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Original research article

Benchmark pregnancy rates and the assessment of post-coital contraceptives: an update

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Abstract

Objective: In 2001, we provided benchmark estimates of probability of pregnancy given a single act of intercourse. Those calculations assumed that intercourse and ovulation are independent. Subsequent research has shown that this assumption is not valid. We provide here an update of previous benchmark estimates.
Study design: We reanalyze earlier data from two North Carolina studies that collected daily urine samples and recorded daily intercourse for multiple menstrual cycles. One study comprised 68 sexually active women with either an intrauterine device or tubal ligation. The second was of 221 women who planned to become pregnant and had discontinued use of any birth control at enrollment. Participants had no known fertility problems. New statistical analyses were based on Monte Carlo simulations and Bayesian methods.
Results: The probability that a single act of intercourse occurs within a woman's fertile window is 25%, compared with 20% in previous calculations. The probability of pregnancy with intercourse on a given menstrual cycle day is correspondingly higher than previously estimated, with the largest increases occurring on menstrual days 12–22. These increases are, however, fairly small (for example, the peak chance of conception on menstrual day 13 increased from 8.6% to 9.7%).
Conclusions: Previous benchmark rates of pregnancy with one act of intercourse were moderately underestimated due to a mistaken assumption about the independence of intercourse and ovulation.
Implications statement: The chance of pregnancy with a single act of unprotected intercourse is greater than previously estimated. Previous benchmarks may underestimate the efficacy of post-coital contraception.
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Keywords: Emergency contraception; Post-coital contraception; Bayesian statistics

1. Introduction

In 2001, we published estimates of the probability of pregnancy given a single act of intercourse on a given menstrual cycle day, taking into account the natural variation in day of ovulation [1]. While this paper has been frequently cited (139 citations, Web of Science, 12 December 2014), the estimates rested on the then untested assumption that intercourse and ovulation are independent. That is, we assumed that the timing of ovulation is not influenced by intercourse and that the physiological events leading to ovulation do not affect the frequency of intercourse.

Subsequent research has shown that this assumption is not accurate: frequency of intercourse rises during the follicular phase, peaks around ovulation and declines thereafter [2]. The biological mechanisms that link intercourse and ovulation are unknown. The link may be due to cycle changes in a woman's libido [3–6], to an increase in male-initiated intercourse [7] in response to female pheromones [8] or to an act of intercourse accelerating ovulation [9,10]. Regardless of the exact biological mechanism, women who engage in unplanned and unprotected acts of intercourse are presumably more likely to do so when they are close to ovulating and thus vulnerable to pregnancy. Previous estimates of pregnancy probability have not taken this pattern into account, which raises questions about the validity of earlier benchmark estimates of conception probabilities. Any changes in these estimates may have

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implications for the evaluation of the efficacy of post-coital emergency contraceptives.

We revisit this question using Bayesian statistics and modeling to estimate the probability of conception given unprotected intercourse, taking into account the non-independence of intercourse and ovulation.

2. Materials and methods

As in our earlier analysis, we use data from two North Carolina studies. In one, 68 sexually active women with either an intrauterine device or tubal ligation provided data for up to three menstrual cycles. Of these women, 38 had a non-hormonal intrauterine device (90 cycles) and 30 had tubal ligation (81 cycles). These women collected daily first-morning urine specimens and kept daily diaries of intercourse and menstrual bleeding. Most participants were white, college educated, parous and in their late 20s or early 30s. All were in a stable sexual relationship and had no chronic illnesses or history of fertility problems. These data were originally gathered to assess hormone patterns in non-pregnant sexually active women of reproductive age and have been extensively described [11,12].

Data were also drawn from a prospective study of early pregnancy conducted in North Carolina. This study comprised 221 women (696 cycles) who planned to become pregnant by discontinuing any use of birth control and who had no known fertility problems. These women also collected daily first-morning urine samples and recorded menstrual bleeding and unprotected intercourse daily. Most were white and well educated, with ages ranging from 21 to 42 years (mean of 30). Further descriptions can be found elsewhere [12,13].

2.1. Identifying day of ovulation

Day of ovulation was identified through serial changes in daily urinary hormones. Daily urinary levels of estrone-3-glucuronide (a primary urinary metabolite of estradiol) and pregnanediol-3-glucuronide (a metabolite of progesterone) were measured using competitive time-resolved fluoro-immunoassays [14]. Day of ovulation was defined using an algorithm based on the rapid change in the ratio of estrogen-to-progesterone metabolites around ovulation [15,16]. This algorithm has subsequently been validated as a marker of ovulation [17,18].

2.2. Statistical analyses overview

Our purpose is to estimate the probabilities of conception following a single act of intercourse, both unconditional and conditional on menstrual cycle day. Ideal data for this purpose would come from a large sample of cycles from non-contracepting, sexually active women with a single act of unprotected intercourse in each cycle and an accurate marker of ovulation day. Such data are unavailable and are unlikely to become available. Women who do not want to become pregnant would not participate in such a study, and women who wish to become pregnant are unlikely to naturally engage in a single act of intercourse every cycle. Furthermore, a woman trying to become pregnant would presumably be unwilling to seek emergency contraception.

Instead, we rely on flexible statistical models that combine data from various sources to obtain indirect but reliable estimates. Specifically, we use statistical models to characterize (i) variability among women and cycles in the lengths of their luteal and follicular phases, (ii) the probability of intercourse on each day of the cycle relative to ovulation and (iii) the probability of conception from a single act of intercourse on a given day of the cycle relative to ovulation. Additional details about the models can be found in subsection 2.3.

The probabilities of interest can then be estimated based on the parameters from these component models. Our Monte Carlo simulations assume for the sake of simplicity that acts of intercourse in the empirical data are independent of one other, that cycle length is not related to the association of intercourse and ovulation and that follicular and luteal phase lengths are independent. We simulate a large number of menstrual cycles with varying cycle lengths, varying days of ovulation and a single act of intercourse. We also simulate whether or not each cycle resulted in conception. This simulation statistically estimates the hypothetical but infeasible clinical study mentioned above. From these simulations, we can directly estimate the probabilities of interest.

2.3. Component models

To model the within- and between-women variability in follicular and luteal phase lengths, we combined data from all datasets described above. This assumes that a woman's cycle length is not influenced by her intercourse behavior or by whether she is trying to conceive. We modeled follicular and luteal phase lengths with two separate log-t hierarchical models. As had been done earlier, we modeled the observed follicular and luteal phase lengths with two different log-t distributions [1]. However, instead of weighting a woman's observed number of ovulatory cycles by the reciprocal of her total number of observed cycles, we included a random effect for women (one effect for luteal phase length and another independent effect for follicular phase length) to prevent less-fertile women from being overrepresented. This approach takes into account the observed right-skewed distributions of phase lengths, while allowing for average follicular and luteal lengths to vary across women. For each phase, we estimated a mean parameter that represented the average phase length for all women, a variance parameter that estimated the variability of a woman's phase lengths and a second variance parameter that estimated how much each woman's average phase length varied relative to the total average. This model provided an excellent fit to the data.

To estimate the probability of intercourse on each day relative to day of ovulation, we excluded the 221 women