**Human Reproduction, Vol.35, No.9, pp. 2107–2112, 2020**
Advance Access Publication on August 5, 2020 doi:10.1093/humrep/deaa156

human reproduction

**ORIGINAL ARTICLE** ***Reproductive epidemiology***

# Peri-implantation intercourse does not lower fecundability

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*Submitted on February 1, 2017; resubmitted on May 29, 2020; editorial decision on June 4, 2020*

**STUDY QUESTION:** Does sexual intercourse in the implantation time window (5–9 days after ovulation) reduce fecundability?

**SUMMARY ANSWER:** After adjustment for intercourse in the fecund window and clustering by couple, there was no association between intercourse in the implantation time window and fecundity.

**WHAT IS KNOWN ALREADY:** Previous research has suggested an association between intercourse in the peri-implantation time window (5–9 days after estimated ovulation) and reduced fecundability.

**STUDY DESIGN, SIZE, DURATION:** We used data from the FERTILI study, a prospective observational study conducted in five European countries, with data collected from 1992 to 1996.

**PARTICIPANTS/MATERIALS, SETTING, METHODS:** Women who were experienced in fertility awareness tracking kept a daily diary of cervical mucus observations, basal body temperature measurements, coitus and clinically identified pregnancy. We estimated the day of ovulation as cycle length minus 13 days. From 661 women, 2606 cycles had intercourse during the fecund window (from 5 days before to 3 days after the estimated day of ovulation), resulting in 418 pregnancies (conception cycles). An established Bayesian fecundability model was used to estimate the fecundability ratio (FR) of peri-implantation intercourse on fecundability, while adjusting for each partner's age, prior pregnancy, the couple's probability of conception and intercourse pattern(s). We conducted sensitivity analyses estimating ovulation as cycle length minus 12 days, or alternatively, as the peak day of estrogenic cervical mucus.

**MAIN RESULTS AND THE ROLE OF CHANCE:** There was no effect of peri-implantation intercourse on fecundability: adjusted FR for three or more acts of peri-implantation intercourse versus none: 1.00, 95% credible interval: 0.76–1.13. Results were essentially the same with sensitivity analyses. There was an inverse relationship between frequency of intercourse in the fecund window and intercourse in the peri-implantation window.

**LIMITATIONS, REASONS FOR CAUTION:** Women with known subfertility were excluded from this study. Many couples in the study were avoiding pregnancy during much of the study, so 61% of otherwise eligible cycles in the database were not at meaningful risk of pregnancy and did not contribute to the analysis. Some couples may not have recorded all intercourse.

**WIDER IMPLICATIONS OF THE FINDINGS:** We believe the current balance of evidence does not support a recommendation for avoiding intercourse in the peri-implantation period among couples trying to conceive.

**STUDY FUNDING/COMPETING INTEREST(S):** No external funding. The authors have no potential competing interests.

**TRIAL REGISTRATION NUMBER:** N/A.

**Key words:** fecundability / time to pregnancy / conception / day-specific probabilities of conception / fertile window / fecund window / sexual intercourse

# Introduction

Fecundability is the probability of a clinical pregnancy occurring in a given menstrual cycle. It is a function of reproductive biology (the potential of the couple to produce offspring) and intercourse in the fecund window (the days prior to and the day of ovulation during which conception is possible) (Barrett and Marshall, 1969; Wilcox *et al.*, 1995; Colombo and Masarotto, 2000). A variety of characteristics of women and men are related to fecundability including age, prior pregnancies and history of menstrual irregularities (Wood, 1994). Understanding the determinants of fecundability is of interest to clinicians in the field of reproductive health, and to couples who are attempting to conceive (Stanford, 2015).

Implantation is a pivotal moment in the establishment of clinical pregnancy. Implantation is recognized to occur in humans approximately 5–9 days after ovulation (Wilcox *et al.*, 1999). This time period is called the peri-implantation window. Exposures that impact the endometrial and intrauterine environment during this time frame could reduce the probability of implantation through various mechanisms, including induction of myometrial contractions, or changes in immune or inflammatory processes of endometrial maturation during the luteal phase (Fox *et al.*, 1970; Fanchin *et al.*, 1998; Shafik et al., 2005).

In a prospective cohort study, Steiner *et al* (2014) studied 564 women without infertility between 30 and 44 years of age who were seeking pregnancy. They found that two or more days of sexual intercourse during the peri-implantation window was associated with lower incidence of clinical pregnancy, when compared with 0 days: fecundability ratio (FR) of 0.62; 95% credible interval, 0.42–0.91. The authors suggested that orgasm induced myometrial (uterine) contractions at the time of expected implantation, or asynchronous immune or inflammatory responses to seminal fluid may reduce the incidence of clinical pregnancy in cycles with a higher frequency of peri-implantation intercourse. If this finding is replicated and confirmed, couples seeking to conceive should be advised to reduce or avoid intercourse in the peri-implantation period. We sought to replicate this finding in a dataset from a different prospective cohort study.

# Materials and methods

## Study population and database

Data from the European FERTILI study were acquired from the University of Padua, Italy. The FERTILI study prospectively enrolled women ages 18–40 who were experienced in use of a natural family planning method to record characteristics of the menstrual cycle daily, including all acts of intercourse. Women were in a stable heterosexual relationship and did not have any medical conditions or indicators of subfertility. The complete data include 7283 cycles from 781 women at seven European sites. Data include woman/couple level variables such as age, prior pregnancy, date of relationship start, birth date and history of hormonal birth control. Also included are cycle level data about timing of ovulation based on mucus peak, daily intercourse, unusual daily disturbances and the occurrence or absence of clinical pregnancy in each cycle. Many of the women in the study avoided intercourse during the fecund window for most of their study cycles in order to space pregnancy; only cycles with intercourse during the fecund window were used for this analysis. (Colombo and Masarotto, 2000).

## Fecund and peri-implantation windows

We followed the approach of Steiner *et al.* (2014) to estimate the day of ovulation and define the fecund and peri-implantation windows. The estimated day of ovulation was designated as cycle length minus 13 days, which is the same as 14 days prior to the first day of the next menstrual cycle. For conception cycles, we used the woman's prior cycle length (Mikolajczyk and Stanford, 2005), or in the case of the first cycle being a conception cycle, the median cycle length based on age (Najmabadi *et al.*, 2020). The fecund window was defined as the interval from 5 days before the estimated day of ovulation to 3 days after, inclusive. The peri-implantation window was defined from 5 days to 9 days after estimated day of ovulation, inclusive.

We conducted several sensitivity analyses around the estimated day of ovulation and the fecund window. We conducted analyses with an expanded the fecund window of 8 days prior until 3 days after the estimated day of ovulation (Lynch *et al.*, 2006). We estimated ovulation to occur 12 days prior to the last day of the cycle, which corresponds to a median luteal phase length of 12 days (Bull *et al.*, 2019; Najmabadi *et al.*, 2020). We also identified the estimated day of ovulation by cervical mucus peak day, i.e. the last day of any 'level 4' mucus observation, i.e. mucus that is slippery, stretchy or clear (Colombo and Masarotto, 2000). The peak day of cervical mucus has been shown to have similar accuracy to the LH surge to identify ovulation (Fehring, 2002; Direito *et al.*, 2013).

## Selection criteria for analysis

The study population was women at risk of pregnancy, meaning a first pregnancy during the study period. Women who became pregnant had subsequent cycles censored from analysis. Cycles were required to have intercourse recorded during the fecund window, in order to be at risk of pregnancy. Cycles known to be not at risk for pregnancy, due to no intercourse in the fecund window, were not informative for our research question.

## Statistical analysis

We conducted a correlation analysis of cycles to determine the relationship between fecund-window intercourse and peri-implantation intercourse. For couples with fecund-window intercourse, we also calculated descriptive statistics associated with the first cycle included in the study, including nulligravida status, location of enrollment and each partner's age. This analysis was stratified by the number of days of peri-implantation intercourse during that cycle, and differences were evaluated using the continuity-adjusted $\chi^2$ test. We also examined the impact of peri-implantation intercourse on cycle fecundability while accounting for the frequency and timing of intercourse during the fecund window by using a Bayesian model proposed by Dunson and Stanford (2005), which was also adapted by Scarpa and Dunson (2006). This Bayesian model, which was also used in the analysis of Steiner *et al.* (2014), allows the estimation of a baseline, cycle, or day-level effect while adjusting for the frequency and timing of intercourse during the fecund window, couple-specific fecundity and the clustering of cycles (i.e. couples having variable numbers of cycles in the analysis). In an adjusted model, we also included the covariates adjusted for by Steiner *et al.*, insofar as they were available to us. Thus, we adjusted for woman's age, gravidity and man's age but were unable to adjust for BMI, race, smoking and history of regular menstrual cycles. Results of the model are interpreted as an FR, with a point-mass at one representing the probability that a parameter has no effect on the model. When the posterior distribution for a given parameter has a very high probability of being one, then a 95% credible interval may include one as a lower or upper bound, which has the interpretation of there being a 95% probability of the parameter either being one or falling between one and the corresponding upper or lower bound of the interval (Pritchard, 2015). All analyses were conducted using R 3.4.1, and RStudio 1.0.143.

# Results

Initially, the FERTILI database included 7283 cycles from 781 women, with 485 pregnancies (conception cycles). The following cycles were excluded, for reasons described in the methods: 443 cycles (6.1% of all cycles) occurred after a first pregnancy in the study; 164 (2.2%) had incomplete data; 4071 cycles (55.9%) were not at risk for pregnancy because there was no intercourse during the known fecund window (see Fig. 1). Thus, 2606 cycles and 418 pregnancies (conception cycles) were included in the analysis. Compared to the 661 couples in the analysis, the 120 couples excluded had older women (30.7 years vs 29.9 years), older men (32.9 years vs 32.1 years) and had higher mean gravidity (1.3 vs 0.9).

The majority of women was less than 30 years of age (60.6%), men were less than 50 years of age (99.9%). Couples were primarily from Milan (34.8%) and Verona (27.3%). The mean number of cycles per woman was 3 (range 1–20). Three hundred and forty-nine (44.7%) women had no prior history of pregnancy (see Table I). During the peri-implantation period of the 2606 cycles at risk of pregnancy, 886 (34.0%) had no intercourse, 933 (35.8%) had 1 day of intercourse, 536 (20.6%) had 2 days of intercourse and 251 (9.6%) had 3 or more days of intercourse.

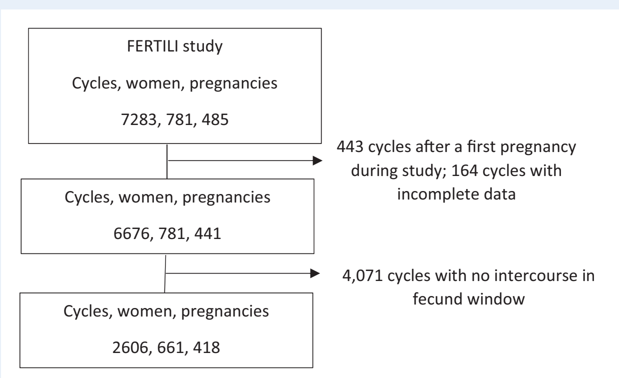


**Figure 1. Cycle eligibility for analysis.** The fecund window is calculated from 5 days before to 3 days after the estimated day of ovulation, which is 13 days before the last day of the cycle (or length of prior cycle).

There was a modest inverse relationship (correlation = −0.0367, *P*-value = 0.0027) between frequency of intercourse in the fecund window and in the peri-implantation window. Days of peri-implantation intercourse were similar for age, parity or study centers, as shown in Table I. After adjusting for intercourse during the fecund window, woman's age, man's age and gravidity, there was no effect of peri-implantation intercourse on fecundability, as shown in Table II. Results in Table II are based on the estimated day of ovulation 13 days before the end of the cycle, and a fecund window of 5 days before to 3 days after the estimated day of ovulation. We also obtained extremely similar null results for an estimated 12-day fecund window [−8, +3], and for the estimated day of ovulation 12 days before the end of the cycle (Supplementary Table SI). When we used the peak day of cervical mucus as the estimated day of ovulation, we had similar null results for a fecund window of [−8, +3] (not shown), and [−5, 0] (Supplementary Table SI).

# Discussion

Our results indicate that there is no significant relationship between the frequency of peri-implantation intercourse and fecundability, though in this population there was a modest inverse relationship between intercourse during the peri-implantation and the fecund windows. These results contradict those of Steiner *et al.* (2014), and do not support a recommendation to avoid peri-implantation intercourse patterns among couples attempting to conceive.

Couples in the FERTILI study were experienced users of the sympto-thermal method of fertility awareness or natural family planning, which incorporates daily observations of cervical mucus (Frank-Herrmann *et al.*, 2007; Frank-Herrmann, 2011). Although cycle intentions were not assessed in the FERTILI study, most couples who had intercourse during the fecund window were more likely to be trying to conceive, or at least receptive to the possibility of conceiving; whereas couples not attempting to conceive did not usually have intercourse during the fecund window and would likely have a greater frequency of intercourse in the peri-implantation period to compensate for less intercourse in the fecund window (Sinai and Arevalo, 2006). This would account for the inverse relationship between the frequency of intercourse in these different time windows in this study. Couples excluded from analysis were older and had higher number of previous pregnancies, characteristics that are associated with higher motivation to avoid pregnancy (Marshall, 1968).

There are important similarities and differences between our analysis of the FERTILI data and the analysis of Steiner *et al.* (2014), using data from the Time to Conceive study. Both studies are based on prospectively collected data from couples who used a daily diary to record intercourse and observations about the cycle. Both studies excluded known subfertile couples. The TTC study consisted of 1332 cycles from 546 couples who were older (ages 30–44). It is possible that there might be a greater effect of peri-implantation intercourse in older women; however, adjustment for woman's and man's age in our model did not alter our results. In the TTC study, all couples were trying to conceive; whereas many couples in the FERTILI study were not trying to conceive. While all couples in the FERTILI study tracked the fecund window and ovulation by cervical mucus and basal body temperature, only some of the couples in TTC did so (by mucus,

**Table I** Study population baseline characteristics by peri-implantation intercourse frequency in first cycle (n = 781).

| | Days of peri-implantation intercourse during first cycle | | | |
|---|---|---|---|---|
| | None (n = 245) | One (n = 257) | Two (n = 182) | Three or more (n = 97) |
| Woman's age (years) | | | | |
| <30 | 140 (57.1) | 148 (57.6) | 116 (63.7) | 69 (71.1) |
| 30–34 | 81 (33.1) | 81 (31.5) | 45 (24.7) | 21 (21.7) |
| 35–37 | 18 (7.4) | 24 (9.3) | 13 (7.1) | 4 (4.1) |
| ≥38 | 6 (2.5) | 4 (1.6) | 8 (4.4) | 3 (3.1) |
| Partner's age (years) | | | | |
| <50 | 245 (100.0) | 257 (100.0) | 182 (100.0) | 96 (99.0) |
| ≥50 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (1.0) |
| Nulligravid | 110 (44.9) | 126 (49.0) | 78 (42.9) | 35 (36.1) |
| Center | | | | |
| Verona | 78 (31.8) | 74 (28.8) | 48 (26.4) | 13 (13.4) |
| Milan | 70 (28.6) | 76 (29.6) | 69 (37.9) | 57 (58.8) |
| Lugano | 4 (1.6) | 4 (1.6) | 3 (1.7) | 2 (2.1) |
| Paris | 31 (12.7) | 42 (16.3) | 23 (12.6) | 8 (8.3) |
| Düsseldorf | 36 (14.7) | 42 (16.3) | 15 (8.2) | 12 (12.4) |
| London | 19 (7.8) | 14 (5.6) | 10 (5.5) | 2 (2.1) |
| Brussels | 7 (2.9) | 5 (2.0) | 14 (7.7) | 3 (3.1) |

Data are represented as n (%).

**Table II** Effects of peri-implantation intercourse on fecundability.*

| | Days of peri-implantation intercourse | | | |
|---|---|---|---|---|
| | None | One | Two | Three or more |
| Number of pregnancies | 157 | 146 | 83 | 31 |
| Number of cycles included | 886 | 933 | 536 | 251 |
| Total number of cycles | 2188 | 2166 | 1554 | 768 |
| Fecundability ratio, 95% CI | REFERENT | 1.00 (0.81, 1.00) | 1.00 (0.89, 1.08) | 1.00 (0.76, 1.13) |

*The model is adjusted for intercourse during the fecund window, woman's age at first included cycle, partner's age at first included cycle and gravidity. The fecund window is calculated from 5 days before to 3 days after the estimated day of ovulation, which is 13 days before the last day of the cycle (or length of prior cycle).

temperature or urine LH). For our analysis, we used exactly the same statistical model and the software used by Steiner *et al.* (2014), which is based on the Bayesian model to adjust for intercourse during the fecund window (Dunson and Stanford, 2005; Scarpa and Dunson, 2006). Following Steiner *et al.*'s (2014) analysis, we indexed the estimated day of ovulation, and hence the fecund and peri-implantation windows to the last day of the menstrual cycle or first day of positive pregnancy test, which is a substantially less precise way to define the timing of ovulation or the fecund and peri-implantation windows (Mikolajczyk and Stanford, 2006). In particular, this approach assumes that all cycles are ovulatory, while in reality 3% or more of cycles may be anovulatory (Lynch *et al.*, 2014; Najmabadi *et al.*, 2020). However, Steiner *et al.* (2014) also conducted a separate analysis using only cycles with urine LH monitoring to identify ovulation (226 cycles, 156 women), which had similar results to their main analysis but without statistical significance (FR for three or more days of peri-implantation intercourse, 0.74; 95% CI, 0.38–1.28). We also conducted a separate analysis using the mucus peak day to identify ovulatory cycles and the timing of ovulation (1583 cycles, 526 women), in which we again obtained null results (FR for three or more days of peri-implantation intercourse, 0.89; 95% CI, 0.54–1.50). Both our analyses and those of Steiner *et al.* adjusted for woman's age, man's age and gravidity. Steiner *et al.* also adjusted for BMI and self-reported history of regular menstrual cycles, variables which were unavailable for our analysis. Ultimately, we found no single definitive explanation for the discrepancy between the results from the TTC and FERTILI studies.

The incomplete recording of intercourse, during the fecund window and/or the peri-implantation window, could bias or distort the findings. Full reporting of intercourse was a key data objective of the original FERTILI study; however, the extent of underreporting of intercourse in our data remains unknown. Further studies of this question and similar questions related to intercourse patterns may require innovative methods to ascertain intercourse patterns more reliably and completely; for example, using a daily question on an app for whether intercourse occurred each day (Jennings *et al.*, 2019).

Further study of the relationship in additional datasets would be helpful to replicate or refute our findings, particularly since they contradict those of Steiner *et al.* (2014). Meta-analysis combined across data sets could allow for more robust assessment of the impact of woman's age and other covariates, as well as of alternative statistical approaches to identifying and modeling the fecund and peri-implantation windows (Kim *et al.* 2012). In addition, this question should be studied in subfertile couples, who would benefit from understanding any possible impact of peri-implantation intercourse.

# Supplementary data

Supplementary data are available at *Human Reproduction* online.

# Acknowledgements

We thank Bruno Scarpa and the University of Padua, Department of Statistics, for access to the FERTILI data; and Bernardo Colombo (deceased) and the FERTILI study investigators for the original collection of the data set. We thank David Pritchard, University of North Carolina, Chapel Hill, for providing the R code and discussing its use for the fecundability model.

# Authors' roles

J.B.S., S.K.W. and J.L.H. had full access to all of the data in the study and take responsibility for the integrity and accuracy of the data analysis. J.B.S. proposed the study question and design. J.L.H. performed the initial statistical analysis, with direct guidance of J.B.S., N.H. and A.T. S.K.W. performed additional statistical analysis, with the direct guidance of J.B.S. J.B.S., N.H. and A.T. aided in interpretation of results. J.L.H. and J.B.S. drafted the manuscript. S.K.W., N.H. and A.T. critically revised the manuscript for important intellectual content.

# Funding

None.

# Conflict of interest

All authors declare no conflict of interest.

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