Cumulative incidence rate of medical consultation for fecundity problems–analysis of a prevalent cohort using competing risks.

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Abstract

Study question

Incidence of medical consultation for fecundity problems in the French population, taking into account pregnancy occurrence and resumption of contraceptive use.

Summary answer

Considering the occurrence of a pregnancy and resumption of use of contraception as competing risks, the cumulative incidence rate of medical consultation for fecundity problems was 9.0% [6.5% - 11.9%] after 12 months of unprotected intercourse and 12.2% [9.6% - 15.3%] after 24 months.

What is known already

Estimates of the prevalence of medical consultation due to involuntary infertility among couples who have sought a pregnancy for more than 12 months range 25%-50%. Most of the studies however are limited by retrospective data collection, without considering the duration of the period since the beginning of the period of unprotected intercourse (PUI) and without considering medical consultation for fecundity problems as a competing risk.

Study design

This study is based on the OBSEFF survey (Observatory of Fecundity in France), a population-based probability survey designed to estimate the frequency of involuntary infertility on a nation-wide basis and to explore the associations with environmental factors. The current analysis was performed among a subsample of 6,577 women recruited before or during a period of unprotected intercourse and followed-up for one year.

Participants/materials, setting, methods

The study sample comprised 940 women who had a PUI between the time of enrolment and the one-year follow-up, and who had not consulted a physician for fecundity problems for the current PUI prior to enrolment.

Women reported all the medical consultations they had because of difficulties becoming pregnant during the current PUI. The date of each consultation was carefully assessed. In France, women can consult a gynaecologist directly without referral by their general practitioner.

The occurrence of a pregnancy and resumption of contraceptive use were considered as informative censoring events, using a competing risk model.

Main results and the role of chance

Using the competing risk survival model, the cumulative incidence rate of first consultation was 9.0% [95% CI: 6.5% - 11.9%] 12 months after the start of the PUI and 12.2% [95% CI: 9.6% - 15.3%] after 24 months. The Kaplan-Meier method, which does not take competing

risks into account, yielded substantially higher estimates: 26.0% [95% CI: 18.8% - 32.5%] at 12 months and 56.8% [95% CI: 44.2% - 66.6%] at 24 months.

Among the 219 women who had attempted to become pregnant for at least 12 months, cumulative incidences of first medical consultations were 28.2% [95% CI: 18.7% - 38.9%] 24 months after the start of the PUI, and 31.2% [95% CI: 21.3% - 42.4%] after 36 months.

The rates were higher among nulliparous but non nulligravid women, followed by nulligravid women, as compared with parous women. Age was not strongly related to the occurrence of medical consultation.

Limitations, reasons for caution

The main limitation of this study is the number of women lost to follow-up (29.7%). Although such an attrition rate is commonly observed in prospective studies in the general population, it could have induced a selection bias that may have led to an underestimation of the rates of medical consultation. Sensitivity analyses, using the inverse probability weighting method suggest that our results are unlikely to be biased.

Wider implications of the findings

This study reveals frequencies of medical consultation for fertility problems (about 9 and 12% after 12 and 24 months), which, after considering competing events such as pregnancy in a relevant statistical model, turn out to be lower than generally reported in the literature. Results also suggest that other factors than medical recommendations may play a role in the patterns of medical seeking behaviours for fecundity problems such as women's reproductive history, socio-economic characteristics or accessibility to infertility services.

Study funding/competing interest(s)

The study was funded by grants from ANR (French Agency for Research, SEST call on Environmental and Occupational Health), ANSES (French Agency for Food, environmental and Occupational Health Safety, EST call on Environmental and Occupational Health), InVS (French Institute for Public Health Surveillance). The team of Environmental Epidemiology applied to Fecundity and Reproduction has been funded by an AVENIR grant from Inserm (2007).

KEYWORDS

Infertility; Consultation; Competing risk; Studies, Incidence; Prevalent Cohort Study

INTRODUCTION

Involuntary infertility affects about 10% of couples worldwide, which represents, according to WHO, 60 to 80 million people (WHO, 2002). All studies evidence a discrepancy between the potential need for medical services for infertility and the use of these services (Boivin, et al., 2007). However, the extent of this discrepancy varies widely between studies, due to differences in the way involuntary infertility (12 months infertility, current infertility, lifetime infertility…) and medical care for infertility are defined and assessed, including study design, study populations and statistical methods (Schmidt and Munster, 1995). Thus, the range in the prevalence of medical consultation due to involuntary infertility among couples who have sought a pregnancy for more than 12 months varies from 25% in the United States (Chandra and Stephen, 2010) to almost 50% according to a Danish study (Schmidt, et al., 1995). In their recent review, Boivin and colleagues estimated that more than half of infertile couples (56% [42% -76%]) seek medical help for infertility in developed countries (Boivin, et al., 2007). In most of the studies however, data were collected retrospectively, which entails several limitations in terms of recall bias and outcome definition. In particular, women were asked about having consulted a doctor for fecundity problems during any of all their past pregnancy attempts. Thus, the occurrence of a medical consultation for infertility was not related to a specific pregnancy attempt. Moreover the timing of the consultation (time elapsed since the beginning of the period of unprotected intercourse) was not considered, although it is a crucial determinant of infertility consultation. Indeed, from a methodological point of view, the occurrence of a medical consultation should be seen as a survival event just like time to pregnancy is taken into account in studies on a couple's fecundity (Scheike and Keiding, 2006). To our knowledge, only one population-based study, conducted in two rural regions in France, used survival analysis to explore medical consultation for fecundity problems: 30% of infertile couples had sought medical care for infertility after 12 months of pregnancy attempt and 64% after 3 years (Moreau, et al., 2010). However, by using Kaplan-Meier life table probabilities, the authors considered that pregnancies occurring before a medical consultation for fecundity problems acted as non informative censoring rather than as a competing risk, yielding an estimation of the probability of medical consultation for fecundity problems in a population where pregnancies does not occur, which is an unrealistic situation.

In the present study, we explore the incidence of reported medical consultation for fecundity problems for a given period of unprotected intercourse (PUI) in a representative cohort of women selected from the general population. The occurrence of a pregnancy was considered as an informative censoring event, using competing risks models.

POPULATION AND METHODS

Study population

This study is based on the OBSEFF survey (Observatory of Fecundity in France), a population-based probability survey designed to estimate the frequency of involuntary infertility on a nation-wide basis and to explore the associations between environmental factors and fecundity. The study received the approval of the relevant French government oversight agency (CNIL, the Commission Nationale de l'Informatique et des Libertés).

The methodology of the recruitment steps of this study has been published elsewhere (Slama, et al., 2006, Slama, et al., 2012). The OBSEFF survey is a two-stage probability sample of 15,810 women aged 18-44 years living in metropolitan France, who were not identified as sterile. A sample of households was selected in 2007 using random digit dialing and one woman aged 18-44 years per household was randomly selected to participate. In this study, a woman was considered as being at risk of a pregnancy if she had a male partner and had unprotected intercourse. Some of these women declared that they were actively seeking to become pregnant, but others did not. The current analysis was performed among a subsample of 6,577 women who had to be contacted one year after enrolment in the study: 936 women who had a PUI at the time of enrolment and a random sample of 5,641 women selected among those who were not having unprotected intercourse at that time. This corresponds to a prevalent cohort design (Keiding, 2006) because some women were recruited during and not at the start of the PUI. Among the 6,577 women, a registered phone contact was available in the database for 5,003 women of whom 3,515 responded to the one-year follow-up interview and 1,488 women were lost to follow-up one year after enrolment. This is mostly due to the fact that these women were never reached, as only 160 openly refused to participate in the follow-up study. Women lost to follow-up were older (36 % were 35 years old or more *versus* 27% among women who completed the follow-up interview). In addition, they were less likely to have ever been pregnant (39% were nulligravid, *versus* 32% of women in the follow-up group).

As the focus of this study was to explore medical consultation for fecundity problems, the analysis was restricted to the 1,184 women who reported that they had unprotected intercourse between the time of enrolment and the one year follow-up interview. Two hundred and forty four of these women had consulted a physician or received a treatment for fecundity problems in the course of the current PUI, prior to the date of enrolment in the study. Since they had already experienced the event of interest before the period of observation, these women were excluded from the analysis. Consequently, our study sample comprised 940 women who had unprotected intercourse between the time of enrolment and

the one-year follow-up, and who had not consulted a physician for fecundity problems for the current pregnancy attempt prior to enrolment (Figure 1).

Questionnaires

Women answered two telephone questionnaires, the first at the time of enrolment in 2007, the second at follow-up one year later. They were asked about their sociodemographic characteristics, their medical history and occupational exposures. They were also asked about their partner's socio-demographic characteristics. Women described all past pregnancies (outcome, date of start and end) and reported all consultations or treatments for fecundity problems in the past. The beginning of the current PUI was identified as the date when the woman or her partner discontinued use of contraception (n=895); if the couple had not used contraception before the PUI, the starting date was the date of end of the last pregnancy (n=33). For 12 women for whom this information was missing, we reconstructed the starting date of the PUI by using proximate data.

Answering to detailed standardized questions, women reported all the medical consultations they had had because of difficulties becoming pregnant during the current PUI. They were asked: "Since the beginning of the current period of unprotected intercourse have you, yourself or your partner, consulted a physician because you thought you had difficulties becoming pregnant?" If they reported that they were not actively seeking to become pregnant, the question was rephrased as "Since you stopped using (name of the contraceptive method) / Since the end of your last pregnancy: have you, yourself or your partner, consulted a physician because you thought you had difficulties becoming pregnant?" The timing and date of each consultation was carefully assessed in order to estimate the time elapsed since the beginning of the PUI and to verify the timing of the consultation relative to the date of enrolment. It should be noticed that, in France, women can consult a gynaecologist directly without referral by their general practitioner (GP).

MAIN OUTCOME AND STATISTICAL ANALYSIS

Time to medical consultation for fecundity problems was defined as the number of months elapsed between the beginning of the PUI and the occurrence of a consultation for fecundity problems.

A total of 404 women in the study sample had started their PUI before study enrolment, but we only considered the medical consultations for fecundity problems that occurred after the study enrolment. It was thus mandatory to use a survival model with delayed entry (Keiding, 2005, Keiding, et al., 1987) to study the cumulative incidence rate of first medical consultation for fecundity problems. Moreover, the probability of consulting a physician for fecundity problems once a pregnancy has occurred becomes null, which implies that pregnancy is to be considered as an informative censorship. Similarly, for those women who

reported that they had resumed using contraception and thereby given up trying to become pregnant, the probability of consulting for fecundity problems also becomes null, so that this event also has to be considered as informative censorship. We therefore used a competing risk model to estimate the cumulative rates of first consultation for fecundity problems (Aalen, 1976). However, in order to compare our results with those of previous studies, in particular those of the previous French study using survival analysis (Moreau, et al., 2010), we also estimated the cumulative rates using Kaplan-Meier analysis in which pregnancy and resumption of contraception are considered as non-informative censoring events.

Because most studies have only included infertile women (often defined as women who had not succeeded in becoming pregnant within the first 12 months of unprotected intercourse (Evers, 2002, Gnoth, et al., 2005, Zegers-Hochschild, et al., 2009)), we also carried out the analysis among the subsample of women who had attempted a pregnancy for at least 12 months.

Finally, we examined cumulative probabilities of consultation for fecundity troubles according to women's age and parity/gestity status, since these factors have previously been shown to influence women's decision to seek medical treatment for fecundity troubles (Moreau, et al., 2010).

All analyses were weighted to take into account the sampling design of the OBSEFF study. In particular, the weighting factors depended on the recruitment area and the number of women aged 18 – 44 years in the household (Slama, et al., 2006). Analyses were conducted using the R package msSurv (Ferguson, et al., 2012) modified by us to account for the weighted sampling design. We used standard Greenwood confidence intervals for the Kaplan-Meier estimates (based on the log-transform and modified to take account of the design weights) and bootstrap confidence intervals for the cumulative incidences, based on 1000 samples with replacement.

Sensitivity analyses were performed using the inverse probability weighting (IPW) method (Groves, et al., 2002, Seaman and White, 2011) to study the potential effect of lost to follow-up on the different estimates. Weights accounting for missing data (women loss to follow up) were calculated according to women's age, parity and educational level, and combined with initial sampling weights. The analyses were re-run with these new weights.

RESULTS

Study population

Women's age at the time of enrolment varied from 18 to 45 years, with a mean age of 31 years; 50% of women had started their pregnancy attempt before the age of 30. Almost half had finished or dropped out of education before 21 years of age and 26 % before the age of 18. More than 60 % had children while 5% were nulliparous but non-nulligravid (they had

been pregnant before but had not given birth to a child) and 31 % were nulligravid. A majority (70%) reported that they were actively seeking to become pregnant at enrolment; the remaining women (30%) reported that they were not actively seeking a pregnancy but were sexually active and were not using any form of contraception (Table I).

Incidence of medical consultation

Between the date of enrolment and the one-year follow-up interview, 104 women reported a first medical consultation for fecundity problems, 533 became pregnant and 60 resumed contraception. Using the competing risk survival model, the cumulative incidence rate of first consultation was 9.0% [6.5% - 11.9%] 12 months after the start of the PUI and 12.2% [9.6% - 15.3%] after 24 months (figure 2a). The Kaplan-Meier method yielded substantially higher estimates: 26.0% [18.8% - 32.5%] at 12 months and 56.8% [44.2% - 66.6%] at 24 months (figure 2b). After restricting to women who were actively seeking to become pregnant (n=696), we obtained similar results (data not shown).

Among the 219 women who had attempted to become pregnant for at least 12 months, 49 became pregnant, 27 resumed contraception and 37 had a first medical visit for fecundity problems during the second year of the PUI. Cumulative incidences of first medical consultations were 28.2% 24 months after the start of the PUI (95% CI [18.7% - 38.9%]), and 31.2% [21.3% - 42.4%] after 36 months (figure 3a). Using the Kaplan-Meier approach, the corresponding figures were 42.3% [26.7% - 54.6%] at the end of the second year of the PUI and 53.5% [34.5% - 66.9%] by the end of the third year (figure 3b).

The cumulative probability of consultation during the first year was 11% among women less than 30 years at the start of the PUI, 5% among women aged 30 to 34 years and 11 % among women 35 years or older (n= 219). These figures increased respectively to 16%, 6% and 16% after 2 years of unsuccessful PUI (figure 4.a).

Concerning woman's parity and gestity status, 6.0% of parous women, 15.0% of nulligravid and 20.0% of nulliparous but non nulligravid women consulted a physician for the first time during the first year of the PUI. Those percentages rose respectively to 8.0%, 21.0% and 25.0% at the end of the second year of the PUI (figure 4b).

Among women who consulted a physician for fecundity problems, almost two thirds (63.3% [51.6 – 73.6]) consulted their regular physician: 84.9% [72.1 – 92.4] of them first consulted their gynaecologist and 15.0 % [7.6 – 27.8] first consulted their GP.

In the sensitivity analyses, using the IPW method, the estimates remained similar (less than 1% point differences in all cumulative rates of the first medical consultation when compared with the reported results).

DISCUSSION

Using a competing risk survival model, we estimated that about 9.0 % of women in France consult for fecundity troubles by the end of the first year of unprotected intercourse and 12.0% within the first 2 years. Those rates were 2.5 times as high among women who had been pregnant before but who never gave birth than among parous women. Conversely, age was not an important determinant of medical consultation in this study.

Our estimates are markedly lower than those of earlier studies, in which probabilities of medical consultation for fecundity problems varied from 25% (Chandra and Stephen, 2010) to more than 50% (Boivin, et al., 2007, Schmidt, et al., 1995), with an average of 56 % of infertile women seeking medical advice in industrialized countries (Boivin, et al., 2007). Several methodological issues may explain these differences: the first relates to the definition of the study population; the second to study design; and the last to the statistical models used.

We estimated the cumulative incidence of first medical consultation for fecundity problems among all women rather than among those who are usually defined as being infertile (often referred to as women who have had at least 12 months of unsuccessful PUI). Indeed our interest was to explore the timing of medical care seeking for perceived fecundity problems including early medical consultations in the general population rather than focusing only on couples who already experienced at least 12-month involuntarily infertility. As a result, our denominator was greater than that used in studies restricted to involuntarily infertile couples, decreasing rates compared with prior publications (Chandra and Stephen, 2010). Nevertheless, when we restricted the analysis to involuntarily infertile couples, our estimates remained lower than those of some previous studies (Schmidt, et al., 1995). The inclusion of all couples at risk rather than a restriction to couples seeking to conceive also possibly entailed lower estimates of medical consultation, although the differences in estimates are small.

Data on medical consultations were collected with a prospective design, and each event was dated. Thus, unlike prior cross-sectional surveys for which the timing of the consultation was not available or collected retrospectively with possible recall bias, we were able to identify and select consultations relative to the current PUI. Recall bias do not only relate to errors on the existence or timing of fertility treatment, but also on the existence of the period of unprotected intercourse, which might be under-reported in studies in which recruitment takes place after the PUI, in particular if the PUI was not followed by a live birth. Our design limited possible misclassifications associated with the use of information not specific to a given PUI, such as “ever having consulted for fecundity troubles” among women who ever had infertility troubles or who had ever been pregnant.

The reconstruction of the chronology of events enabled us to use survival models to assess not only the frequency but also the timing of medical consultation, using the same approach as in the French study conducted in Normandy and Brittany (Moreau, et al., 2010). However in the Normandy-Brittany study, pregnancy was considered as a non-informative censoring event, which conceptually implies that one aims to estimate the rate of medical consultation under the assumption that pregnancies never occur, which is an unrealistic situation. In the present study, we sought to address this methodological issue by using competing risk models (Aalen, 1976). Our results illustrate that the way pregnancies and resumption of contraceptive use are considered in the analysis as informative or non-informative censoring generates substantial differences in estimates of incidence rates of medical consultation. In a different but related problem (analysing waiting time from first consultation for fecundity troubles until occurrence of 'natural pregnancy' with start of assisted reproduction treatment (ART) as competing event), Van Geloven et al (Van Geloven, et al.) also found much higher estimates from the Kaplan-Meier estimator derived from an unrealistic assumption of independent censoring (in their case: by ART) than from the appropriate cumulative risk model. It is well-known that the higher the probability of pregnancy, the larger the gap between Kaplan Meier and competing risk model estimates (Alberti, et al., 2003). Consistently, the difference in estimates was much smaller among the subgroup of couples with a PUI of 12 months or more, who reported fewer pregnancies during the follow-up period (figure 3).

The low rate of consultation observed in this study suggests the existence of a difference between the potential need (assessed by the involuntary infertility rate) and the actual use of medical care for fecundity problems (assessed by the cumulative incidence rate of medical consultation for fecundity problems). In the OBSEFF study, the estimated involuntary infertility rate was 24% [19 – 30%] within 12 months of PUI (Slama, et al., 2012) while the cumulative incidence rate of medical consultations for fecundity problems was 9.0 % [6.5 – 11.9] within 12 months of PUI. The gap between these 2 percentages (calculated among the same sample of women) is thus consistent with the literature (Boivin, et al., 2007, Chandra and Stephen, 2010). This calls for more research to explore whether barriers to medical care may exist and explain the discrepancy observed. As found in previous studies, our results suggest that parous women are less likely to seek medical care than others (Chandra and Stephen, 2010, Farley Ordovensky Staniec and Webb, 2007, Moreau, et al., 2010, Schmidt, et al., 1995). However, our results show that women who had a history of unsuccessful pregnancies were more likely to consult than women who had never been pregnant (nulligravid women). Prospective data allow accurately describing the sequence of reproductive events relative to the outcome of interest (in this case medical consultation for fecundity troubles): this may enable to capture more efficiently the influence of past

reproductive histories on subsequent medical care seeking behaviours. Unlike previous studies conducted in the USA (Bunting and Boivin, 2007, Chandra and Stephen, 2010), our results show no obvious relationship between woman's age and medical consultation. This result should be taken with caution as few women of our study sample were aged over 35. Moreover, our study population included all women at risk rather than only infertile women, which may account for the difference observed with the US National Survey of Family Growth (NSFG) data (Chandra and Stephen, 2010, Stephen and Chandra, 2000). In any case, further analysis of factors associated with medical consultation, including partner characteristics, among all women at risk of conceiving are warranted to better understand couple's motivations, socio-economic and structural barriers to access medical services for infertility. In particular, geographical disparities in access to specialized healthcare services should be explored in future studies (Bhattacharya, et al., 2009, Bunting and Boivin, 2007, Chandra and Stephen, 2010, Farley Ordovensky Staniec and Webb, 2007, Moreau, et al., 2010, Stephen and Chandra, 2000).

We had expected incidence of consultations to increase more rapidly after 12 months and/or after 24 months of unsuccessful unprotected intercourse, under media influence or according to GP's advice (National Collaborating Centre for Women's and Children's Health, 2003) . Although there are no official medical recommendations in France, these key thresholds serve as a medical criteria for the diagnosis of infertility and are used by doctors to inform their patients about future options for treatment (Belaish-Allart, 2009, ESHRE, 2008). These time-frames are also often mentioned in articles on infertility published in magazines or posted on generalist websites (WebMD, 2011). However, our data are rather compatible with a continuous and regular increase in the incidence of first consultation with no surge at 12 and 24 months, even after controlling for woman's age.

The main limitation of this study is the number of women lost to follow-up estimated to be 29.7%. However, such proportions of individuals lost to follow-up are commonly observed in prospective studies in the general population (Razafindratsima, 2004). High rates of loss to follow-up reduce sample sizes, thus limiting the statistical power and precision of the analysis. A second problem lies in the potential for selection bias, which would occur if women lost to follow-up had different patterns of use of medical services for fecundity problems then others. Women who were lost to follow-up in this study were less likely to have ever been pregnant and were significantly older than women included in the analysis. Our results, as well as those of previous studies, have shown that nulliparous women (Chandra and Stephen, 2010, Moreau, et al., 2010, Schmidt, et al., 1995) are more likely to seek medical help for fecundity problems. As discussed above, while our results show no effect of age, other research reports higher probabilities of medical consultation for infertility among older women (Chandra and Stephen). Thus, our consultation rates may be

underestimated. However, when using the same statistical model (Kaplan Meier life table probabilities), our results were similar to those published in the population-based study in Normandy-Brittany in France (cross-sectional study collecting retrospective data) (Moreau, et al., 2010). Finally, the estimates obtained with the IPW method were similar to the results presented and discussed in this manuscript, which suggests that our results are unlikely to be biased by loss to follow-up.

CONCLUSION

Based on a national prospective cohort of couples who reported having unprotected intercourse, and using competing risk modelling, this study reveals frequencies of medical consultation for fecundity troubles of about 9 and 12% after 12 and 24 months of unprotected intercourse respectively. These rates are lower than generally reported in the literature. Results also suggest that the timing of consultation shows no obvious increase in the incidence of consultations just after 1 or 2 years of unprotected intercourse, and that the probability of medical consultation is influenced by the parity/gestity status of women. Thus, other factors than medical recommendations may play a role in the patterns of medical seeking behaviors for fecundity problems such as women's reproductive history, socio-economic characteristics or accessibility to infertility services. Beyond medical consultation, the frequency, timing and determinants of treatment initiation are important indicators to consider while assessing the overall patterns of medical care for fecundity troubles in the general population.

AUTHOR'S ROLES

Duron S.: analysis and interpretation of data, draft of the article
Slama R.: conception and design, acquisition of data, revision of the article
Ducot B.: conception and design, acquisition of data, revision of the article
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Bouyer J.: conception and design, analysis and interpretation of data, acquisition of data, revision of the article

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

ETHICAL APPROVAL

The study received the approval of the relevant French government oversight agency (the Commission Nationale de l'Informatique et des Libertés).

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TABLE I: CHARACTERISTICS OF THE STUDY POPULATION (N=940 WOMEN).

	n	weighted %
Age at inclusion (years)		
18-29	433	49 %
30-34	288	31 %
35 or more	219	20 %
Age at the beginning of the pregnancy attempt		
18-29 years	443	50 %
30-34 years	313	34 %
35 years or more	184	16 %
Age when stopped school/university		
18 or less	110	26 %
19-20	166	23 %
21-25	541	46 %
More than 25	105	5 %
Missing	18	
Lives with partner at the time of inclusion		
No	33	7 %
Yes	907	93 %
Actively seeking to become pregnant during the follow-up		
No	244	30 %
Yes	691	70 %
Missing	5	
Parity/gestity at the time of inclusion		
Nulligravid	307	31 %
Nulliparous but non nulligravid	62	5 %
Parous	570	64 %
Missing	1	
History of infertility treatment before the start of pregnancy attempt		
No	896	96 %
Yes	44	4 %

FIGURE 1: FLOW CHART FOR STUDY OF THE CUMULATIVE INCIDENCE RATE OF MEDICAL CONSULTATION FOR FECUNDITY PROBLEMS.

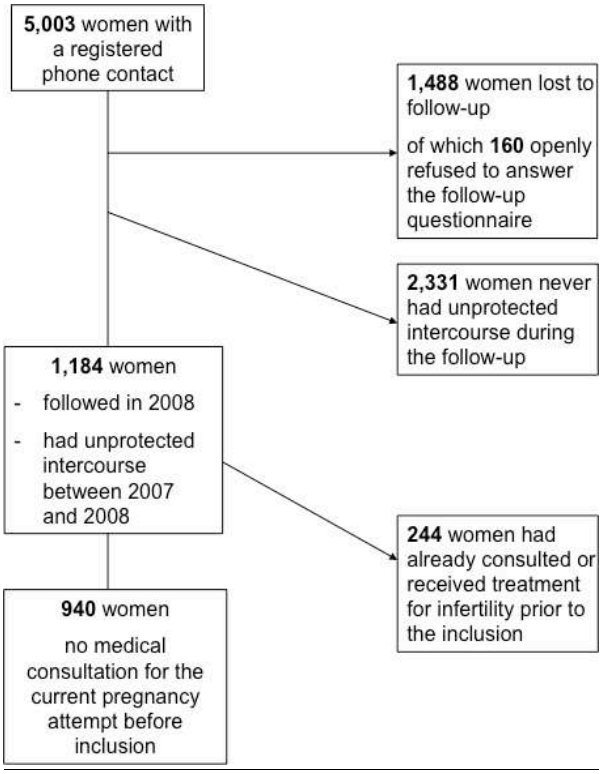
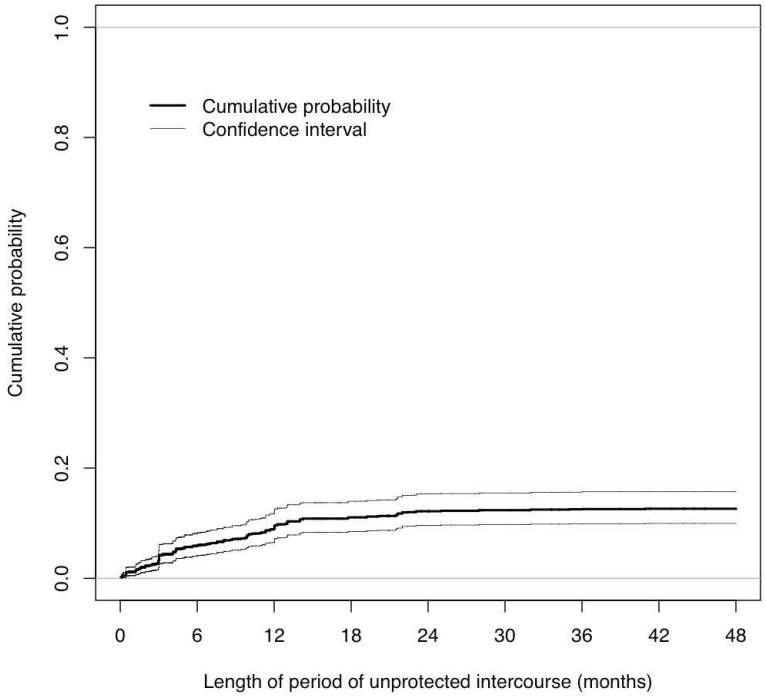


FIGURE 2: FIRST MEDICAL CONSULTATION FOR FERTILITY TROUBLES AS A FUNCTION OF THE DURATION OF PUI (940 COUPLES)

A. CUMULATIVE INCIDENCE FUNCTION OBTAINED WITH A COMPETING RISKS MODEL



B. CUMULATIVE PROBABILITIES ESTIMATED BY A KAPLAN-MEIER APPROACH.

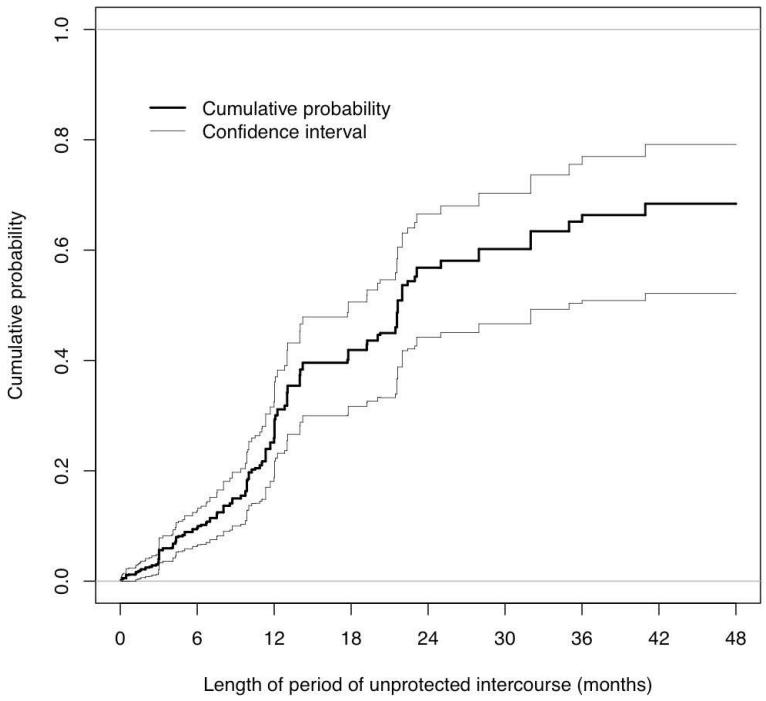
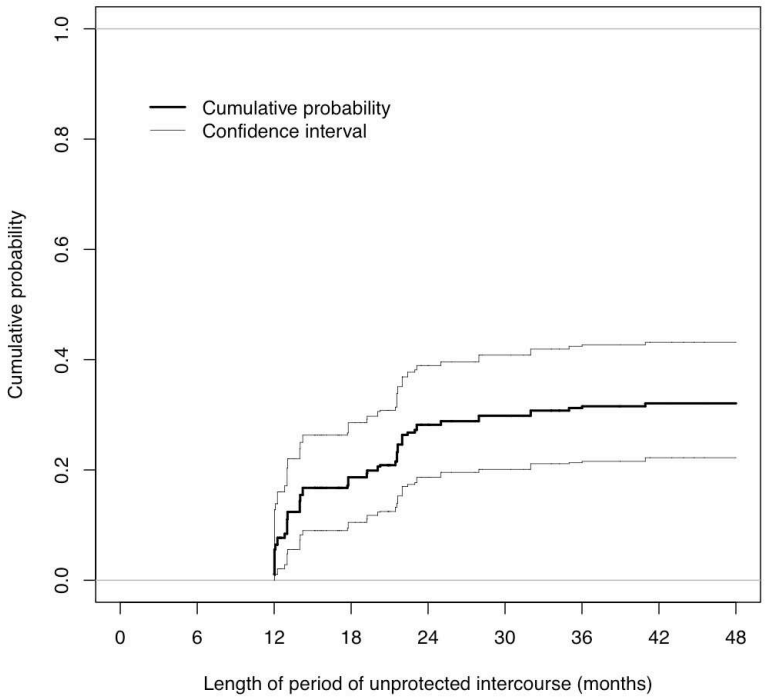


FIGURE 3: FIRST MEDICAL CONSULTATION FOR FERTILITY TROUBLES AS A FUNCTION OF THE DURATION OF PREGNANCY ATTEMPT AMONG WOMEN WHO HAD A PUI OF AT LEAST 12 MONTHS (219 COUPLES)

A. CUMULATIVE INCIDENCE FUNCTION OBTAINED WITH A COMPETING RISKS MODEL



B. CUMULATIVE PROBABILITIES ESTIMATED BY A KAPLAN-MEIER APPROACH.

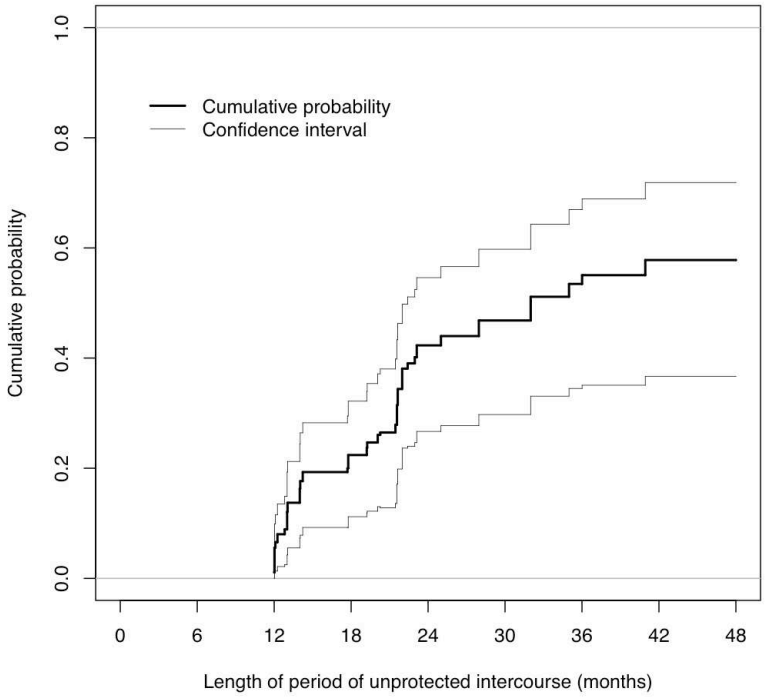
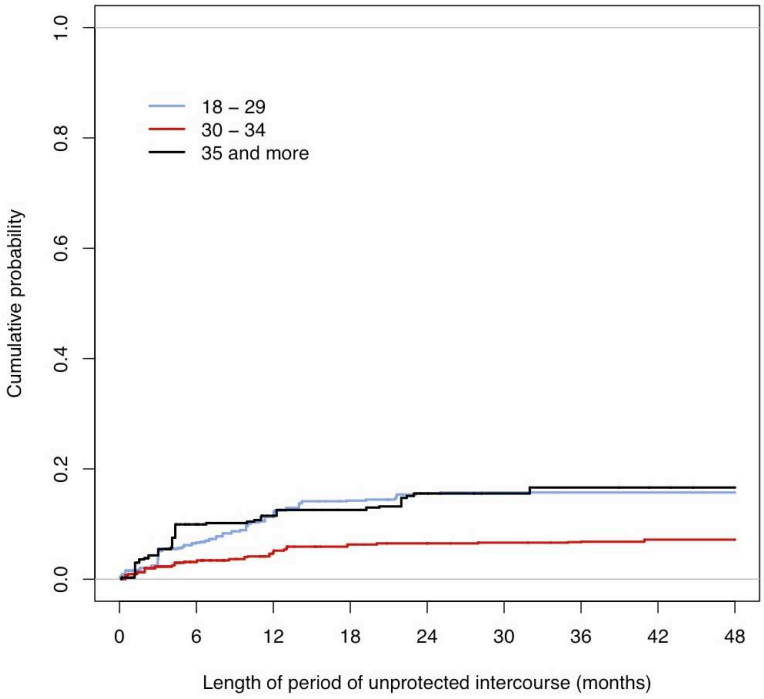


FIGURE 4: FIRST MEDICAL CONSULTATION FOR FERTILITY TROUBLES AS A FUNCTION OF THE DURATION OF THE PUI ACCORDING TO WOMAN'S CHARACTERISTICS (OBTAINED WITH A COMPETING RISK MODEL)

A. CUMULATIVE INCIDENCE FUNCTION ACCORDING TO WOMAN'S AGE AT THE BEGINNING OF PUI



B. CUMULATIVE INCIDENCE FUNCTION ACCORDING TO WOMAN'S PARITY/GESTITY STATUS.