Feasibility of surveillance of changes in human fertility and semen quality

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There is concern that male fertility is declining, but this is difficult to study because few men volunteer for studies of semen quality, and recruitment bias may over-represent the subfertile. The Human Reproduction Programme of the World Health Organization developed a protocol for multicentre studies of fertility involving a questionnaire for pregnant women to obtain time to pregnancy (TTP): the number of menstrual cycles taken to conceive. Male characteristics and semen quality will be determined in a subset of the partners. Our aim was to validate the TTP questionnaire, and to examine potential recruitment bias and feasibility of conducting large-scale surveillance of fertility. The questionnaire was administered to 120 pregnant women (16–32 weeks). Validation included internal reliability by consistency of responses, test–re-test reliability by repeat administration (20 women) and accuracy by comparison of gestational age from first antenatal ultrasound and menstrual dates. Internal reliability was high. Agreement between categorical responses on re-testing was very good (k > 0.8). In both the re-test and gestational age analysis, differences in TTP of 1 cycle were found (standard deviation <0.25 cycles). In this small pilot study there was no evidence of recruitment bias. Response rates indicate the feasibility of surveillance of fertility in large maternity centres.

Key words: fecundability/human fertility/questionnaire validation/recruitment bias/time to pregnancy

Introduction

Concern has been raised that there has been a decline in human sperm concentration over the past 50 years, and also a corresponding increase in the incidence of abnormalities of the male reproductive tract such as testicular cancer, undescended testes and hypospadias (Carlsen et al., 1992; Sharpe and Skakkebaek, 1993; Kavlock et al., 1996). A postulated cause of a downward trend in male fertility is the prenatal exposure to chemicals in the environment called ‘endocrine disruptors’ that act like oestrogens (Sharpe and Skakkebaek, 1993).

The Sharpe and Skakkebaek (1993) hypothesis arose from knowledge of the results of exposure to diethylstilboestrol (DES) and chemicals such as dichlorodiphenyltrichloroethane (DDT). Between 1945 and 1971, millions of pregnant women were prescribed the synthetic oestrogen DES in the hope of preventing miscarriages (Sharpe and Skakkebaek, 1993). A controlled trial showed that DES was ineffective in preventing miscarriage, but follow-up revealed that it predisposed the female offspring to specific abnormalities such as vaginal adenocarcinoma. The male offspring had an increased risk of genital malformations and reduced sperm concentration (Crisp et al., 1998). However, the effects on males were minor, and male fertility was found not to be impaired (Wilcox et al., 1995). DES was withdrawn for use in humans in 1971.

Wildlife studies exemplify the effects of endocrine disruptors on reproductive health. In 1980, Lake Apopka in Florida was contaminated with DDT as a result of a chemical spill. Subsequently, alligators inhabiting the lake displayed a variety of reproductive disorders (Crisp et al., 1998). In the UK, fish in water containing oestrogenic sewage effluent exhibited an increased incidence of hermaphroditism (Sumpter and Jobling, 1995).

Given the extent of modern chemical use, the possibility of
ill health in general (and infertility in particular) has caused considerable disquiet. However, the reports that semen quality has declined (Carlsen et al., 1992; Auger et al., 1995; Adamopoulos et al., 1996; Irvine et al., 1996; Van Weeleghem et al., 1996) are balanced by others showing no decline (Bujan et al., 1996; Fisch et al., 1996; Paulsen et al., 1996; Benshushan et al., 1997). There are also concerns about the reporting of other reproductive disorders such as testicular cancer and cryptorchidism (Kavlock et al., 1996).

The World Health Organization (WHO) Special Programme of Research, Development and Research Training in Human Reproduction (HRP) has developed a multicentre collaborative epidemiological study, ‘Sentinel Surveillance of Semen Quality and Time to Pregnancy’ to determine whether or not human fertility is declining. This study is to be conducted in settings in Africa, South America, Asia/Pacific regions and Russia. It will complement independent studies being undertaken in Europe, Japan, and the Study of Families in the USA.

One method of assessing changes in semen quality over time is to select at intervals random samples of males from the population and submit them to fertility tests, including semen analysis. This approach is not possible since few men volunteer, and previous experience indicates that volunteers disproportionately represent those who are concerned about their fertility, either because of previous testicular disorders or suspected infertility (Handelsman, 1997; Larsen et al., 1998a). Moreover, such a study fails to address whether any deterioration in semen quality is accompanied by a reduction in human fertility. This can be measured by assessing changes in the time taken to achieve a pregnancy. The WHO HRP study consists of repeat samples from the population of currently pregnant women, coupled with an assessment of semen quality in partners of the women. It is accepted that assessing TTP in women who are currently pregnant will exclude those who are infertile and some who are subfertile. Also, TTP may not change in direct relation to a decline in sperm concentration or other semen characteristics. However, TTP is a useful and sensitive measure of human fertility (Joffe, 1997). It has been used successfully to study environmental effects, and it will allow bias in the male volunteers to be assessed (Weinberg et al., 1994).

TTP, which can be assessed by questionnaire, is defined as the time from when a woman starts trying to conceive, or is first exposed to the risk of a pregnancy, until conception occurs (Baird et al., 1986; Weinberg et al., 1993). TTP is recorded in months or menstrual cycles (Spira, 1998). TTP based on cycles rather than months may be more useful because conception is usually only possible once during an average cycle length of 28 days (Weinberg et al., 1994). Fecundability, defined as the probability of pregnancy in each menstrual cycle, can be estimated from TTP. A long TTP is indicative of low fecundability (Basso et al., 1997). TTP has been used to study the effects of environmental, occupational, health and lifestyle factors on fertility (Baird and Wilcox, 1985; Wilcox et al., 1988; Weinberg et al., 1989; De Cock et al., 1994; Spinelli et al., 1997; Larsen et al., 1998b; Sallmen et al., 1998). Regional differences in fertility have also been studied (Joffe, 1996; Tuntiseranee et al., 1998; Juul et al., 1999).

TTP can be studied either retrospectively or prospectively. Prospective TTP studies involve selection of non-pregnant subjects who are followed until a pregnancy or birth occurs (Joffe et al., 1993). A prospective design has the advantage of accuracy of TTP data, but the disadvantage of the expense of follow-up and possible problems with selection bias (Baird et al., 1994; Weinberg et al., 1994; Zinaman et al., 1996; Kold Jensen, 1997; Bonde et al., 1998).

Retrospective TTP can be obtained with a short questionnaire which is inexpensive, feasible, and has good validity and high compliance rates (Baird et al., 1986; Joffe, 1997; Olsen et al., 1998). However, it is necessary to control for confounding factors and bias (Baird et al., 1986, 1994; Weinberg et al., 1994). Also, determining exposure in retrospective studies can be difficult (Joffe, 1997). Theoretically, retrospective measures of TTP have questionable validity as they are indirect observations. That is, they rely upon the subjects’ ability to remember dates correctly for calculation of the TTP (Joffe et al., 1995; Spira, 1998). It has been found that at group level, valid data on TTP could be obtained retrospectively with a recall of TTP greater than 14 years (Joffe et al., 1995). In addition, data obtained retrospectively correlate well with those obtained prospectively, and with different questionnaires (Joffe, 1989; Baird et al., 1991; Zielhuis et al., 1992; Joffe et al., 1993, 1995). The internal reliability was checked (Joffe, 1989), and a test–re-test study of a TTP questionnaire carried out (Zielhuis et al., 1992).

For the WHO surveillance studies, TTP and factors affecting it will be assessed by a short questionnaire administered to currently pregnant women. In selected male partners more detailed information will be obtained by a further questionnaire, clinical examination and semen analysis. The surveillance will be done at intervals of 3 years (years 1, 4 and 7) with different subjects drawn from the same source population. It is not intended to establish cause and effect relationships, for example between spermatogenic defects and specific exposures to endocrine disruptors, but some exposure data will be collected to generate hypotheses for more specific studies. All women between 16–32 weeks pregnant by dates will be invited to participate in the TTP study. To be eligible for the semen study men must be aged between 18 and 50 years, reside in the district, both he and his mother must have been born in the country of the participating centre, and the couple must have received no infertility treatment for the current pregnancy.

The aim of this pilot study was to further develop, pilot and validate a draft TTP questionnaire from WHO. Subsidiary aims were to provide estimates of compliance rates and to examine possible bias in the recruitment of male partners. Compliance rates would enable more precise calculations of the number of subjects to be interviewed, the number of personnel to perform the interviews, and the overall cost of the intended WHO study.

Materials and methods

Subjects

The aim of this pilot study was to recruit 120 pregnant women between 16 and 32 weeks gestation from the antenatal clinic at the
Royal Women’s Hospital, Melbourne, between June and August 1999. Women were approached in the waiting areas and given a ‘participants’ information statement’ outlining the nature of the study and the questionnaire. All women interviewed gave written informed consent. Institutional Ethics Committees approved the project.

**Questionnaire**

The draft TTP questionnaire developed by WHO was initially modified to suit Australian participants. The structure and wording of the questionnaire was further revised after pilot testing face to face with 10 women. The revised questionnaire contained 57 questions which elicited information on pregnancy, reproductive and contraceptive history, socio-demographic characteristics and some exposures such as smoking (Appendix I). The 120 women were interviewed face to face by one of three people (female research nurses or a student). The questionnaire took ~15 min to administer. The questions were rank tests were used to assess the significance of differences between life-tables. Cox regression analysis was used to determine the effect of 24 potential explanatory variables on pregnancy rate (Table I), and to examine recruitment bias on the presumption that women who have a longer TTP might be more likely to have their partners participate in the semen study. Three responses (Yes, No and Don’t know) to two questions about the women’s perceptions of their partner’s willingness to participate in semen studies were analysed.

**Results**

**Participation**

Of the 132 women approached, 120 agreed to participate (90%). Those who declined to be interviewed did so for various reasons, with tiredness by far the most common reason. None refused to be interviewed because the questionnaire was seen to be intrusive or too sensitive.

Sufficient and consistent information from which TTP could be calculated accurately was obtained from 85 (70%) women with planned pregnancies. Of the other 35 women, 15 had contraceptive failure [oral contraceptive pill (n = 6), condoms (n = 5), intrauterine device (n = 2), rhythm (n = 1)], injection of Depo-Provera (medroxyprogesterone acetate) (n = 1)], three used contraceptives irregularly, four had secondary amenorrhoea, one was raped, and six conceived with infertility treatment. TTP could not be calculated for six women because of missing information.

**Gestational age by ultrasound and menstrual dates**

There was good agreement between gestational age calculated from the menstrual dates and ultrasound (Figure 1). The results did however show some variation because ultrasonologists used different methods to estimate and report gestational age. Also, approximately one-third of the women in the study had their first ultrasound after 24 weeks of pregnancy when ultrasound estimates of gestation are less accurate. This probably accounts for the increasing variability in discrepancy with gestational age seen in Figure 1.

**Internal and re-test reliability of questionnaire**

Only 5% of 120 women had minor discrepancies of a few days in their responses to different questions about the timing of cessation of contraception. These did not influence calculation of TTP. With the re-test validation, the 20 women
Table I. List of explanatory variables analysed by Cox regression

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Frequency of intercourse (7 categories)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Educational level (4 categories)</td>
<td>Infertility treatment (yes/no)</td>
</tr>
<tr>
<td>Marital status (yes/no)</td>
<td>Specified medical conditions (yes/no)</td>
</tr>
<tr>
<td>BMI</td>
<td>Illicit drug use (yes/no)</td>
</tr>
<tr>
<td>Gravida (primigravid/multigravid)</td>
<td>Smoking (yes/no)</td>
</tr>
<tr>
<td>Contraceptive use around the time of conception (yes/no)</td>
<td>Activities involving chemical exposure (yes/no)</td>
</tr>
<tr>
<td>Oral contraceptive use (ever/never)</td>
<td>Employment (yes/no)</td>
</tr>
<tr>
<td>Use of Depo-Provera injection (yes/no)</td>
<td>Employment (male partner) (yes/no)</td>
</tr>
<tr>
<td>Use of IUD (yes/no)</td>
<td>Activities involving chemical exposure (male partner) (yes/no)</td>
</tr>
<tr>
<td>Planned pregnancy (yes/no)</td>
<td>Australian born male partner (yes/no)</td>
</tr>
<tr>
<td>Menstrual cycle pattern (regular/irregular)</td>
<td>Knowledge of fertile phase (yes/no)</td>
</tr>
<tr>
<td>Timing of intercourse to fertile phase (yes/no)</td>
<td></td>
</tr>
</tbody>
</table>

Some were binary variables such as marital status and education, some categorical such as frequency of intercourse, and some continuous such as BMI and age. Variables such as desire for pregnancy, smoking, activities involving chemical exposure (both male and female), timing of intercourse to fertile phase, frequency of intercourse, infertility treatment, illicit drug use, employment (both male and female) and menstrual cycle pattern were for the period between commencing trying to become pregnant and conception. BMI = body mass index [weight (kg)/height (m)²]; Depo-Provera = medroxyprogesterone acetate; IUD = intrauterine device.

responded consistently to the questioning on contraceptive history. In reporting their LNMP, 17 (85%) women were able to do so consistently, with three (15%) having minor discrepancies in their responses (± 2 days). Questions pertaining to the use of contraception around the time of conception were answered consistently by all women (k = 1.00). In describing their menstrual pattern, 19 women responded consistently, with one reporting inconsistently about regular cycles (k = 0.83). In the reporting of shortest and longest menstrual cycles, 85% of women were able to answer consistently, although 15% reported minor discrepancies (± 3 days). One woman, who was re-interviewed after an interval of 2 weeks, gave two different estimates of when she resumed sexual intercourse after her last pregnancy, altering the TTP estimate by 1 cycle. Thus, the measurement error of TTP is small in this study: in the test-retest study [mean difference 0.05 ± 0.22 (SD) cycles], 1 month in 1 of 85 women for ultrasound-confirmed gestational age (mean difference 0.11 ± 0.01 cycles), and overall there was a difference of 2 cycles in 105 women (mean difference 0.02 ± 0.14 cycles).

Distribution of TTP

Figure 2 compares histograms of TTP for the total population (n = 114) and for women with planned pregnancies (n = 85). For the total population, TTP could not be calculated for six women. Women with birth control failure were included as conceiving in cycle 1 (n = 15). For women whose current pregnancy was the result of infertility treatment (n = 6), the duration of infertility until treatment commenced was used as TTP. Periods of time in which contraception was used irregularly were counted as half-cycles and rounded to even numbers.

Feasibility of WHO Study

The WHO protocol aims to recruit 5000 women and 300 men at each centre for each phase of the study. In addition, the male study may be confined to couples with first pregnancies only. Of the 85 women with planned pregnancies for whom TTP could be calculated, 55% had partners who were eligible for the semen study. The responses of these women to two questions about possible participation of their partners in the semen quality study are listed in Table II. Twenty one women (44.7%) were uncertain whether their partners would agree to participate, but they would pass on the invitation. When the women were interviewed, about half were accompanied by
Figure 2. Time to pregnancy (TTP, cycles) for total population \( (n = 114) \) and for planned pregnancies \( (n = 85) \). The average TTP was 4.6 and 4.4 cycles respectively.

Their partners, and the questions pertaining to possible participation in the semen study were also directly addressed to the men. Surprisingly, after being advised of the requirements of the study involving a physical and semen analysis, most indicated they would agree to participate in the male study, even though their partners had strongly believed that they would refuse.

From the results of this study, 47 women had partners who were eligible for the semen study, and 43 indicated they would pass on the invitation to their partners. Assuming that 50% would comply, we estimate that 18% (95% CI 12–26%) of women interviewed would result in the subsequent recruitment of a man for the semen study. Therefore, 1700 (95% CI 1100–2500) women would need to be approached in order to recruit 300 men. As only 22% of women were pregnant for the first time, 7600 (95% CI 5200–11 400) women would need to be approached to recruit 300 partners of primigravidas. To obtain useable TTP data from 5000 couples with planned pregnancies, 7800 (95% CI 6900–8900) women would need to be approached. However, if all data for which TTP could be estimated were used, the figure would be reduced to 5800 (95% CI 5100–6600) women.

**Recruitment bias**

The possibility that women who have a longer TTP may be more likely to have their partners participate in the male studies was examined. The mean TTP for the 15 women who thought their partner would agree to participate was 3.3 \( \pm 3.2 \) cycles. For the 35 who did not believe their partner would participate, the mean TTP was 4 \( \pm 3.1 \) cycles, and for the 35 who did not know it was 5.1 \( \pm 6 \) cycles. Using Cox regression analysis without or with known co-variates of fecundability included in the model, the three responses to questions on potential male participation were also not significant. Thus, there was no evidence that partners of women with a long TTP would be more likely to participate.

None of the 24 factors known or suspected to affect fertility included in the Cox regression models (Table I) was statistically significant, although use of the oral contraceptive pill \( (P = 0.06) \) and exposure of the male partner to chemicals \( (P = 0.08) \) were associated with lower fecundability and close to statistical significance. Age had a small \( P \) (PH, proportional

**Table II. Women’s responses where the male partner was eligible to be recruited \( (n = 47) \)**

<table>
<thead>
<tr>
<th>‘Do you think your partner (husband) would agree to participate in semen quality studies?’</th>
<th>‘Would you agree to pass an invitation to your partner to participate in the study?’</th>
<th>No. of women (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>Yes</td>
<td>12 (25.5)</td>
<td>14–40</td>
</tr>
<tr>
<td>No</td>
<td>No</td>
<td>4 (8.5)</td>
<td>2–20</td>
</tr>
<tr>
<td>No</td>
<td>Yes</td>
<td>10 (21.3)</td>
<td>11–36</td>
</tr>
<tr>
<td>Don’t know</td>
<td>Yes</td>
<td>21 (44.7)</td>
<td>30–60</td>
</tr>
<tr>
<td>Don’t know</td>
<td>No</td>
<td>0 (0)</td>
<td>0–8</td>
</tr>
</tbody>
</table>
Figure 4. Life-table pregnancy rates for 38 women aged <30 years and 47 women aged ≥30 years.

hazards) value (0.03), indicating a violation of the proportional hazards model assumption and that a different type of analysis was required. Inspection of Figure 4 suggests that women <30 years had a higher pregnancy rate than the older women. Both the log rank \((P = 0.36)\) and Peto tests \((P = 0.20)\) were not significant, although there was a significant difference in the first month: 44% of women aged <30 years conceived in cycle 1, compared with only 23% of women aged ≥30 years \((\chi^2 = 4.33, P < 0.04)\). Removal of cycle 1 resulted in superimposable life-table curves for both age groups (log rank \(P = 0.76, n = 57\)), indicating that the pregnancy rates were the same after the first month.

Discussion

The aim of the WHO surveillance study is to establish whether human fertility is changing in different regions of the world. Specifically, cross-sectional studies conducted at 3-year time intervals over a 7-year period aim to determine whether the average TTP is increasing and semen quality decreasing with time. The information in the TTP questionnaire will also be used to assess possible recruitment bias in the male study. The purpose of the present study was to validate the WHO TTP questionnaire and examine potential recruitment bias and other aspects of the feasibility of the proposed study.

The questionnaire was validated by internal and re-test reliability and comparison of gestational ages determined by menstrual dates and ultrasound. Overall, the results from internal and re-test reliability demonstrated consistent and reliable data on TTP from the questionnaire. The re-test study was performed with 20 women as a reasonable proportion of the total pilot study and at least 2 weeks after the initial interview. Longer times would have taken some subjects out of the inclusion criterion of 16–32 weeks gestation. A difference in TTP of 1 cycle was seen in one of 20 women in the re-test study, but the SD of the difference was only 0.22 cycles. The measurement error in a re-test study of 89 women showed a SD of 1 month for TTP obtained by telephone interviews or mailed questionnaires with a re-test interval of 3–5 weeks (Zielhuis et al., 1992).

Other studies have validated retrospective TTP questionnaires with previously obtained prospective data (Baird et al., 1986; Joffe, 1989; Zielhuis et al., 1992; Joffe et al., 1995). The present study however is unique in that it compared TTP obtained from menstrual dates with that from ultrasound-measured gestational age. Only one subject had a significant underestimation of gestation time because of early pregnancy bleeding. This occurrence is rare, and has only a minor impact on the error of TTP (SD 0.01 cycles).

Previous studies have demonstrated that TTP can be reliably obtained retrospectively, even after periods ranging from 2 to >14 years after pregnancy (Joffe, 1989; Baird et al., 1991; Zielhuis et al., 1992; Joffe et al., 1993, 1995). The present study shows that recruiting women who are currently pregnant provides very reproducible results since they can recall with precision the events leading up to the pregnancy, such as the timing of cessation of contraception. Both the internal and retest reliability studies support this contention.

The 90% participation and 95% completion rates obtained in this study suggest that administration of the questionnaire by face-to-face interview maximizes compliance and completeness of data collection. This is in keeping with previous investigations (Zielhuis et al., 1992) where different retrospective TTP approaches were tested (face-to-face interviews, mailed questionnaires, telephone interviews) and showed that face-to-face interviews provided the best data.

Of particular concern for studies of semen quality using volunteers is the likelihood of recruitment bias, specifically subjects participating because of concern about their fertility. An unrecognized and uncorrected recruitment bias in the study would limit generalization of the findings to the whole population. A strategy to assess recruitment bias is to monitor pregnant women and recruit a proportion of their male partners for detailed study. Comparing characteristics of the responders and non-responders would allow the possible effects of recruitment bias to be estimated. In this pilot study, we assessed whether women with a longer TTP were more likely to have their partner participate in the semen study. The TTP for those likely to participate was not significantly different between women who thought their partner would participate, would not participate, or were uncertain if he would participate. Cox regression analysis including known co-variates of pregnancy rate showed no evidence that TTP was related to the likelihood of male participation. However, because it is not possible to obtain a random sample of men for this type of study, recruitment bias remains likely and a larger study may show that the subfertile are over-represented among the volunteers. It is also argued that assessing TTP in women who are currently pregnant will include only those who have higher fecundity, and exclude those who are infertile. This could lead to loss of sensitivity to detect reduced fertility in the population, and would miss entirely a trend of increasing sterility which is not accompanied by a general decline in fecundity. To overcome this in the proposed WHO study, the proportion of currently pregnant women who conceived as a result of treatment and the duration of infertility until treatment commenced, provide indirect measures of such a pattern.

Compliance rates for this study were high (90%). Few
women refused to be interviewed. Approaching women in the hospital antenatal clinic may have contributed to the high compliance rates because they often welcome the distraction while waiting to be seen. The high compliance rate is in keeping with the findings from other retrospective TTP studies (Zielhuis et al., 1992; Joffe et al., 1995). The compliance rate may be further improved by a second approach at a subsequent visit to the clinic for those women who had previously declined to be interviewed because of tiredness.

TTP could be calculated accurately in a high proportion of the volunteers (70%) with planned pregnancies. TTP is difficult to calculate for pregnancies that result from birth control failure or irregular use of contraception. Of note is the relatively high proportion of unplanned continuing pregnancies >16 weeks in this category (19 of 120). The frequency of pregnancies in women with secondary amenorrhoea also requires that they be recorded, and rules devised to include them in the surveillance studies. For example, both birth control failures and pregnancies occurring during amenorrhoea could be regarded as first-cycle pregnancies. Cycle data involving irregular contraceptive use could also be included by appropriate weighting, such as half-cycles (Baird et al., 1991). Infertility treatment was involved in 5% of the pregnancies. TTP for these could be the duration of infertility before an effective treatment commenced. Such approaches would enable the use of TTP data in a high proportion (95%) of the women.

There was a high first-cycle pregnancy rate in women aged <30 years. When contraception failures and pregnancies from rape and during amenorrhoea were also included as first-cycle pregnancies, over 46% of women fell into this category. In the general population it is expected that approximately 20–30% of women will conceive in cycle 1 (Basso et al., 1997). While the high rate in cycle 1 is probably explained by the small sample sizes (n = 85 and 114), it is likely there is an important proportion of highly fertile couples that conceive easily in the general population, and their existence may cause difficulties with standard methods of statistical analysis.

Certain aspects of the feasibility of large-scale surveillance studies remain uncertain. Foremost is funding. While some groups have been funded by National agencies, and WHO plans to fund work in some countries, monitoring changes in fertility is not necessarily a research priority in others. Subject numbers are also of concern. To recruit 300 men for the semen study we have estimated from this pilot study that between 1100 and 2500 women would need to be approached. This is feasible at a large maternity centre. However, if it is intended to recruit 300 partners of women with first pregnancies and obtain data for accurate calculation of TTP from 5000 women with planned pregnancies, it is estimated that up to 11 400 and 8900 women would need to be approached respectively. This would require more centres and staff to be involved. Alternatively, the questionnaire content could be reduced, though at the expense of potentially important exposure information and a reduced chance of developing rapport between researchers and participants that might be crucial for recruiting the male partners. The present study has highlighted the need for strategies to encourage women to at least ask their partners to consider participating in the semen study.

In conclusion, the most significant finding from this study is the high proportion of women who would ask their partners to participate in the semen study. A primary concern of the surveillance studies of male fertility and semen quality is the likelihood of recruitment bias. In this small pilot study, there was no evidence that partners of women with a long TTP would be more likely to participate. However, it is yet to be established that the predicted numbers of subjects actually volunteer and the men are representative of the general population, and the TTP data remain a necessary part of the strategy for checking recruitment bias.

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Appendix I. World Health Organization. Semen quality and time to pregnancy project

Pregnant Women—Interview

(modified for use in an Australian population)

General UR number

1. Family name
2. Given name
3. Date of interview
4. What is your date of birth?
5. Suburb of residence (include postcode)
6. Country of birth
7. City (include postcode)
8. What is the highest level of education (completed) you attained?
   1 Primary school
   2 Secondary school
   3 Vocational/technical
   4 University or higher
9. Ethnic group
   Caucasian
   Asian
   Aboriginal/ Torres Strait Islander
   Other
10. Do you belong to any religion?
    Buddhism
    Judaism
    Christianity
    Other Religions
    Hinduism
    No religion
    Islam
11. Are you married?
    Yes
    No
   (a) If No, do you have a regular partner?
    Yes
    No
12. What were your height and weight before this pregnancy?
    Height (cm)
    Weight (kg)

Contraceptive history

13. Have you ever used the pill for birth control?
    Yes
    No
   (a) If Yes, when did you last take the pill? (month/year)
14. Have you ever used Depo-Provera for birth control?
    Yes
    No
   (a) If Yes, when was your last injection? (month/year)
15. Have you ever used Norplant for birth control?
    Yes
    No
   (a) If Yes, when was your last Norplant removed? (month/year)
16. Have you ever used an IUD for birth control?
    Yes
    No
   (a) If Yes, what is the total length of time you have used an IUD?
   (b) How many IUDs have you had inserted?
   (c) When was your last IUD removed? (month/year)

Pregnancy history

17. Prior to your current pregnancy, were you ever pregnant?
   (Include all pregnancy outcomes, e.g. miscarriage, ectopic, abortion, live or still births)
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Yes No
(a) If No, go to Question 18
(b) If Yes, how many times have you been pregnant? (including this pregnancy)
   *What was the outcome of your previous pregnancies? (in order of occurrence, and the date the pregnancy ended, i.e. date of birth)
   *Which of these pregnancies were with your current partner?
   (c) How many live births have you had?

18. How many weeks are you currently pregnant?
19. What is your estimated date of delivery?
   (a) By date
   (b) By ultrasound

Reference date
20. What was the first day of your LNMP before this pregnancy?
21. Were you using contraception or a method of family planning around the time you became pregnant?
   Yes No
   (a) If No, go to Question 22.
   (b) If Yes, what was the main method of family planning you were using?
      1 Pill (oral contraceptive)
      2 Injection
      3 Implant
      4 IUD
      5 Condom
      6 Diaphragm
      7 Withdrawal
      8 Rhythm
      9 Jelly, cream or foam
      10 Other, specify
   (c) Did you use any additional method?
      Yes No
   (d) If Yes, which method did you use?
   (e) Were you using this (primary) method in a regular and consistent manner around the time of conception?
      Yes No
   (f) If No, when did you start using the method irregularly or inconsistently? (month/year)
22. Did you decide to stop using contraception in order to become pregnant?
   Yes No
23. When did you stop using all forms of contraception, i.e. synthetic (condoms, pill, etc.) or natural (withdrawal, rhythm etc)? (month/year)

Women with a previous pregnancy
(Refers to the last pregnancy only, includes: live birth, miscarriage, termination or other)
24. Have you used a method of contraception or family planning since your last pregnancy?
   Yes No
   (a) If Yes, what method and when did you stop using it? (month/year)
25. Did your menstrual periods start again after your last pregnancy?
   Yes No
(a) If No, go to Question 18
(b) If Yes, when did your periods start again? (month/year)
26. When did you start having sexual intercourse again after your last pregnancy? (month/year)
27. Did your periods start again before you had sexual intercourse?
   Yes No
28. Did you breastfeed your last child?
   Yes No
(a) If Yes, how long was breast milk the child’s only source of food or drink?

All women
Reference date (month/year) = Date of first exposure
29. How many menstrual periods did you have between the <REFERENCE DATE> and this pregnancy?

Health factors
30. How would you describe your menstrual pattern around the time of <REFERENCE DATE>?
   1 Regular
   2 Irregular
   (a) What was your shortest and longest menstrual cycle? (e.g. 21 to 28 day cycle)
31. In <REFERENCE DATE>, were you trying to become pregnant?
   Yes No
32. Do you know when the fertile phase occurs in the menstrual cycle?
   Yes No
   (a) If No, go to Question 33
   (b) If Yes, when does the fertile phase usually occur in your cycle?
      (c) In order to conceive this pregnancy, did you ever time sexual intercourse to coincide with the fertile phase?
         Yes No
33. How often did you have sexual intercourse around <REFERENCE DATE>?
   1 Daily
   2 Every other day
   3 Three times a week
   4 Once a week
   5 Once every 2 weeks
   6 Once a month
   7 Other
34. In <REFERENCE DATE>, was there any month that you did not engage in sexual intercourse? For example, due to shift work, travel or illness.
   Yes No
   (a) If Yes, when did you not engage in sexual intercourse, and for how long?
35. Did you or your partner (husband) seek any medical advice to help you conceive this pregnancy?
   1 No
   2 Yes, my partner (husband) did
   3 Yes, I did
   4 Yes, we both did
   (a) If No, go to Question 36.
   (b) If 2, 3 or 4, when did you first seek help?
(c) Did you or your partner receive any of the following treatments for this pregnancy?
1 ICSI
2 IVF, GIFT
3 Artificial insemination
4 Ovulation induction
5 Other, specify
Yes No
(d) If Yes, specify type of treatment (1, 2, 3, 4 or 5)

Life style, medical and work history
36. In which city/suburb were you living in <REFERENCE DATE>?
   (a) Postcode
   (b) How long did you live there?
37. In <REFERENCE DATE> did you smoke?
   Yes No Never smoked
   (a) If never smoked, go to Question 38
   (b) If No, go to (e)
   (c) If Yes, are you still smoking?
      Yes No
   (d) If Yes, go to Question (g)
   (e) Did you smoke prior to that date?
      Yes No
   (f) If Yes, when did you stop smoking? (month/year)
   (g) What did you smoke?
      1 Cigarettes
      2 Cigars
      3 Pipe tobacco
   (h) How many cigarettes did you smoke per day?
      1–10
      11–20
      Over 20
38. Have you had any major illnesses in the past?
   Yes No
   (a) If Yes, specify
   (b) Were you taking any medication around the time you became pregnant?
      Yes No
   (c) If Yes, what and what for?
   (d) Have you ever had any of the following infections, diseases or operations?
      If ‘Yes’, in which year were you first told?
      1 Pelvic inflammatory disease (e.g. infection in Fallopian tubes or ovaries)
      2 Chlamydia infection
      3 Gonorrhoea
      4 Other sexually transmissible infections
      5 Endometriosis
      6 Ovarian cysts
      7 Fibroma in the uterus (fibroids)
      8 Operations on the uterus, tubes, ovaries or cervix
      9 Cervical dysplasia (i.e. abnormal cells, CIN 1, CIN 11, CIN 111)
      10 Thyroid disease
      11 Appendicitis
      12 Diabetes/gestational diabetes
      13 Chemotherapy or radiation therapy for cancer
      14 Other chronic illnesses (specify)
      (a) Postcode
      (b) How long did you live there?
      (c) Did you or your partner receive any of the following treatments for this pregnancy?
      1 ICSI
      2 IVF, GIFT
      3 Artificial insemination
      4 Ovulation induction
      5 Other, specify
      Yes No
      (d) If Yes, specify type of treatment (1, 2, 3, 4 or 5)
      (e) Did you smoke prior to that date?
      Yes No
      (f) If Yes, when did you stop smoking? (month/year)
      (g) What did you smoke?
      1 Cigarettes
      2 Cigars
      3 Pipe tobacco
      (h) How many cigarettes did you smoke per day?
      1–10
      11–20
      Over 20
      (i) If Yes, in which year were you first told?
      (j) Did you have a paid job in <REFERENCE DATE>?
      Yes No
      (a) If No, go to Question 42
      (b) If Yes, in what kind of industry or business were you working?
      (c) What was your job title?
      (d) What kind of work did you do?
      (e) Did you have an unpaid job in <REFERENCE DATE>?
      Yes No
      (a) If No, go to Question 43
      (b) If Yes, what kind of unpaid work did you have?
      (c) During the <REFERENCE DATE> were you involved in any activity in which you were exposed to chemicals such as pesticides, herbicides, paint thinners, photographic chemicals, etc.
      Yes No
      (a) If Yes, please specify.

Infant’s father
44. What is the date of birth of the infant’s father?
45. Was his mother born in Australia?
   Yes No Don’t know
46. Where was he born?
   (a) Country
   (b) City
47. What is the highest level of education (completed) he attained?
   Primary school
   Secondary school
   Vocational/technical
   University or higher
48. Did he have a paid job in <REFERENCE DATE>?
   Yes No
   (a) If No, go to Question 49
   (b) If Yes, in what kind of industry or business did he work?
   (c) What was his job title?
   (d) What kind of work did he do?
49. Did he have an unpaid job in <REFERENCE DATE>?
   Yes No
   (a) If No, go to Question 50
   (b) If Yes, what kind of unpaid work did he have?
50. During the <REFERENCE DATE> was he involved in any activity which exposed him to chemicals such as pesticides, herbicides, paint thinners, photographic chemicals, etc.
   Yes   No
   (a) If Yes, please specify.

Screening eligibility check list
51. Was his mother born in Australia?
   Yes   No
52. Was he born in Australia?
   Yes   No
53. Does he live in Victoria?
   Yes   No
54. Is he aged between 18 and 50?
   Yes   No

55. Has either partner had any infertility treatment for this pregnancy?
   Yes   No
   If ‘Yes’ to Questions 51–54 and ‘No’ to Question 55, the male partner is eligible for the semen study

Invitation for eligible participants
56. Do you think your partner (husband) would agree to participate in semen quality studies?
   Yes   No   Don’t know
   (a) If No, give reason why:
57. Would you agree to pass an invitation to your partner to participate in the study?
   Yes   No

\textbf{Feasibility of surveillance of human fertility}