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Regional differences in waiting time to pregnancy: pregnancy-based surveys from Denmark, France, Germany, Italy and Sweden

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The objective of this study was examine geographical variation in couple fecundity in Europe. The study was based upon all recently pregnant (or still pregnant) women within well-defined geographical areas in Europe (Denmark, Germany, Italy, Sweden and France) at a given time period in 1992. Altogether, 4035 women responded to a highly structured questionnaire. Highest fecundity was found in Southern Italy and Northern Sweden; lowest fecundity was seen in data from the East German centre. Approximately 16% of the study population had a waiting time of more than 12 months to become pregnant. Most of the pregnancies were planned (64%) and approximately 14% were the result of contraceptive failures. The study shows that smoking, body mass index, age and parity did not explain the differences in fecundity found between the centres. Regional differences in fecundity exist and the causes may be genetic or due to variations in behavioural and environmental exposures.

Key words: environment/fecundity/infertility/pregnancy

Introduction

There is evidence to suggest a decline in sperm quality over time (Carlsen *et al.*, 1992), but this finding may be biased by geographical differences, differential selection, changes in the measuring or changes in other circumstances (Olsen, 1994). If the decline in sperm quality is real, it should have an impact on couple fecundity (Bonde *et al.*, 1998). Unfortunately, there is surprisingly little evidence about trends in couple fecundity over time. There is also very little known about geographical differences and, if they exist, they should be taken into consideration when studying secular changes in semen quality or concentration.

In Europe, several investigations have provided a wide range of estimates of the prevalence of infertility, from 6% to 20% (Rachootin and Olsen, 1981, 1982, 1983; Hull *et al.*, 1985; Rantala and Koskilles, 1986; Page, 1989; Templeton *et al.*, 1990; Thonneau and Spira, 1990; Thonneau *et al.*, 1991; Wagner and Stephenson, 1992). However, the applied methods vary and results are thus not comparable. In order to obtain comparable data, a European study group was established in 1990 (ESIS, European Studies of Infertility and Subfecundity) which implemented comparable studies on infertility and subfecundity in different European countries.

ESIS conducted both population-based and pregnancy-based surveys, using highly structured questionnaires. In this report we present findings on time to pregnancy (TTP) from the studies based upon pregnant women.

Materials and methods

Concepts and definitions

Terms to describe fecundity are used differently by demographers, clinicians and epidemiologists. In the demographic context, the term fertility refers to the actual reproductive behaviour as expressed by the number of childbirths; clinicians often use the term to describe the biological ability to conceive, or the ability to produce live offspring. We use the term fecundity for the biological ability to give birth or to achieve a recognized pregnancy, subfecundity for evidence of decreased fecundity, and sterility for inability to conceive, e.g. due to hysterectomy or sterilization.

Fecundity is estimated for a population by the time to pregnancy (TTP): the time span, or the number of menstrual cycles exposed to unprotected intercourse, until conception (Baird *et al.*, 1986). To determine TTP, the starting date of unprotected cohabitation and the date of conception are required. A TTP of one year or more is often used as a measure of subfecundity (Rowe and Farley, 1988).

Questionnaire and interview

A questionnaire was developed by a collective process during several cycles of pilot testing in most of the participating countries. The master questionnaire was in English, and ambiguity in the wording was checked by independent translations to other European languages and back-translation to English. The questionnaire was designed for self-administration, but in two centres in Italy it was administered by female interviewers.

The main contents of the questionnaire were: health and education, reproductive history, starting date and TTP for the current or recent pregnancy, exposures around the starting date, and intent to become pregnant (planning). A copy of the questionnaire is available on request (S.Juul).

The questionnaire was structured according to the past reproductive

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experience in order to better define the starting time (start of unprotected intercourse). The TTP question was phrased: 'How long was it from that 'starting time' until you became pregnant? (the date you became pregnant is the date you conceived)'. The women's response could be expressed in weeks, months or years.

Interviews/responding typically took 15–25 min. The unit of analysis was a pregnancy, and the mothers were used as informants.

Population

The surveys were conducted in five European countries between February 1992 and December 1992. The target group consisted of women who had just given birth to a live child or women who were pregnant. In Sweden and France, only part of the data were collected during pregnancy.

The women were approached either immediately after having given birth at a hospital or birth clinic or at a visit to an antenatal care centre after 20 weeks of gestation. The institutions were selected because they served geographically well-defined populations, and all pregnant women during the period of data collection were asked to participate. The sampling method excluded women who did not attend prenatal services or who gave birth at home, but $<5\%$ were excluded for this reason in any centre.

Statistical methods

TTP was recorded as weeks and/or months and/or years, e.g. a TTP of 3.5 months was recorded as 3 months + 2 weeks. For short TTP, up to three menstrual cycles to pregnancy were also recorded, as pilot experience showed that women recalled longer waiting times as months rather than as menstrual cycles. For this reason, the data in this paper were analysed according to passage of time. By using time as the outcome, TTP measures cover not only sexual activity and ability to conceive and sustain a conception, but also menstrual irregularities. For pregnancies occurring despite contraception, TTP was considered to be undefined and thus missing.

In this paper the TTP distribution was described as the cumulative proportion of pregnancies occurring up to a given waiting time.

Comparisons of TTP in different centres were also based upon Cox regression, using continuous TTP (not cycles) as the outcome. Observations longer than 12 months were censored. By design, there were no censorings within the first 12 months, and TTP was measured in continuous time, and it was therefore not considered appropriate to use a discrete time model. The term 'pregnancy ratio' was used for the Cox regression coefficients, which should not be considered as fecundability ratios, as there were no data on TTP not leading to pregnancy. With this reservation, the pregnancy ratio was considered to be that between incidence rates of pregnancy, the incidence rate being the reciprocal of TTP.

Coding and data entry were performed locally, but combined to an anonymous dataset, using SPSS. Analyses were performed using SPSS for Windows.

Results

Sample size, participation rates and administration of the questionnaire by centre are detailed in Table I. The overall participation rate was 83%, varying from 66% in East Germany to 98% in the Rome area.

The reproductive experiences of the participants are described in Table II. The variations in age and in reproductive experience reflect the actual age distribution and reproductive pattern in the regions included. The highest parity was seen in Umeå, Sweden, and the lowest in Rome and Milan, Italy. Table II also details the distribution of potential confounders for the geographical comparisons.

Overall, 14% of the pregnancies were the result of contraceptive failures, with a high value of 21% in Milan/Bergamo and a low of 9% in Paris (Table III). Most (64%) of the pregnancies were described as planned by the women, ranging from 81% in Paris to 41% in Halle and Rostock (East Germany). Similar figures were found for those who expected (or who had just had) their first baby. Information on TTP was obtained for almost all of the pregnancies not due to contraceptive failure.

TTP was recorded with some digit preference, with excess recordings of 12 and 24 months, compared with the neighbour categories. Thus, the cumulative TTP distribution for <12 months and TTP for $\leqslant 12$ months is presented in Table IV. The average proportion of TTP >12 months was 16%, with a low of 10% in Southern Italy and a high of 24% in East Germany. The TTP distribution did not differ significantly in the first pregnancy compared with other pregnancies. For planned pregnancies, the average proportion of TTP >12 months was 13%, with the same relative distribution between regions. For unplanned pregnancies, the proportion was 24%.

To adjust for confounders, the TTP distributions were compared in Table V, using Cox regression analysis. The significant differences in the TTP distributions remained after adjustment for regional differences in body mass, smoking,

Table I. Description of the samples from the different European countries

	Odense, Denmark	West Germany	East Germany	Umeå, Sweden	Milan, Italy	Rome, Italy	Paris, France	Total
No. of participants	503	832	486	774	423	440	577	4035
Participation rate (%)	83.0	72.5	66.5	93.0	95.5	97.8	87.2	82.8
Status at data collection (%)								
Pre-partum				81			22	19
Post-partum	100	100	100	19	100	100	78	81
Administration of questionnaire	Self-administered	Self-administered	Self-administered	Self-administered	Interview	Interview in hospital within 24 h of delivery	Self-administered	
Regions (urban/rural)	Odense (urban)	Freiburg (urban) Hamburg (urban) Tubingen (rural)	Halle (urban) Rostock (rural)	Umeå (mixed)	Milan/Bergamo (urban)	Rome (urban) Terni (urban)	Paris (urban)	

Table II. Reproductive history and potential confounders

	Odense, Denmark	West Germany	East Germany	Umeå, Sweden	Milan, Italy	Rome, Italy	Paris, France	Total
No. of prior pregnancies								
0	34	41	41	35	43	45	36	39
1	34	32	30	30	32	38	33	32
2	19	15	15	18	17	12	17	16
3+	13	12	14	17	8	5	14	13
Mean	1.21	1.05	1.17	1.32	0.95	0.81	1.22	1.12
No. of prior live births								
0	48	51	51	49	52	55	47	50
1	37	36	33	32	37	38	38	36
2	13	10	10	13	9	6	9	10
3+	2	3	6	6	2	1	6	4
Mean	0.69	0.66	0.77	0.79	0.62	0.53	0.76	0.70
Age (years) at starting date								
<19	3	3	19	2	3	1	4	5
20–24	22	20	47	27	19	18	28	25
25–29	52	45	26	41	41	40	43	42
30–34	20	26	6	22	29	31	20	22
>35	3	6	2	8	8	10	5	6
Mean	27.5	28.1	23.8	27.8	28.4	29.0	27.2	27.4
Body mass index								
<17.9	3	4	10	2	5	5	7	5
18–24.9	79	78	73	84	81	78	82	79
25–29.9	15	14	11	11	11	14	8	12
>30	3	4	6	3	3	3	3	4
Mean	22.4	22.4	22.1	22.2	21.8	22.2	21.6	22.2
Smoking								
No	59	68	56	77	65	68	59	65
1–9/day	8	10	23	9	16	13	12	13
>10/day	33	22	22	14	19	19	29	22
Planned pregnancy	83	67	47	73	80	85	86	74
Intercourses per week								
⩾1	73	63	67	76	83	87	71	73
<1	20	19	14	17	12	7	7	14
No answer	7	18	19	7	5	6	22	13
Ever used oral contraception	88	89	83	87	56	45	84	79
Ever used IUD	32	16	3	17	7	13	13	15
Ever suffered from sexually transmitted or pelvic inflammatory disease	35	19	21	28	14	13	10	21

Values are percentages.

Table III. Main information about time to pregnancy

	Odense, Denmark	West Germany	East Germany	Umeå, Sweden	Milan, Italy	Rome, Italy	Paris, France	Total
All pregnancies								
1 No. of participants	503	832	486	774	423	440	577	4035
2 Not contraceptive failure (% of 1)	456 (90.7)	702 (84.4)	416 (85.6)	665 (85.9)	333 (78.7)	360 (81.8)	525 (91.0)	3457 (85.7)
3 Planned pregnancy (% of 1)	380 (75.5)	478 (57.5)	200 (41.2)	487 (62.9)	269 (63.6)	307 (69.8)	466 (80.8)	2587 (64.1)
4 Information on TTP (% of 2)	453 (99.3)	694 (98.9)	413 (99.3)	663 (99.7)	333 (100.0)	359 (99.7)	523 (99.6)	3438 (99.5)
No prior live births								
1 No. of participants	243	422	245	376	222	243	270	2021
2 Not contraceptive failure (% of 1)	221 (90.9)	358 (84.8)	222 (90.6)	324 (86.2)	184 (82.9)	212 (87.2)	244 (90.4)	1765 (87.3)
3 Planned pregnancy (% of 1)	187 (77.0)	254 (60.2)	117 (47.8)	227 (60.4)	153 (68.9)	184 (75.7)	222 (82.2)	1344 (66.5)
4 Information on TTP (% of 2)	220 (99.5)	354 (98.9)	222 (100.0)	322 (99.4)	184 (100.0)	212 (100.0)	243 (99.6)	1757 (99.5)

Table IV. Cumulated distribution of time to pregnancy (percentages) by region

Months	Odense, Denmark	West Germany	East Germany	Umeå, Sweden	Milan, Italy	Rome, Italy	Paris, France	Total
All pregnancies (*n*)								
	453	694	413	663	333	359	523	3438
⩽3	56.3	52.2	46.7	62.7	47.1	66.0	48.2	54.5
⩽6	73.3	67.4	62.0	79.3	70.0	79.7	68.1	71.5
<12	81.0	79.0	73.1	87.0	77.5	86.9	79.3	80.8
⩽12	83.0	82.9	75.8	89.6	81.1	90.3	82.8	83.9
<24	88.1	89.5	83.3	93.8	85.3	93.9	90.6	89.6
⩽24	90.7	91.1	85.5	94.1	88.3	94.7	92.0	91.2
No prior live births (*n*)								
	220	354	222	322	184	212	243	1757
⩽3	55.5	49.4	44.1	62.4	48.4	65.1	46.1	53.2
⩽6	70.0	64.7	59.0	78.6	73.9	78.2	63.8	69.7
<12	78.6	76.8	71.6	87.6	79.9	87.7	74.9	79.7
⩽12	80.5	80.5	74.8	90.7	81.0	91.0	79.0	82.8
<24	83.6	89.5	83.8	95.0	86.4	95.3	90.9	89.6
⩽24	87.7	91.8	86.5	95.3	89.7	95.8	92.6	91.6

Table V. Pregnancy ratios (PR) according to geographical region. Cox regression on time to pregnancy in months

Region	*n*	Crude	Adjusted
		PR 95% C.I.	PR 95% C.I.
Odense, Denmark	453	1.00	1.00
West Germany	694	0.93 (0.81–1.06)	0.91 (0.80–1.04)
East Germany	413	0.79 (0.68–0.92)	0.81 (0.69–0.95)
Umeå, Sweden	663	1.24 (1.09–1.42)	1.16 (1.01–1.32)
Milan, Italy	333	0.89 (0.76–1.04)	0.85 (0.72–0.99)
Rome, Italy	359	1.32 (1.14–1.53)	1.22 (1.04–1.42)
Paris, France	523	0.87 (0.76–1.00)	0.77 (0.67–0.89)

C.I. = Confidence interval.
Adjusted for: mother's age (four levels), gravidity (1,2+), body mass index (five levels), smoking (four levels), pregnancy planning (yes, no), frequency of intercourse (four levels), previous sexually transmitted disease or pelvic inflammatory disease (yes, no). All TTP >12 months were censored at 12 months

frequency of intercourse and sexually transmitted diseases. After these adjustments, the French centre had the longest TTP and Southern Italy the shortest.

Discussion

The study shows substantial variations in fecundity between the centres, as estimated by the TTP distribution. To our knowledge this is the first international study on fecundity which is based upon an unselected population of pregnant women or mothers, a common protocol, and the same questionnaire. Results based upon a less comparable design have shown better couple fecundity in Finland than in the UK (Joffe, 1996). In spite of our use of a common protocol, however, the differences may be due to bias, e.g. related to comparability of populations and quality of information.

Comparability of populations

In all sites, the sampling included almost all pregnancies leading to a live birth or a pregnancy exceeding a duration of 20 gestational weeks within the stated time periods. Participation rates varied considerably, and this may have introduced a bias of unknown direction and magnitude in the comparison of fecundity.

Pregnant women were selected late in pregnancy in order to avoid pregnancies leading to miscarriages, and women who aborted after recruitment were excluded from the sample according to the protocol. Since subfecundity correlates with abortion (Basso *et al.*, 1997a), bias may have been introduced if not all abortions were excluded, though the bias would be small if present.

Of much more serious concern is the fact that the study relied upon a similar drive in pursuing a pregnancy attempt in all centres, since those who gave up are not included in the sample. We did, however, find similar results when restricting the study to pregnancy planners who are expected to provide better data on TTP and to have a more similar behaviour. Differences in the willingness to become pregnant hardly explain all the findings.

The locations included in the study are not representative of areas greater than regions, and the study provides no information on variation between countries.

Quality of information

The questionnaire was developed during several cycles of pilot testing, and the experience from the translation–back-translation process indicated that language differences give rise to few problems of comparability. However, cultural differences in pregnancy planning habits, use of contraceptive methods, etc. might lead to differences in the reporting of TTP, but this potential source of bias hardly explains the marked differences in fecundability.

The interviewers reported that the interviewees accepted being asked about reproductive and sexual experience, and they had the impression that the women provided honest answers. However, the tendency to digit preference indicates that the recall of TTP duration is not perfect at an individual level in spite of a short recall period. A previous study (Joffe *et al.*, 1993) concluded that long-term recall of TTP duration is quite reliable, and we find no reason to believe that the quality of recall is different during pregnancy and shortly after delivery.

When the questionnaire was self-administered, some of the women had difficulties in finding the relevant questions.

The difference in the frequency of a TTP >12 months as a function of pregnancy planning (13% for planners and 24% for those who had unprotected sexual intercourse without planning a pregnancy) shows that TTP measures strongly depend upon how the key questions are phrased. A similar conclusion was reached in a study from USA (Marchbanks *et al.*, 1989). These results warn against comparing data based upon different questionnaires, or questionnaires using different wordings of key questions.

In conclusion, interpretation of the TTP distribution in a pregnancy-based study is somewhat complex, since the pregnancy-based TTP distribution is conditional on a pregnancy actually occurring. On the other hand, geographical factors that potentially affect fecundity can be studied, since most determinants prolong TTP rather than cause sterility (perhaps with the exception of infections). The target population of a pregnancy-based study is easier to identify and to approach than the target population of a population-based study, and recall problems when reporting TTP are less since recall is short.

Fertility is a function of many factors, and fecundity plays a rather limited role in most countries with low fertility. We found low fecundity in areas with high fertility (East Germany) and high fecundity in areas with low fertility, such as Italy.

Many (36%) of the pregnancies (19% in France, 59% in East Germany) were not planned, and 14% of the pregnancies (from 9% in France to 21% in Northern Italy) occurred despite contraception. All these pregnancies had passed the gestational age for induced abortion which was available within the first 12 gestational weeks in all participating countries.

The study shows regional differences in couple fecundity which should be taken into consideration when studying how fecundity develops over time. In the search for environmental factors of importance for fecundity, such as hormonal disruptions acting in fetal life, geographical variation may give important clues and ecological studies related to environmental exposures are needed.

We have previously analysed data according to selected determinants (Basso *et al.*, 1995, 1997b; Bisanti *et al.*, 1996; Bolumar *et al.*, 1996, 1997; Olsen *et al.*, 1997), and the most important of these are mother's age, smoking habits and body mass index. Regional differences in these determinants did not explain the variation between the centres. Unfortunately, we probably have no good data on previous sexually transmitted infections or previous induced abortions. It is possible that these factors partly explain the geographical variation in TTP, but it is of course also possible that genetic factors play a role. The main aim of this study was to describe geographical variation, rather than to identify underlying reasons for the differences.

The study shows that differences in fecundity in Europe do occur, and resources should be devoted to finding out why. The use of simple survey methods may provide valuable and direct measures of couple fecundity, and monitoring TTP distribution over time for the same population may provide valuable data on major secular changes in couple fecundity. Great care should be taken when selecting proper data collection instruments, and uniform sampling criteria must be used.

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