

Alternative measures of fertility compromise

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Fertility has been defined in many ways—from the demographers practice of simply recording the number of children born, to the precise (but difficult to measure) monthly probability of conception. Infertility is likewise variably defined, making comparison of data across studies difficult. Furthermore, there is debate about which measures/indicators/contributors are the most useful to try to track when trying to understand fertility/infertility, fecundity/subfecundity trends. (Fertil Steril® 2008;89:e27–9. ©2008 by American Society for Reproductive Medicine.)

Fertility, the ability of people to produce offspring, was a concept formerly applied only to the female. However, fertility is one of the few measures that reflect the joint health of two individuals, and we have only recently begun to appreciate the extent to which fertility depends on the health and environment of both the male and female partner, as well as the interaction between partners. In asking how the environment affects fertility, it is important to examine the contribution of environmental agents to subtle changes in both male (e.g., semen quality) and female (e.g., hormonal patterns during menstruation) reproductive physiology.

The answer to the question, “Has fertility declined” varies, depending upon one’s definition of fertility and infertility. Demographers define fertility as the average number of children per woman; by this measure fertility has declined dramatically worldwide since 1965. For example, the number of children per woman decreased 45% worldwide, from 4.9 in 1965–1970 to 2.7 in 2000–2005. The more developed countries experienced a somewhat smaller decline (from 2.4 to 1.6) in the same period (1).

The terminology is confusing. If you are not “fertile” (e.g., have not born a child), you are not necessarily “infertile”; this may be because of choice, and may not reflect “infertility.”

What, then, defines infertility? Definitions vary widely. Using alternate definitions the age-adjusted prevalence of history of infertility in a single population ranged from 6.1% (for self-report of an M.D. diagnosis) to 32.6% (for self-report of unprotected intercourse for 12 months without conception over the lifespan).

The National Survey for Family Growth classifies a woman as having “12-month infertility” if, at the time of interview, she has not conceived during the past 12 months and also satisfies the following criteria: 15–44 years old, married, not surgically sterilized, and sexually active but not practicing contraception in each of the 12 preceding months. “Percent

infertile” is the number of women classified as having “12-month infertility” divided by women 15–44 who were married at the time of interview. The denominator includes all women, regardless of whether they were trying to have a baby or were even “at risk” of pregnancy. Women are included in the denominator regardless of the length of time they were married, their sterilization status, and their level of sexual activity. Additionally, women who were infertile but who became pregnant through medical treatment during the preceding 12 months would not be considered as having “12-month infertility” (because they had, indeed, conceived). They would, however, be included in the denominator, further reducing the constructed “percent infertile” measure. By this measure, infertility is declining (2).

The risk of infertility may be better reflected by a second measure used by the National Survey of Family Growth (NSFG) (3), that of “impaired fecundity.” A woman is classified as having “impaired fecundity” if: [1] she reports a long (36-month) interval without conception; [2] it is physically impossible for her to have a child or for her husband to father a child; or [3] it is physically possible, but difficult, for her and her husband to have a child. The “percent impaired fecundity,” which uses all married women 15–44 as a denominator, appears to be increasing, as can be seen in Figure 1, taken from latest NSFG report (3), reaching 15% in 2002. Unlike “percent with 12-month infertility,” the “percent with impaired fecundity” (about 15% in 2002) (4) is quite consistent with the estimates of infertility rates based on prospective studies. By this measure infertility is increasing.

META-ANALYSIS OF TIME TO PREGNANCY

Time to pregnancy (TTP) the number of months (cycles) of unprotected intercourse until conception is a measure that is far more useful for epidemiologic purposes. It is more precisely defined and more consistently used than other measures. It is also the measure most suitable for cross-study comparisons. Perhaps the most commonly used measure, both clinically and epidemiologically, is that of TTP >12 months. Studies frequently report the proportion of the population that satisfies this criteria; we call this the % subfertile.

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TABLE 1**Time to clinically recognized pregnancy in four prospective studies.**

	United States			Europe
	Tietze (1968) (7)	Wilcox (1988) (8)	Zinaman (1996) (9)	Bonde (1998) (6)
Sample size	611	221	200	430
Study years	1963–1968	1983–1985	1994	1992–1995
Study area	USA	NC, USA	DC, USA	Copenhagen, DK
Ethnicity	Not stated	96% White	94% White	Primarily White
Socioeconomic status	Not stated	Middle-high	Middle-high	Union members
Rate of clinically recognized pregnancy after:				
3 cycles	0.60	0.56	0.51	0.40
6 cycles	0.76	0.69	0.71	0.70
9 cycles	0.83	0.70	0.78	NA
12 cycles	0.86	NA	0.80	NA

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We conducted a meta-analysis of all English-language studies published 1950–2001 that report the % subfertile in the study population by doing a Medline search for English language studies using multiple key words (time to pregnancy, time to conception, cycles to pregnancy, cycles to conception, fecundability, subfecundity, and natural fertility). We identified 51 studies (with $N \geq 50$), including 133,000 pregnancies or pregnancy attempts. We grouped these populations into three “regions”: Europe (67%), North American (26%), and elsewhere (7%). In our multivariate analysis we controlled for a number of variables including: length of recall, parity, whether pregnancy planned, whether all couples in the study conceived, and whether the pregnancy had to result in alive birth.

We found a wide range of estimates from 2.8% to 31.8%, with a mean, worldwide, of 12.8% (median 11.7%). These data are very variable, and although trends in North America and Europe are significant statistically, they are opposite in direction and difficult to interpret. A critical factor contributing to this wide variation may be the “wanted ness of the pregnancy,” which is difficult to ascertain, particularly retrospectively. Time to pregnancy is poorly defined for *unplanned pregnancies* and most useful for couples planning pregnancy. However, 49% of pregnancies in the US (not ending in miscarriage) in 1994 were unplanned (5). Therefore, even this measure of impaired fecundity has serious limitations.

ALTERNATIVE APPROACHES

A novel and promising approach, is to determine how long a cross-section sample of women had been “trying” when called: the “current duration” approach. In a phone survey conducted in Paris, of 1,204 women (aged 18–44). The cur-

rent duration since the beginning of unprotected intercourse was defined for 69 women (5.7%). In addition, 15 women (1.2%) were planning to start trying to become pregnant within the next 6 months. Slama and colleagues estimated that 34% of women would have a TTP > 12 months had they been followed prospectively. They also estimated that tobacco smoking by the woman was associated with a doubling in the median duration of unprotected intercourse before pregnancy.

An alternative is to enroll couples at the time they stop using an effective method of contraception and following them closely to see how long it takes them to conceive. There are few such studies because identifying such couples and enrolling them at precisely the right time is logistically difficult and costly.

Table 1 gives results from four such studies, from different countries and years. Although rates of pregnancy varied somewhat across these, after six cycles, the percents of participants that have conceived were quite similar (69%–76%).

In conclusion, population surveys can provide data on fertility trends, but will remain controversial and cannot address environmental causes of impaired fertility. Time to pregnancy, if used in a consistent manner across studies, can give consistent yield results. However, such studies can only address environmental causes if conducted prospectively, or using the current-duration approach. Finally, prospective studies of pregnancy planners have the highest degree of consistency and can examine risk factors for infertility, but only in a highly motivated (and therefore nonrepresentative) population. In short, this area remains difficult and controversial. However, important advances have occurred in recent years, and long-term cohort studies underway in the United States and Europe should yield more precise estimates

and make it possible to identify the role of environmental factors in fertility compromise.

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