Infertility

PUBLIC HEALTH IMPORTANCE

Physicians in the United States typically classify couples as infertile if they have been unable to conceive a pregnancy after 12 months or more without contraception. In 1988, this definition could be applied to about 2.3 million U.S. couples with wives aged 15–44 years, or one in 12 married women (1). Another useful measure of infertility is impaired fecundity, which includes unmarried as well as married women and encompasses problems with pregnancy loss as well with becoming pregnant. In 1988, 4.9 million women—or one in 12 females aged 15–44 years—had impaired fecundity. Among married women, 3.1 million, or one in 10, had impaired fecundity.

The rates of infertility in less industrialized nations are markedly higher, and infectious diseases are responsible for a greater proportion of infertility than in the United States and other industrialized nations (2–5). Despite the low and relatively constant levels of infertility over the past three decades, a number of demographic and social factors have contributed to the misperception of an **infertility epidemic** in the United States (1–6).

- Delayed childbearing and the aging of baby boomers have increased the absolute numbers of couples trying to have their first children at ages when it is considerably more difficult. Because older couples have fewer years in which to achieve their desired family size, they may seek help more quickly, thereby inflating the demand for infertility services.
- Dramatic increases in physician visits for infertility have drawn immense media interest. In 1968, 600,000 office visits

were for infertility services compared with 1.7 million in 1991. Between 1982 and 1988, the number of women reporting a visit for infertility services in the previous year grew by 25%.

- The number of physicians trained to provide specialized infertility services has soared over the past 20 years.
- New infertility drugs and treatment procedures have been developed in the last two decades. With each new treatment option, tremendous publicity has been generated about infertility and the resulting medical, legal, and ethical issues of infertility services. As more hope for overcoming infertility is created, more people may be motivated to seek medical help.
- The decreased number of infants, especially white infants, available for adoption has increased the proportions of couples of all ages who seek medical and legal assistance to have a baby (7).

Although infertility does not represent a serious public health threat in the United States, it carries significant personal, societal, and economic consequences that call for surveillance and action. Diagnosis and treatment are very costly, time-consuming, and invasive, and they can place immense stress on marital and family relations. Clearly, the financial and personal costs pose a significant barrier to many who face the disappointments of infertility. National data sources describing infertile couples may suggest

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ways to prevent infertility and improve access to infertility services.

One of the Public Health Service's year 2000 national health objectives is to reduce the prevalence of infertility from 8% to 6.5% (8). Much of this reduction will depend on our success in identifying risk factors for infertility and lowering the rates of risk factors that are preventable primarily sexually transmitted diseases (STDs) and pelvic inflammatory disease (PID). Because of the relatively high prevalence and young age distribution of STDs in the United States, their impact on PID, ectopic pregnancy, and infertility may not be seen for many years (9). Only by regularly monitoring these trends can we accurately estimate the total need for infertility services in the coming decades.

The wide social and economic disparities in infertility services sought by American women represent yet another reason for monitoring infertility in the United States. Women who seek infertility services are not representative of all women who are infertile (10,11). Continued surveillance is critical for shedding light on these inequities and identifying the barriers that women face in meeting their childbearing goals. For both men and women, infertility frustrates one of the most basic of human desires (6).

Moreover, as greater numbers of couples seek medical help with infertility, the need to ensure the quality and cost-effectiveness of the services received becomes more urgent. Medical care for persons with infertility poses unique challenges to professionals striving to ensure standardization and quality control, largely because the potential to help infertile couples varies widely. Many demographic, behavioral, and clinical factors determine the prognosis for each infertile couple. In addition to identifying predictors of success, infertility services research has addressed other questions such as these (12):

- What constitutes a standard infertility workup?
- What are the most accurate and costeffective diagnostic tools for specific classes of infertility?

- How are treatment success rates affected by the diagnostic mix of patients and the different definitions of success?
- How much should services cost, and to what extent should insurance cover these costs?

The national surveillance data presented in this chapter cannot answer these questions directly, but they provide the demographic and epidemiologic backdrop needed to evaluate clinicbased studies, which are known to be based on highly selected groups of infertile individuals namely, those who actually pursue medical help (for additional information about related topics and surveillance activities, see the Contraception and Sexually Transmitted Diseases chapters).

HISTORY OF DATA COLLECTION

In the United States, only one source has provided reliable national data on infertility: the National Survey of Family Growth (NSFG) and its predecessor surveys, the Growth of American Families Study in 1955 and 1960 and the National Fertility Survey in 1965 and 1970 (see the Contraception chapter for background information). Since 1973, CDC's National Center for Health Statistics (NCHS) has periodically conducted the NSFG to ask national samples of women about their pregnancies, reproductive health, infertility, and basic social and economic characteristics. To date, four NSFGs have been conducted—in 1973, 1976, 1982, and 1988. Work is presently underway on the 1994 NSFG, which will contain an enhanced set of infertility questions.

Between 1978 and 1984, the World Health Organization conducted a multinational, multicenter study of infertility in both developed and developing countries, collecting data on 2,500 couples. The chief purpose of this study was to provide a standardized approach for diagnosing infertility. Because the study was clinic-based, investigators were unable to estimate the prevalence of infertility. Nevertheless, these findings represent the largest database of demographic, epidemiologic, and clinical information on couples seeking medical help for infertility (2).

Several data sources provide information on infertility services and service providers. In addition to collecting data on services in the 1982 and 1988 NSFGs, NCHS has conducted the National Ambulatory Medical Care Survey and found that nearly 400,000 new patients are seen for infertility each year-at more than double the rate in 1966. In 1991, 1.7 million physicians' visits were made in which infertility was mentioned as at least one of three top reasons for the visit. In 1985, the Alan Guttmacher Institute surveyed private physicians in four specialties: obstetrics/gynecology, urology, general/family practice, and surgery. These data sources, along with several European studies (6,13,14), have given comparable pictures of the levels and predictors of service-seeking among infertile couples. On average, less than two thirds of infertile couples seek medical help, and the rates of service-seeking are highest among persons who are well educated, older, and of a higher-than-average income status.

CDC SURVEILLANCE ACTIVITIES

Definition of Terms

The NSFG produces data on two measures of infertility: **infertility status** and **impaired fecundity**. **Infertility status** reflects the standard medical definition of infertility used in the United States—a case in which a married couple is not surgically sterilized, has not used contraception, and has not become pregnant for at least 12 months (15).

In the 1982 and 1988 NSFGs, an **impaired fecundity** measure was formulated to determine if it was difficult, impossible, or dangerous for a woman to become pregnant or carry a pregnancy to term. This broader measure of infertility has potentially greater utility for planning and monitoring services because it 1) includes women regardless of marital status, and 2) encompasses problems with pregnancy loss as well as with getting pregnant. The goal of individuals with fertility problems is, after all, to have a healthy baby.

Women who did not report any sterilizing operations (e.g., tubal ligation, hysterectomy) were classified as having impaired fecundity on the basis of their answers to the following series of questions:

- Some women find it physically impossible to have (more) children. As far as you know, is it physically possible or impossible for you to conceive a(nother) baby, that is, to get pregnant (again)?
- What about your husband? Is it physically possible or impossible for him to father a(nother) child?
- Some people are able to have a baby but have difficulty getting pregnant or holding onto the baby. As far as you know, is there any problem or difficulty for you (and your husband) to conceive or deliver a(nother) baby?
- Does your husband have any difficulty fathering a child?
- Has a doctor ever told you never to become pregnant (again)?

Women were considered to have impaired fecundity if they gave any of the following responses:

- They said it was impossible or physically difficult to conceive or deliver a baby.
- They said that a doctor had told them never to become pregnant again because the pregnancy would pose a danger to them, the baby, or both.
- They said they or their husbands were infertile (were continuously married, did not use contraception, and did not become pregnant) for 36 months or more.

^{*} The impaired fecundity measure was used in the 1976 NSFG, but the 1982 NSFG was the first cycle to include women of all marital statuses. Trends since 1976 can be examined for currently married women only.

Use of Medical Services for Infertility

In the 1982 and 1988 NSFGs, all women, regardless of marital or contraceptive status, were asked the following questions about using infertility services:

- Have you (or your husband) ever been to a doctor or clinic to talk about ways to help you become pregnant?
- (Not counting routine care or advice about a pregnancy), have you (or your husband) ever been to a doctor or clinic to talk about ways to help you prevent a miscarriage?

Women who answered "yes" to either of these questions were considered to have sought medical help for infertility. In the 1982 survey, women were asked an open-ended question about specific services they or their husbands received, and in the 1988 survey, women identified specific services from a list (Table 1).

GENERAL FINDINGS

NSFG data indicate that one in 12 currently married American women (8%) was infertile in 1988. This overall rate did not change **significantly** between 1965 and 1988, nor did infertility rates change within specific age-groups (Figure 1).

In the 1988 NSFG, about 4.9 million married and unmarried females aged 15–44 years (one in 12) were found to have impaired fecundity. Among women who were married at the time of the survey, about 3.1 million women (roughly one in 10) had impaired fecundity compared with 2.3 million women (one in 12) who were infertile. These rates had changed little since 1982.

The precise role of factors such as age on infertility is challenging to identify because risk factors

Type of service	Number of women (in thousands)	Percentage of women who ever used services	Percentage of all females aged 15–44 years (N=57.9 million)	
Any infertility services	6,756	100.0	12	
Advice on becoming pregnant (e.g., timing of intercourse)	3,537	52	6	
Tests on male partner	2,224	33	4	
Tests on female partner	2,105	31	4	
Ovulation drugs	1,901	28	3	
Bed rest	1,560	23	3	
Treatment of blocked tubes	1,018	15	2	
Advice on starting or stopping contraception	946	14	2	
Artificial insemination	369	6	1	
In vitro fertilization	145	2	0.3	
Other	1,070	16	2	

TABLE 1. Use of infertility services among females aged 15-4 years - United States, 1988



FIGURE 1. Prevalence of inferility among married females* aged 15–44 years — United States, 1965–1988

* Excluding surgically sterilized females.

and demographic characteristics are often highly intercorrelated. The NSFG, as a primarily demographic fertility survey, gives us data on factors such as age, parity, race, and the use of infertility services, whereas epidemiologic studies provide information pertaining to important medical and behavioral factors related to infertility.

Because the definition of impaired fecundity includes unmarried women and women having difficulties carrying to term, we focus on this broader measure of infertility when presenting NSFG data. For the most part, the 12-month infertility status measure shows similar trends, levels, and correlates, and we discuss these issues when appropriate.

Age and Parity

Population- and clinic-based research studies have demonstrated that fertility declines as women get older; the debate generally centers on the critical age, with most studies showing substantial declines after age 35 or 40 years (16,17). Age and parity (the number of live births) are discussed together here because their role in fertility problems is closely linked.

Impaired fecundity increases with age, particularly after age 35, and the rates are higher among women with no previous births (parity 0) (Table 2). These nulliparous women are referred to as having **primary** impaired fecundity, whereas women experiencing difficulty having a second or higher-order birth are referred to as having **secondary** impaired fecundity. Among women who have had one or more births, impaired fecundity does not increase significantly with age, largely because surgical sterilization occurs more frequently among older women, and fewer older women are **at risk** of impaired fecundity.

Using the 12-month definition among currently married women and excluding surgically sterilized women, CDC researchers found that age-specific infertility rates (all parities taken together) have remained fairly constant in the United States since 1965 (within the sampling error of each survey), but they observed a distinct rise in infertility with increasing age (Figure 1). With regard to parity, between 1965 and 1988, the proportion of infertile couples trying to have a first birth (i.e., primary infertility) increased dramatically, from one in six to one in two married infertile couples. These figures reflect the trends of delayed marriage and delayed childbearing in marriage throughout the past 30 years.

Education and Occupation

Education level and occupational status are frequently used as proxy measures for socioeco-

Parity, by age	All women (no. in thousands)		Surgically sterile (%)		Impaired fecundity (%)		Fecund (%)	
	1988	1982	1988	1982	1988	1982	1988	1982
All parity								
15–44 years	57,900	54,099	28.0	25.2	8.4	8.4	63.6	66.3
15–24 years	18,592	20,150	2.2	2.3	4.8	4.3	93.0	93.4
25–34 years	21,726	19,644	25.6	25.9	9.6	10.0	64.7	64.2
35–44 years	17,582	14,305	58.3	57.0	10.6	12.1	31.0	31.0
0 parity								
15–44 years	25,129	22,941	4.3	3.1	8.8	8.4	86.9	88.5
15–24 years	14,978	15,547	0.2	0.1	4.1	4.1	95.7	95.8
25–34 years	7,252	5,628	4.7	5.1	13.4	14.7	82.0	80.2
35–44 years	2,899	1,766	25.0	23.0	21.4	25.7	53.6	51.3
≥1 parity								
15–44 years	32,771	31,158	46.1	41.7	8.1	8.5	45.8	49.9
15–24 years	3,164	4,603	10.5	9.6	7.7	5.2	81.8	85.2
25–34 years	14,474	14,016	36.1	34.2	7.8	8.1	56.1	57.8
35–44 years	14,683	12,539	64.8	61.7	8.5	10.1	26.7	28.1

 TABLE 2.
 Number of females aged 15–44 years and percentage distribution* of those who are fecund, by fecundity status, parity, and age — United States, 1982 and 1988

nomic status, but they have some limitations. NSFG data from 1982 suggest that infertile women (using the 12-month definition and including only married women) were less likely to have an education level beyond high school, and they were more likely to work in lower-status jobs (10,18). When all women are included, regardless of marital status, however, education and occupation are unrelated to impaired fecundity (11). These factors are closely linked to the use of medical care for infertility, which contributes to the impression that infertility is more frequent among women with higher education or higher-status jobs.

Race and Ethnicity

Analyses of 1982 NSFG data had suggested that infertile couples are more likely to be black than white and that this race gap is widest for couples with secondary infertility (18). The apparent link between race and infertility, particularly infertility due to tubal or pelvic problems, is confounded by socioeconomic differences in factors associated with infertility as well as in patterns of seeking services for infertility. For example, rates of STDs and PID have been found to be higher among blacks than among whites (9, 10). Infertile black women are less likely to seek medical help than infertile white women (10, 11, 18). This is probably related to the fact that black women, on average, have lower levels of education and income than white women.

CDC investigators found that neither race nor Hispanic origin is related to impaired fecundity after controlling for a history of PID treatment (*Wilcox LS, Mosher WD, unpublished data,* 1994).

Behavioral Factors

The National Fertility Survey and NSFG data do not include sufficient details for assessing behavioral factors; however, numerous epidemiologic and clinical studies have well characterized the behavioral risk factors for specific classes of infertility. Cigarette smoking has been tied to longer time to conception, ovulatory and tubal disorders, and fetal and early infant death. In addition, women whose mothers smoked during pregnancy were found to take longer to become pregnant themselves (19). The precise effects of caffeine consumption, alcohol use, and other drug use are still under investigation and pose many difficulties in defining and measuring exposure. The role of certain birth control methods, such as intrauterine device (IUDs) and oral contraceptives, also continue to be investigated. Only specific types of IUDs (e.g., the Dalkon Shield) and high-estrogen-dose birth control pills appear to place women at risk of developing fertility problems (20,21). The complex mechanisms whereby sexually transmitted infections can lead to PID, ectopic pregnancy, and infertility have been described elsewhere (9).

Use of Services

The 1982 and 1988 NSFG found that the most common service sought was advice on becoming pregnant; more than half of the women who received any services reported getting instructions on timing intercourse during the fertile period of the menstrual cycle or measuring basal body temperature to predict the time of ovulation. Nearly one third of service-seekers reported infertility testing for themselves or their husbands. Ovulation drug treatment was the most common specialized treatment—sought by 28% of service-seekers and 3% of all females aged 15–44 years (Table 1).

Between the 1982 and 1988 NSFG surveys, the number of women who reported using infertility services in the previous 12 months increased 25%—from 1.08 to 1.35 million women (1). Service-seekers in both surveys were more likely to be white, college-educated, married, and of a higher-income status than infertile women who never sought medical help for infertility (10,11,18).

In 1988, users of infertility services were more likely than nonusers to be non-Hispanic white, college-educated, of a higher income status, >30 years of age, nulliparous, or ever married (Table 3). For example, infertile women >30 years of age who had never been pregnant were 1.5 times as likely to seek medical help than were their counterparts <30 years of age (58% vs. 39%). The percentage of women who received infertility services rose steadily with income, ranging from 24% to 52%. College-educated women were 50% more likely to have received services than were high school graduates (60% vs. about 40%). Thus, women who use infertility services represent a highly selected subgroup of the population of infertile females. Studies in other industrialized nations have reached similar conclusions—that the need for infertility services is unmet among persons with low incomes and less education (2,4,13,14).

INTERPRETATION ISSUES

Numerous studies have shown that the way that infertility is defined can affect the estimates of

by selected characteristics — United States, 1988					
Characteristic	Any service				
Total	43				
Race/ethnicity					
Hispanic	31				
Non-Hispanic white	47				
Non-Hispanic black	30				
Education (years) ⁺					
0–11	32				
12	40				
13–15	42				
≥16	60				
Income [§]					
0–149	24				
150–399	43				
≥400	52				
Age/parity ¹					
15–29/0	39				
15–29/ <u>≥</u> 1	29				
30–44/0	58				
30–44/ <u>≥</u> 1	42				
Marital status					
Never married	24				
Currently married	48				
Previously married	38				
* Among 5.3 million females with impaired fe	ecundity				
Among women aged 20–44 years.					
Percentage of poverty level income; among women aged 20–44 years.					
¹ For age/parity groups, 15–29/0 and 15–29 women aged 15–29 years with 0 or ≥1 par 30–44/0 and 30–44/≥1 indicate women ag years with 0 or ≥1 parity.	/≥1 indicate ity; ed 30–44				

 TABLE 3.
 Percentage of females* aged 15–44

 years receiving any infertility services,

 by selected characteristics —

prevalence, the identification of risk factors, and prognosis (2, 22-24). For example, the standard medical definition in the United States is 12 months of unprotected intercourse without pregnancy, whereas the World Health Organization and many European countries use a 24-month criterion. The results of demographic studies of conception indicate that the average waiting time to conception is 7.5 months, which means that about 10% of women will not become pregnant after 12 months of trying, and about 5% will not become pregnant after 24 months (25). The NSFG prevalence estimate of 8% of married women is well in line with these figures. Some infertile women, identified in the NSFGs or in clinical studies, may simply represent the tail of the normal distribution of waiting times to conception; after additional months, some of them may become pregnant, regardless of whether they receive medical help. Amidst this statistical debate, we should further consider that the usefulness of the 12-month or 24-month criterion depends on many other factors-most importantly, age and medical history. For example, a woman whose fallopian tubes are completely blocked or whose husband produces no sperm (azoospermia) will be infertile after one month as well as after many years of trying to conceive, unless medical help is obtained.

In addition to the time frame used to define infertility, another methodologic issue affecting prevalence and prognosis is the definition of primary and secondary infertility (26). Secondary infertility, in which a prior pregnancy has occurred, generally carries a better prognosis for future fertility than primary infertility, in which no prior pregnancy has occurred. Clinicians recognize that infertility is often a couple-based problem-that is, either partner may be able to get pregnant with someone else, but they have difficulty conceiving with each other. Clinicians have not reached a consensus, however, about how to define prior fertility status. A couplebased definition of primary infertility would require that no prior pregnancy had occurred in the partnership, whereas secondary infertility would mean that one or more pregnancies had occurred. Woman-based definitions are often used in clinical practice. Under these definitions, a woman who has never been pregnant would be classified as having primary infertility,

whereas a woman who has ever been pregnant would be classified as having secondary infertility. When presenting their published results, investigators do not always clarify which definitions of primary and secondary infertility they used, and this omission can lead to confusing estimates of prevalence and prognosis.

EXAMPLES OF USING DATA

Although the NSFG does not provide infertility data for individual states, this survey, along with other surveillance and epidemiologic research on infertility, has been used extensively over the past 15 years to formulate and justify state-level, infertility-related legislation in numerous areas (6):

- Insurance policies.
- Standardization of diagnosis and treatment procedures, and other quality-control measures.
- Registry of in vitro fertilization procedures and other assisted reproductive technologies.
- Targeted prevention programs.

More recently, national surveillance efforts have played a key role in encouraging the enactment of federal statutes for the regulation and quality control of infertility services (e.g, the In Vitro Fertilization Registry conducted by the American Fertility Society) and insurance coverage in a growing number of states.

FUTURE ISSUES

Results on infertility and infertility services from the 1994 NSFG should be available in 1996. This survey design includes periodic follow-up interviews that will allow us to examine factors associated with infertility and the use of services over time.

Although we have limited new information on the population prevalence and other epidemiologic characteristics of infertile couples, several recent studies (12) may help us acquire a more complete picture of who is infertile, who seeks services, and what services are most helpful. These studies have focused on the epidemiologic and psychosocial evaluation of specific aspects of infertility services:

- Evaluations of the prognostic value and cost-effectiveness of some standard diagnostic techniques, such as the postcoital test and the timed endometrial biopsy.
- Establishment of more accurate prognostic guidelines for the use of various treatments, most notably in vitro fertilization and artificial insemination.
- Identification of more accurate and clinically relevant diagnosis groups to minimize fruitless or inappropriate treatment.
- Investigation of adverse effects of infertility treatments on women and their babies as well as the short- and long-term effects of service-seeking on personal and family wellbeing.

Future studies should address the difficult economic, legal, and ethical questions raised by infertility. For example, surrogate motherhood and donor embryos spark considerable debate over a person's **right** to have children and draw further public attention to infertility. Another challenge for translating data into policy is evident with research on fertility and age. Given that infertility rates generally increase with a woman's age, particularly over age 35 or 40, **and** given that the trends of delayed marriage and childbearing are unlikely to reverse, policies and interventions should focus on better educating women about their fertility prognosis and helping them achieve their desired family size.

Furthermore, because epidemiologic studies have given mixed results on risk factors, including age and STD history, more multidisciplinary research is needed to clarify the effects of these factors on fertility as well as the ramifications of specific prevention goals. This information will be critical for targeting prevention efforts more appropriately and realistically as well as for making services more responsive to the needs of infertile individuals.

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