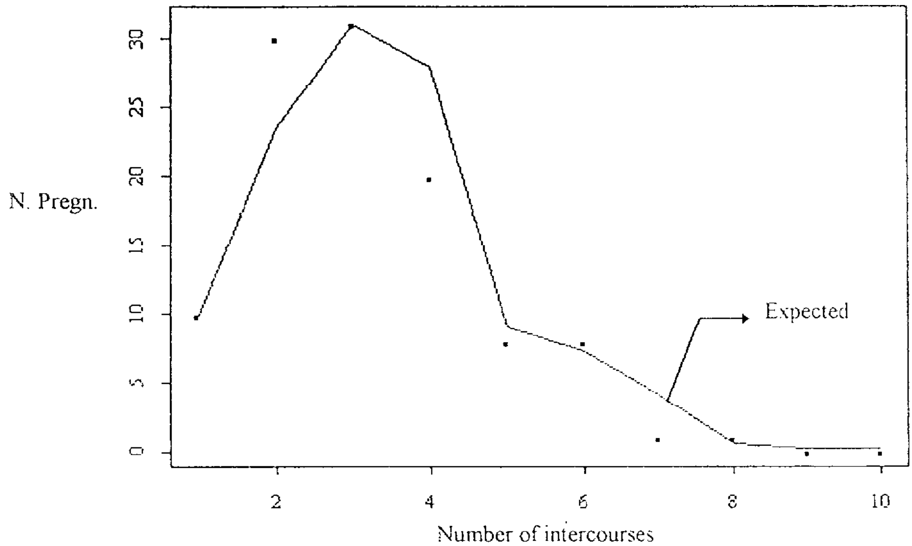

Figure 1. Quality of fit in relation to frequency of intercourse

associated with a feeling of 'wet, slippery and smooth'. The age of the woman was not significant ($p = 0.729$). Table 4 shows the estimates of the remaining parameters. Table 5 shows some values of k for various combinations of the three covariates included in the model. The large range of these values is noteworthy.

Some checks on the basic assumptions of the SBM model

We made some numerical and graphical checks on some of the assumptions of the SBM model.

Goodness of fit in relation to the frequency of intercourse

Figure 1 shows that observed and expected pregnancies classified according to the events of intercourse occurring in the fertile window are in good agreement. Using the number of intercourse events as an additional covariate did not improve the fit ($p = 0.105$).

Independence between the cycles

The results of subsection 2.3 are based on the assumption that the considered factors are able to explain all the variations in fecundity between the couples. Violations of

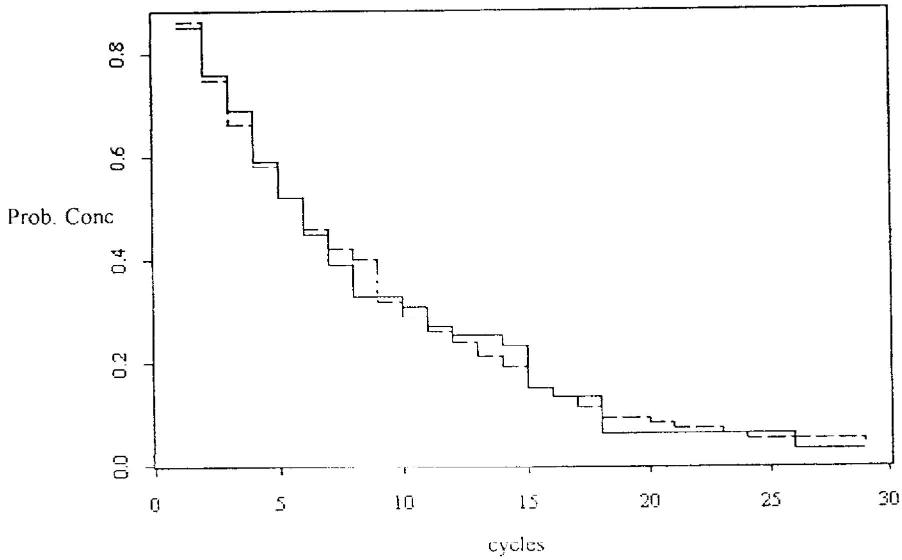

Figure 2. Distribution of the number of cycles that a couple need to conceive. Continuous line: observed distribution. Broken line: expected distribution

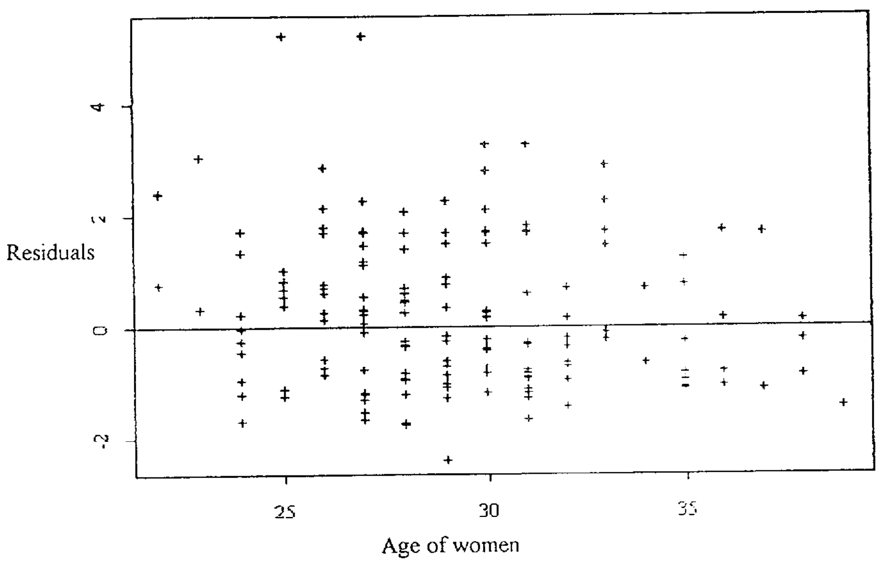

Figure 3. Pearson residual versus age of the woman

this hypothesis can result in some bias, since the most fertile couples conceive sooner and so they contribute a smaller number of cycles.

Now, let N_i be the number of women that provide information on at least i cycles, P_i the number of observed pregnancies during the i-th cycle. The observed distribution of cycles that a couple need to achieve a pregnancy can be estimated by:

$$S_i = [1 - \frac{P_1}{N_1}] \ldots [1 - \frac{P_i}{N_i}],\ i = 1,2, \ldots \quad (3)$$

In a similar way the distribution expected under the model can be obtained. Figure 2 shows the two graphs. No large difference can be seen.

To obtain a different check, we add to the the covariates also the number of previous cycles without conception. The improvement in fit is not significant ($p = 0.841$).

Age of the woman

The age of the woman was not significant. Since this variable is correlated with the age of the partner and with the number of children, we fit a model with only the age of the woman. However, the age of the woman was still not significant. ($p = 0.998$).

A graphical check of this finding can be obtained in the following way. Let y_{ij} be the observed outcome (1 = conceive or 0 = not conceive) for the i-th woman during the j-th cycle. Furthermore, denote by η_{ij} the probability of conception for that woman and that cycle predicted by the SBM model without covariates. Then a Pearson-like residual can be computed as

$$r_i = [\sum_j (y_{ij} - \eta_{ij})] / \sqrt{\sum_j \eta_{ij} (1 - \eta_{ij})} \quad (4)$$

Figure 3 shows a plot of the r_i against the age of the woman. No particular pattern can be observed.

Discussion

These findings are derived from limited data which will need to be confirmed by the total database. Additionally these results cannot be taken as representative of conditions pertaining the whole population. The sample excludes, for instance, cases of sterility or subfertility. They are valid for a population with the biological characteristics of potential clients of a natural family planning clinic. In addition, some refinements in the modelling strategy seem necessary. For example, it seems important to let also the π_js depend upon some possible covariates (e.g. type of mucus on day j, previous intercourse, age of the partners, in particular the man). In this way, information about couple-to-couple and cycle-to-cycle variation in the length of the fertile window can be obtained. Furthermore, these data can be used to address such questions as the relation between sex of the baby and timing of sexual intercourse.

Level of fecundity

Our estimates of the probabilities of conception are lower than those previously reported in the literature. For example, our estimate of k is 0.25. The point estimate of the same parameter computed by Schwartz *et al.* [5] using data collected by Marshall in the 1960s was 0.52. Weinberg *et al.* [6] obtained an estimate of 0.38 using data collected during the Early Pregnancy Study conducted in the United States about ten years ago. This finding is suggestive since it points to a decrease in fecundity over the last three decades. However, it should be noted that the observed differences are, at least in part, due to differences in designs of studies and to statistical errors. With regard to the first point, for instance, Marshall [1] included also women over forty and of 'proven fertility'. With reference to precision of the estimates, it should be mentioned that a 95% likelihood based confidence interval for k can be computed in [0.32,1] on the basis of the data used by Schwartz *et al.* [5] and in [0.20,0.32] using our data.

BBT rise or peak of the mucus

Bearing in mind that the sample is not large and that the difference between the day of the BBT rise and the peak is something more than 2 days on average, the patterns of the probabilities of conception, around the two reference points, look similar. However, the fitted probabilities decrease faster if BBT is used. This may suggest that time of ovulation is more correlated with the BBT rise than with the peak.

Age of the partners

Our data point to a strong effect of the age of the man on the probability of conception. We found no evidence of a similar impact of the age of the woman. It should be appreciated that the women participating in the study are less than 40 years old, at least at the time of first contact. Hence, it can only be concluded that the ability of a woman to conceive does not vary between 20 and 40 years of age.

Mucus

The number of days with 'most fertile' mucus is a factor that could explain cycle-to-cycle variations in fecundity. Our results suggest using a model of fecundity based jointly on basal body temperature and mucus. This kind of model would seem to have potential for natural family planning application.

Couple heterogeneity

We found that the number of previous children affects fecundity. This variable can be viewed as a proxy for the differences in the biological capability to conceive between couples not explained by the other covariates.

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