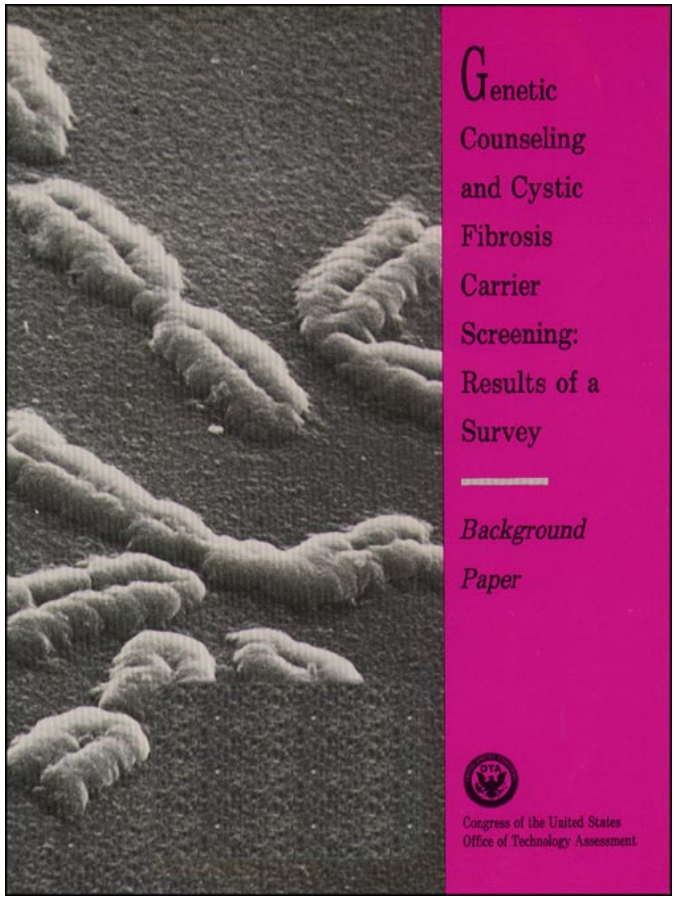
Genetic Counseling and Cystic Fibrosis Carrier Screening: Results of a Survey

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Foreword

For years, experts have theorized about the consequences of increased knowledge of human genetics. In the early 1990s, development of a DNA-based test to identify carriers of cystic fibrosis (CF) moved the debate from the theoretical to the practical. The CF carrier assay is but one of many tests to come that will place genetic counselors and nurses working in genetics at the front line on the issues raised by assimilation of DNA tests into clinical practice.

This OTA Background Paper presents results from a 1991 OTA survey of 431 genetic counselors and nurse geneticists. It was conducted to better understand the environment in which the average genetic counselor or nurse in genetics works, to describe the infrastructure and tools available to these professionals, to assess the state of practice in the provision of CF carrier screening, and to evaluate their attitudes regarding CF carrier screening. The survey supports OTA's August 1992 assessment *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening; the* full assessment was requested by the House Committee on Science, Space, and Technology, the House Committee on Energy and Commerce, and Representative David R. Obey.

The survey data collected by OTA reflect the tensions and concerns surrounding the widespread implementation of CF carrier screening. Those who currently oppose routine carrier screening for CF raise concerns about the sensitivity of the test, the numbers of individuals that would be potentially screened—and the subsequent effect on the clinical genetics infrastructure--and the possibilities of stigma, discrimination, and poor quality in services. Those who think CF carrier screening should be widely available believe the information provided by the test increases patient autonomy and lowers uncertainty regarding reproductive futures.

OTA was assisted in preparing the survey instrument and Background Paper by a panel of advisors, contractors, workshop participants, and reviewers selected for their expertise and diverse points of view. We gratefully acknowledge the contribution of each of these individuals. OTA, however, remains solely responsible for the contents of this Background Paper.



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1 Through December 1991

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Chapter 1
Introduction and Background

Cystic fibrosis (CF) is the most common, life-shortening, recessive genetic disorder affecting Caucasians of European descent. From 1,700 to 2,000 babies with CF are born annually in the United States. The diagnosis of an infant with CF often reveals the first and only clue that the genetic trait exists in the family.

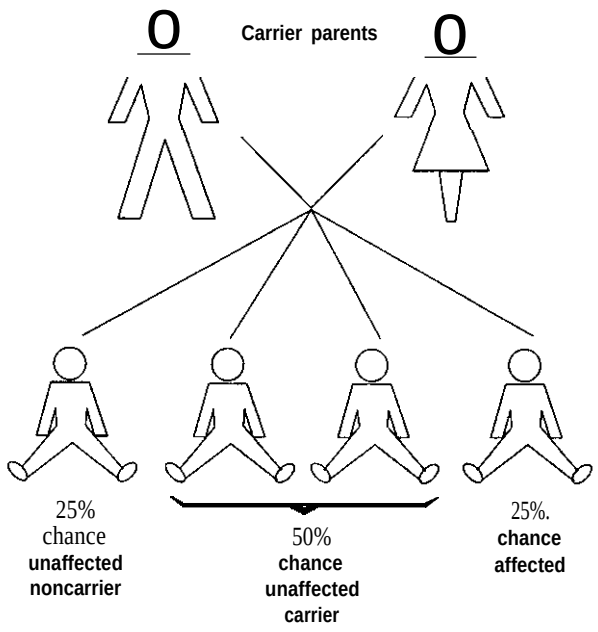
Parents of a child with CF are, by definition, obligate CF carriers. They have no symptoms of CF, but with each pregnancy are at 1 in 4 risk of having a child with CF and 1 in 2 risk of having a child who is a carrier (figure l-l). Such couples are sometimes referred to as carrier couples, or couples who are positive/positive (+/+). If a couple is positive/negative (+/-)—the father is a carrier, but the mother is not, or vice versa—their offspring can be CF carriers, but cannot have CF. Couples are not at risk of having a child with CF if only one or neither partner is a carrier.

Four of five individuals with CF are born to families with no previous history of the illness. Beyond the approximately 30,000 Americans who have CF, as many as **8** million individuals could be CF carriers. With no knowledge of a family history of CF, American Caucasians have about a 1 in 25 risk of being a CF carrier. The risk of carrier status increases when an individual in a family is diagnosed with CF, with risks calculated by relationship to the affected individual (table l-l).

Prior to 1989, the absence or presence of CF in one's family, as well as ethnic and racial background, were the only indicators available to determine risk of carrier status. In 1989, however, scientists identified the most common change, or mutation, in the genetic material-deoxyribonucleic acid (DNA)-that causes CF. Following this discovery came tests to detect mutations in the specific area of DNA—the CF gene-that is responsible for the disease.

The Office of Technology Assessment (OTA) report *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening* (1) focuses on using these DNA tests to screen and identify CF carriers among the general population before they have a child with CF. This background paper, conducted in support of the OTA assessment, reports the results of an OTA survey of 431 members of either the National Society of Genetic Counselors (NSGC) or the International Society of Nurses in Genetics (ISONG). Conducted in summer 1991, the survey was designed to evaluate genetic counseling attitudes and practices regarding widespread CF carrier screening, a prospect that has been viewed with mixed feelings.

Figure I-l—Inheritance of Cystic Fibrosis



SOURCE: Office of Technology Assessment, 1992.

Table I-l—A Priori Carrier Risks for Cystic Fibrosis

Negative family history	
Caucasian	1 in 25 (4%)
African American	1 in 60 to 65 (1.5 to 1.7%)
Asian American	1 in 150 (0.79'.)
Hispanic American	1 in 40 to 50 (2 to 2.5%)
Positive family history	
Parent of child with CF	1 in 1 (1OO%)
Sibling with CF	2 in 3 (67%)
Aunt or uncle with CF[a]	1 in 3 (33%)
First cousin with CF	1 in 4 (25%)
Niece/nephew with CF[a]	1 in 2 (50%)

[a] Consanguineous.

SOURCE: Office of Technology Assessment, 1992.

Consensus exists that individuals who have relatives with CF should be told about the availability of CF carrier tests; the disagreement is whether *everyone* should be informed about the assays, since 80 percent of babies with CF are born to couples with no previous family history of the condition. Concern about the scientific, legal, economic, ethical, and social implications of the prospect that large numbers of people might be screened for their CF carrier status led the House Committee on Science, Space, and Technology, the House Committee on Energy and Commerce, and Representative David R. Obey to request the OTA assessment.

WHAT IS CYSTIC FIBROSIS?

CF is not a new disease. First described in 17th century folklore, medical literature has long documented that CF compromises many functions throughout the body--chiefly the respiratory, gastrointestinal, and reproductive systems and the sweat glands.

Many affected babies are not immediately diagnosed as having CF Although the disease is always present at birth in affected individuals, the onset of recognizable clinical symptoms varies widely. Physicians diagnose CF using a combination of clinical criteria and diagnostic laboratory tests. Although an assay called the sweat test remains the primary diagnostic test for CF DNA mutation analysis can diagnose more than 70 percent of cases.

CF exerts its greatest toll on the respiratory and digestive systems, and the severity of respiratory problems often determines the quality of life and survival. There is no cure for CF Treatment focuses on managing the respiratory and digestive symptoms to maintain a stable condition and lengthen lifespan. Because of CF's varied progression, the regimen and level of therapy depends on the individual. Most therapy involves home treatment (e.g., chest physical therapy to clear mucus from the lungs), outpatient care at one of more than 110 clinics devoted specifically to CF health care, and occasional hospital stays. Today, physicians can look to an ever-expanding array of new pharmaceutical options to manage the care of CF patients; on the horizon are hopes for gene therapy.

Over the last half-century, treatment of CF has evolved so that an illness nearly always fatal in early childhood is now one where life expectancy into adulthood is common. Fifty years ago, most infants born with CF died in the frost 2 years of life. In 1990, median survival was 28 years--i.e., of the individuals born with CF in 1962, half were alive in 1990.

THE CYSTIC FIBROSIS GENE

CF is a genetic illness transmitted from parents to their children via genetic directions stored in DNA. In humans, these directions, including those responsible for CF are stored among genes arrayed on 46 structures called chromosomes. The gene responsible for CF lies on chromosome 7 and results in a product called the cystic fibrosis transmembrane conductance regulator (CFTR). In most people with CF a three-base pair deletion in both of their CF alleles results in a faulty CFTR, which leads to CF pathology. This three-base pair mutation occurs at position number 508 in the CFTR and is abbreviated as delta F508 (AF508). More than 170 additional mutations in the CF gene also lead to faulty CFTRs. Individuals with CF have two of the same, or two different, mutations. CF carriers have only one mutation; their second CF allele produces normal CFTR.

About 70 percent of CF carriers have the AF508 mutation.[1] International studies demonstrate ethnic and regional variation in the frequency distribution of this mutation; as expected, the multicultural nature of the United States reflects this variation. Most of the other 170+ mutations appear in a small fraction of individuals or families, although a few occur at a frequency as great as 1 to 3 percent. Some symptoms (or their lack of severity) correlate with particular mutations. Digestive difficulties from pancreatic insufficiency, for example, generally associate with ΔF508.

CYSTIC FIBROSIS MUTATION ANALYSIS

With localization of the CF gene, ΔF508, and other CF mutations, it is now possible to directly analyze DNA from any individual for the presence

[1] Quoted mutation frequencies for ΔF508 and other CF mutations always depend on racial and ethnic background. Throughout this background paper, OTA presents current expert estimates of appropriate ranges of detection frequencies or sometimes uses a specific figure with qualification (e.g., about 90 percent; approximately 95 percent). OTA adopts such language to avoid restating each time that a frequency depends on racial and ethnic background, not to underemphasize the importance in the distribution variation of CF mutations. In some cases-made clear within the text-a specific frequency is chosen for illustrative or hypothetical purposes.

of CF mutations. Using today's technologies, CF mutation analysis is usually a one-time test that can inform an individual whether he or she carries any of the CF mutations for which tests are conducted. Carrier *screening* for CF (or CF carrier screening) refers to performing CF mutation analysis on DNA from an individual who has no family history of CF

Current technology, however, can leave ambiguity, but not because the tests per se are imprecise. Properly performed, DNA-based tests for CF mutations are accurate and specific-meaning if the ΔF508 mutation (or another CF mutation) is present in the individual's genome and an assay is performed to search for that mutation, the test will detect it more than 99 percent of the time, absent laboratory error. Instead, ambiguity stems from the intrinsic nature of the cause of the disease: Besides ΔF508, more than 170 mutations in the CF gene also cause CF

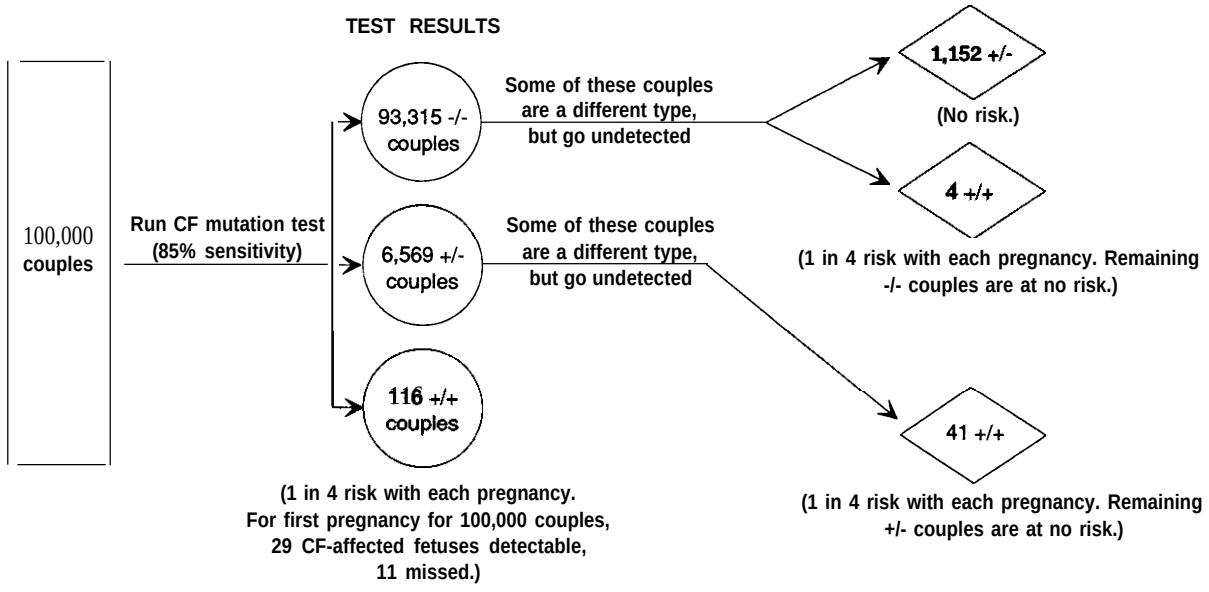
In the United States, about 1 in 25 Caucasians carries one CF mutation. Current assays use ΔF508 plus 6 to 12 other CF mutations (ΔF508+6-12) and identify about 85 percent of CF carriers (in Ashkenazic Jews, ΔF508+6 identifies about 95 percent of carriers). Thus, using ΔF508+6-12 means 10 to 15 percent of actual carriers go undetected. In other words, since tests to detect 170+ mutations are impractical, a negative test result does not guarantee that a person is not a carrier.

Using DF508+6-12 means that some couples receive test results that indicate one partner is a carrier and one is not, when in fact the negative partner carries one of the rare CF mutations that is not assayed. Thus, while most couples whose test results are +/- are at zero risk of having a child with CF some couples with a +/- test result actually are couples whose genetic status is +/+ (but goes undetected) and who are at 1 in 4 risk of a child with CF for each pregnancy. Couples with a +/- test result, then, might misunderstand that their reduced risk of bearing a child with CF is not zero risk (figure 1-2).

CONTROVERSY ABOUT CYSTIC FIBROSIS CARRIER SCREENING

Prospects of routine CF carrier screening polarize people. No mandatory genetic screening programs of adult populations exist in the United States. OTA has found it highly unlikely that CF carrier screening will set a precedent in this regard (l). People agree that persons with a family history of CF should have the opportunity to avail themselves of CF mutation analysis, yet controversy swirls around using the same tests in the general population.

Figure 1-2—Cystic Fibrosis Mutation Test Results at 85 Percent Sensitivity



SOURCE: Office of Technology Assessment, 1992.

Proponents of a measured approach to CF carrier screening express concern about several issues that might be raised if use of CF carrier tests becomes routine. Invariably, discussions about CF carrier screening raise concerns about the use of genetic information by insurance companies (2) and become linked broader social concerns about health care reform in the United States. Related to this are concerns about commercialization of genetic research, i.e., that market pressures will drive widespread use of tests before the potential for discrimination or stigmatization by other individuals or institutions (e.g., employers and insurers) is assessed. Also expressed are questions about the adequacy of quality assurance for DNA diagnostic facilities, personnel, and the tests themselves. Others also wonder whether the current number of genetic specialists can handle a swell of CF carrier screening cases, let alone cases from tests for other genetic conditions expected to arise from the Human Genome Project. Finally, the extraordinary tensions in the United States about abortion affect discussions about CF carrier testing and screening.

Those who advocate CF carrier tests for use beyond affected families are equally concerned about these issues. They assert, however, that individuals should be routinely informed about the assays so they can decide for themselves whether to be voluntarily screened. Proponents of providing such information believe that failing to inform patients now about the availability of CF carrier assays denies people the opportunity to make personal choices about their reproductive futures, either prospectively-e. g., by avoiding conception, choosing to adopt, or using artificial insemination by donor-or by using prenatal testing to determine whether a fetus is affected.

SCOPE AND ORGANIZATION OF THIS BACKGROUND PAPER

One of the tasks of genetic specialists is to provide the educational and counseling services necessary to successful implementation of new technologies. Increasingly, genetic counselors and nurses working in genetics will be at the front line on the issues raised by DNA technologies' assimilation into practice.

The OTA survey was conducted to better understand the environment in which the average genetic counselor or nurse in genetics works, to describe the infrastructure and tools available to these professionals, to assess the state of practice in the provision of CF carrier screening, and to evaluate their attitudes regarding CF carrier screening. The results of the survey are reported in chapters 2 and 3. A summary appears in chapter 4. A description of the survey methodology is in appendix A, and the survey instrument is reproduced in appendix B.

CHAPTER 1 REFERENCES

1. U.S. Congress, Office of Technology Assessment, ***Cystic Fibrosis and DNA Tests: Implications of Carrier Screening, OTA-BA-532*** (Washington, DC: U.S. Government Printing Office, August 1992).
2. U.S. Congress, Office of Technology Assessment, ***Genetic Tests and Health Insurance+Results of a Survey, OTA-BP-BA-98*** (Washington, DC: U.S. Government Printing Office, October 1992).

Chapter 2
Providers, Clientele, and Genetic Services

The purpose of the OTA survey was to evaluate the extent to which genetic counselors and nurses in genetics are routinely offering carrier screening for cystic fibrosis CF to their clientele, to assess their attitudes and beliefs about the appropriateness of such screening, and to obtain a sense of the environment in which they work. While members of the National Society of Genetic Counselors (NSGC) and the International Society of Nurses in Genetics (ISONG) are by no means the only health professionals providing genetic counseling, they comprise a professional segment devoted explicitly to that end. Physicians, social workers, public health workers, and research scientists also provide genetic services. Those groups were not included in this survey.

To better understand the setting in which routine carrier screening for CF might take place, OTA gathered data regarding not only counselors' attitudes and practices regarding CF carrier screening (ch. 3), but also the settings in which they work, the numbers and types of clients they serve, clinical practices, work routines, fees charged, and third-party payment options available to their clientele. Understanding the environment in which CF carrier screening takes place was a critical part of the analysis reported in *Cystic Fibrosis and DNA Tests: Implications of Carrier Screening (10).*

THE SURVEY POPULATION

Of the **703** members of the NSGC who received questionnaires, 351-or 50 percent—responded. Of the 110 members of ISONG who received the questionnaire, 80-or 73 percent—responded. Thus, 80 percent of the respondent group are members of NSGC and 20 percent are members of ISONG.[1]

As preliminary analysis revealed no significant difference in question response between the two populations, all data were combined for the final analysis. The combined response rate is 53 percent.

Genetic Counselors

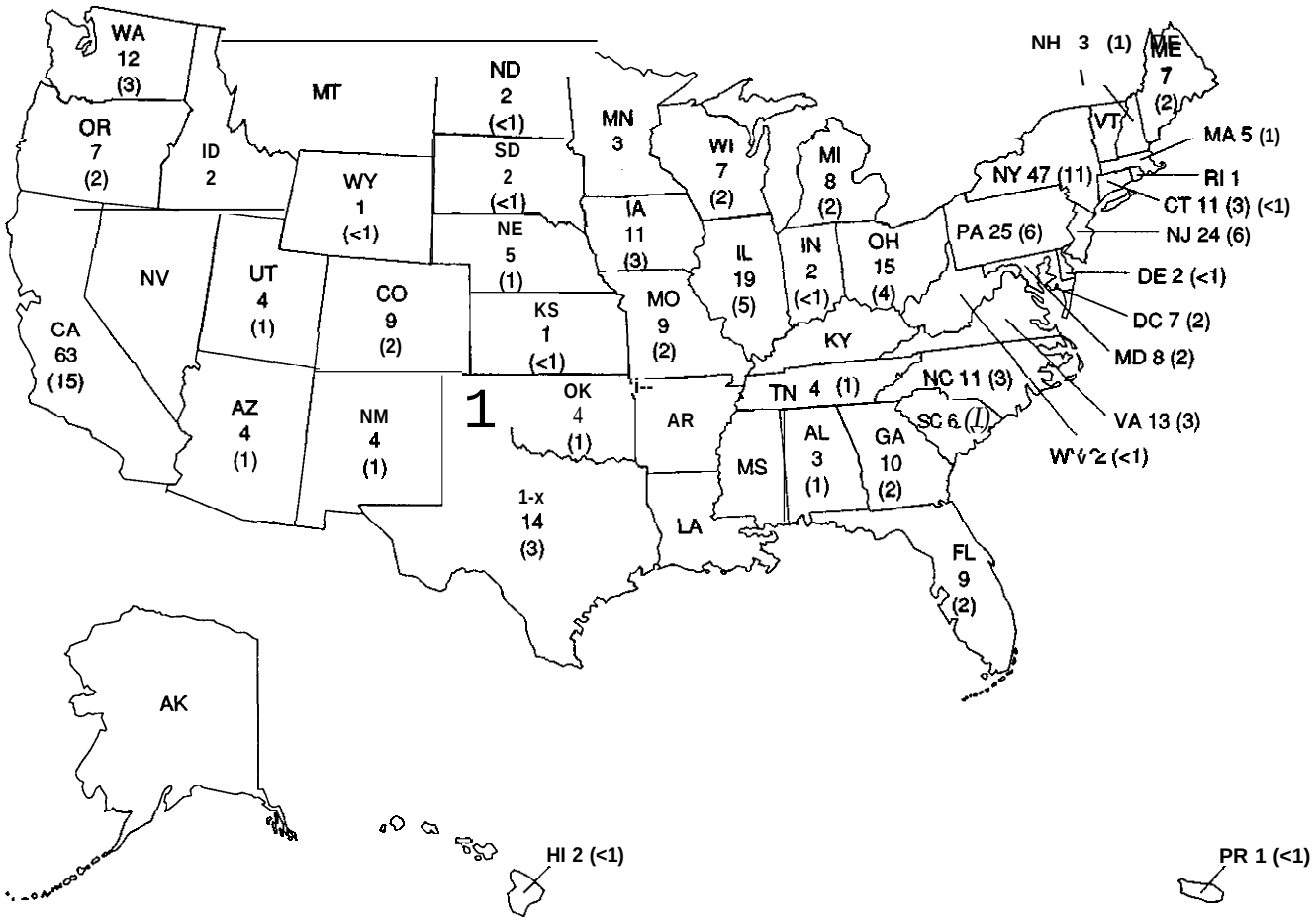
The master' s-level genetic counselor is a relatively new addition to the health care system. In 1971, 10 graduates of the first such program entered the workforce; in 1979, the NSGC was incorporated as a professional organization. Today, there are approximately 1,000 master' s-level genetic counselors practicing in the United States.

Master' s-level genetic counselors receive specialized multidisciplinary training and experience to prepare them for counseling related to a wide variety of genetic disorders and birth defects. They are typically graduates from a 2-year master's degree program, during which time they receive didactic course work in the principles and application of human genetics, clinical and medical genetics, genetic laboratory methods, and interviewing and counseling. Genetic counselors are also trained in social, ethical, legal, and cultural issues relating to genetic diseases, principles of public health and health care delivery systems, and education for the lay and professional community (12). Over the past 20 years, master' s-level graduate programs in genetic counseling have increased to 15, and combined, they produce approximately 75 graduates each year (7). At the time of the OTA survey, there were 703 genetic counselors who were full members of NSGC (associate, student, and foreign members were not surveyed). Of all respondents to the survey, 70 percent had a master's degree in genetic counseling. An additional 10 percent held a master's degree in another area, and 8 percent had a Ph.D.

Genetic counselors receive a minimum of 400 hours of supervised clinical trainingin at least three clinical settings, including a general genetics clinic, a prenatal diagnosis clinic, and a speciality disease clinic. Until 1992, graduates were eligible to sit for the certification examination in genetic counseling by the American Board of Medical Genetics (ABMG), but continuing certification of these individuals by this body is uncertain. In the past, counselors were required to submit their credentials and a logbook of 50 cases obtained in a clinically accredited training

[1] These response rates are typical of other mail surveys reported in the literature (1,6). One review found response rates for a two wave survey (initial mailing and one followup) ranged from 37 to 58.4 percent (6). OTA's aggregate response rate clearly falls within this range, as does the response rate of the genetic counselors; the response rate of the nurses in genetics exceeds it.

Figure 2-I-Geographic Distribution of Survey Respondents[a]



[a]Actual number of respondents from a State is listed, with the percentage the number represents in parentheses.
SOURCE: Office of Technology Assessment, 1992.

site before taking the exam (7). Most survey respondents survey were board certified (65 percent) or board eligible (19 percent).

Nurses in Genetics

There are nearly 2 million registered professional nurses in the United States, many involved in maternal and child health nursing. These professionals provide a unique potential to contribute to the effective delivery of genetic services. Efforts are under way to encourage the incorporation of clinical genetics into the curricula of schools of nursing at both the graduate and undergraduate level (4). The need for better genetics education in nursing stems from the recognition that genetics generally has been within the realm of tertiary care; thus, genetics specialists are not always in the position to screen every individual needing genetics referral (4). That is, individuals in need of genetic services must first be identified by the primary health care professiona1, and in some settings-such as community, occupational, or school health-nurses are the only link with the health care system (3). Thus, nurses can assist in the identification, education and counseling, and followup of patients (2,4). Though nurses can be a valuable part of genetics services, to date they are a largely untapped resource (3).

Opportunities for clinical genetics experience in nursing programs vary. Genetics is generally a part of the nursing school curriculum, but variability exists among programs (3). Four of the 200 universities in the United States that offer graduate degrees

in nursing have established programs providing a master 's-level genetics major (3). A small number of nurses, particularly those in maternal and child health nursing, have focused on genetics in order to sit for the genetic counseling examination given by the American Board of Medical Genetics (ABMG) (3,5). There are over 100 nurses employed in genetics who also belong to ISONG and therefore received OTA's questionnaire. It is likely that many more nurses deliver genetic services but are unidentifiable through current databases. Of the total survey respondents, 12 percent reported having either an R.N. or B.S.N. degree. Nurses might also have a master's degree or Ph.D. and could be included in the 80 percent of respondents who reported having a master's degree or the 8 percent who reported having a Ph.D.

Demographic Profile of Survey Respondents

The typical individual working as a genetic counselor or nurse in genetics is likely to be female (92 percent), in her mid-30s (mean age of 37), Caucasian (96 percent; 2 percent are Hispanic, 1 percent African American, 1 percent Asian American), and married (70 percent). On average, she is likely to have been in practice for 6 to 7 years, having received her degree in 1985. Eight-seven percent of these individuals speak only English; 5 percent also speak Spanish, and 8 percent speak English and a language other than Spanish.

Respondents represented every State except Arkansas, Louisiana, Kentucky, Mississippi, Montana, and Nevada (figure 2-1). There is a heavy concentration of counselors in five States, with 43 percent of respondents located in California, Illinois, New Jersey, New York, and Pennsylvania, and 23 percent located in three northeastern States, New Jersey, New York, and Pennsylvania (table 2-l). California had the highest representation at 15 percent. These data are consistent with those collected and biannually reported by the NSGC (8). Hence, OTA's survey respondent pool is representative of the NSGC membership and no sample weighting was necessary.

WORK ENVIRONMENTS

The majority of respondents (83 percent) are currently engaged in providing genetic counseling. Seventeen percent work in an environment where they are not encountering direct patient contact, perhaps serving as administrators, educators, or researchers. The primary work settings for all respondents are presented in table 2-2. Most counselors and nurses are employed in a university medical center (36 percent) or a private hospital or medical facility (36 percent). The remainder work in a variety of settings, such as public health departments, health maintenance organizations, colleges or universities, private group practices, free standing clinics, or commercial laboratories. Again, these data are consistent with the data collected by NSGC on a biennial basis for its professional status survey (8).

Table 2-l-Geographic Concentration of Survey Respondents

State	Number (percent)
California	63(1 5)
New York	47(1 1)
Pennsylvania	25(6)
New Jersey	24(6)
Illinois	19(5)
Total	178 (43)

SOURCE: Office of Technology Assessment, 1992.

Table 2-2—Primary Work Setting

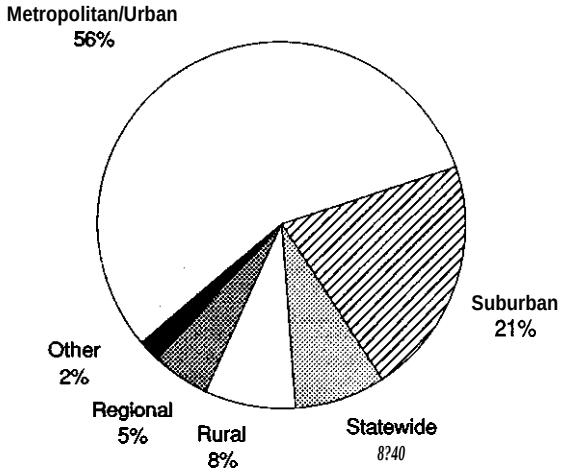
	Number (percent)
University medical center	151 (36)
Private hospital or medical facility	150(36)
Public health department	22(5)
Health maintenance organization	15(4)
College or university	14(3)
Private group practice	11 (3)
Free-standing clinic	10(2)
Commercial laboratory	9 (2)
Other	31 (7)

SOURCE: Office of Technology Assessment, 1992.

Centers of expertise in clinical genetics tend to be located at large urban medical centers, often with a teaching mission. The work location and setting of the survey population reflect that tendency. Respondents are most likely to work in a metropolitan or urban setting (58 percent) (figure 2-2). Counselors and nurses in genetics are less likely to be found working in rural settings. Counselors tend to work with M.D. geneticists, Ph.D. geneticists, other genetic counselors, and a variety of support staff. Most rural centers are unable to support this level of professional personnel and often rely on regional service areas. Five percent of respondents reported working in a regional genetics area.

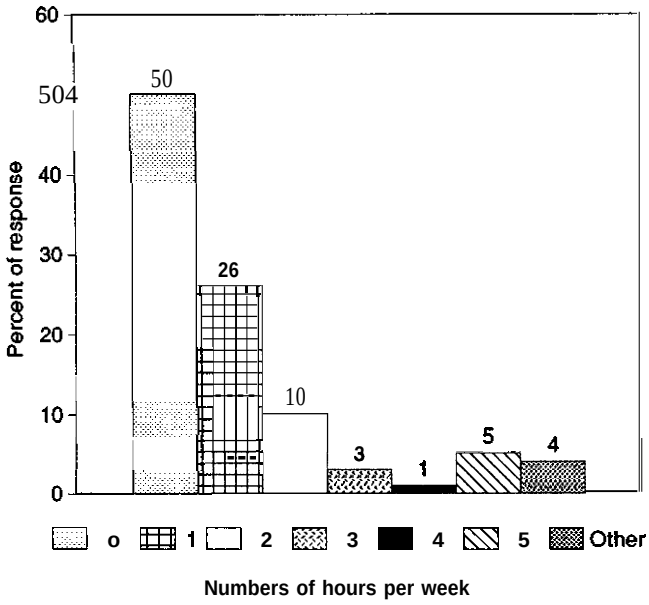
Respondents spend nearly two-thirds (65 percent) of their work week—about 26 hours per week-on patient activities, whether direct patient contact

Figure 2-2—Primary Service Areas of Respondents



SOURCE: Office of Technology Assessment, 1992.

Figure 2-3—Average Hours Spent Per Week on Public Education



SOURCE: Office of Technology Assessment, 1992.

(e.g., intake or counseling) or indirect (e.g., written communication, scheduling, and management of referrals) (table 2-3). An additional day is spent on administrative procedures. This leaves little time for other activities such as educating other health professionals or the general public. On average, counselors and nurses in genetics spend little time on public education. Fifty percent report spending no time on this activity, while 26 percent report spending, on average, an hour a week on public education (figure 2-3). Individual counseling sessions are time and labor intensive and are the primary format for delivering genetic information (table 2-4). Respondents report that they seldom if ever rely on group counseling (67 percent) or videotape with counseling (76 percent).

On average, each genetic counselor and nurse in genetics saw 482 patients in 1990. Averages do not, however, speak to the great variability among practices. Responses ranged from 10 to 2,300 clients. Counselors and nurses providing prenatal diagnosis and followup for elevated maternal serum alpha-fetoprotein (MSAFP) screening tend to have more clients.

In routine genetic counseling, the genetics specialist elicits the reasons for testing or screening and discusses the implications of possible outcomes. The counselor prepares the individual for both positive and negative test results. A genetic counseling session is also the time to discuss risk reduction strategies, irrelevant, and the nature and severity of the disorder for which the test is being done. One task of the genetics professional is to communicate risks to the client-a job not easily performed. The more complex the information, or the more emotionally laden, the more time might be required. Survey respondents estimate that the time needed to conduct routine prenatal counseling is 1 hour. Counseling for

Table 2-3-Average Weekly Schedule of Genetic Counselor or Nurse in Genetics

Activity	Hours per week
Direct patient contact	15
indirect patient activities.	11
Administration/management	7
Educating health professionals	3
Research	2
Educating the general public.	1
Marketing/business	1

SOURCE: Office of Technology Assessment, 1992.

Table 2-4-Formats for Genetic Counseling

	Predominant response (%)
individual counseling sessions	Almost always (84)
Group counseling	Seldom if ever (67)
Videotape alone	Seldom if ever (98)
Videotape with counseling	Seldom if ever (76)
Written educational materials.	Very often (24)
Slide-tape	Seldom if ever (88)
Interactive computer.	Seldom if ever (97)

SOURCE: Office of Technology Assessment, 1992.

newly diagnosed genetic disorders in newborns, children, or adults takes more time and more visits. Carrier testing for families with a positive family history for CF was estimated to take, on average, two visits involving more than 1 hour each. Counseling for CF carrier screening, with no family history, however, was estimated to take one visit of less than an hour. The need for sufficient and appropriate pretest education and post-test counseling is discussed in depth in the full OTA report (10).

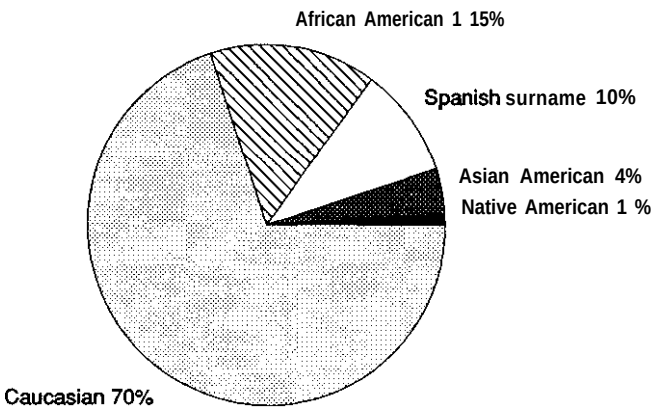
GENETICS CLIENTELE

Genetic counselors and nurses in genetics work in a variety of settings and often the setting in which they work dictates the types of clients they encounter. For example, working in a department of obstetrics and gynecology is likely to mean that the majority of one's clients are pregnant or undergoing family planning prior to pregnancy. Employment in a department of pediatrics or a children's hospital means that most clients are likely to be children and their families. Some counselors work in specialty clinics, such as cranio-facial clinics or sickle cell screening centers. Thus, their clientele are more likely to be adult or African American, respectively. The OTA survey results are reported in the aggregate and fail to illustrate that some practitioners work in specialized settings, often with one type of clientele.

The majority of individuals seen by genetic counselors and nurses in genetics are Caucasian (70 percent) (figure 2-4). Respondents report an ethnic and racial breakdown that is reflective of national population averages. For example, approximately 15 percent of genetics clientele are reported as African American; this minority group represents 12 percent of the U.S. population. These data do not provide information, however, about equitable allocation of genetic services locally or regionally. African Americans or Asian Americans might find genetic services accessible in one city or one region but not in another. Genetics services in cities with large minority populations might be more likely to hire health care providers with language or cultural skills suitable to certain populations.

Ninety-two percent of genetics clientele are English speaking. As mentioned earlier, 13 percent of genetic counselors and nurses reported fluency in a language other than English, but no effort was made by OTA to correlate provider fluency with clientele needs.

Figure 2-4—Racial/Ethnic Background of Clinical Genetics Clientele

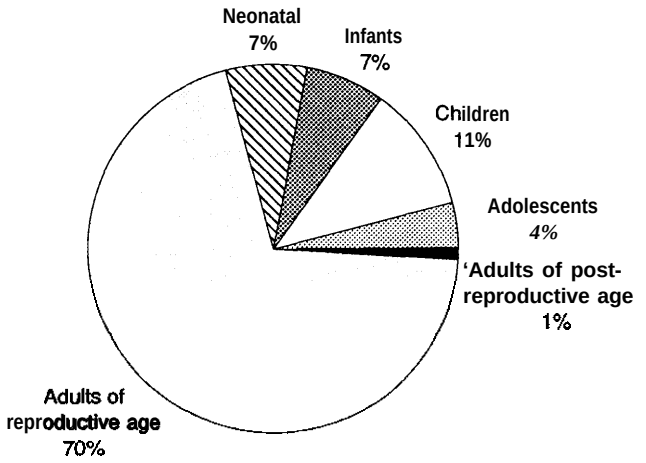


SOURCE: Office of Technology Assessment, 1992,

A variety of age groups are seen, but adults of reproductive age comprise 70 percent of the average clinic clientele. The second largest group of individuals seen are children (11 percent). Infants and neonates collectively comprise 14 percent of genetics clientele (figure 2-5).

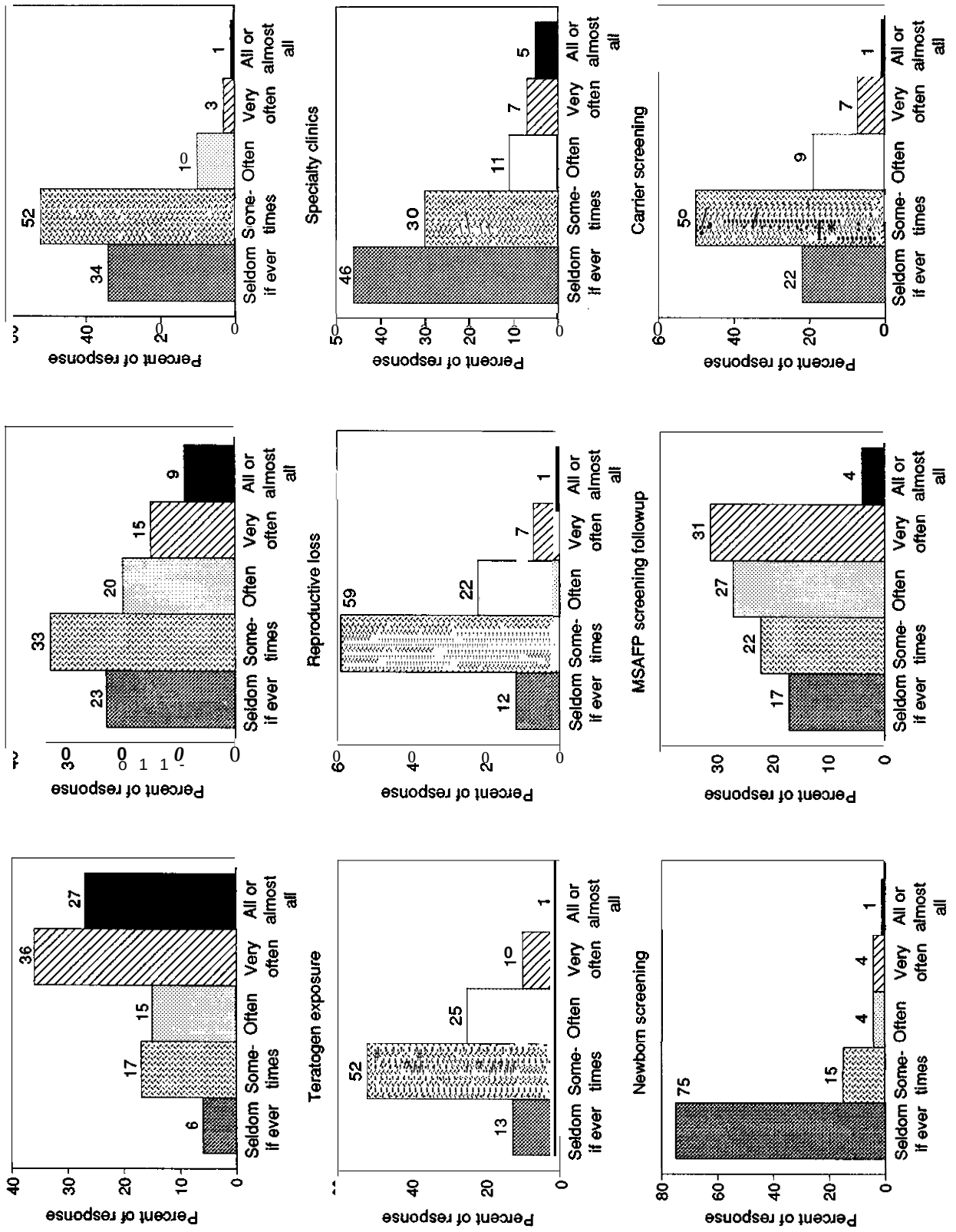
Most of the adults of reproductive age are seen for prenatal diagnosis (figure 2-6), most likely for advanced maternal age. Prenatal genetics patients were reported as being seen very often or almost always by nearly two-thirds of respondents (figure 2-6). Clearly, prenatal diagnosis is a primary reason for individuals to have contact with the clinical genetics setting. Respondents also reported that

Figure 2-5—Age Distribution of Genetics Clientele



SOURCE: Office of Technology Assessment, 1992.

Figure 2-6—Frequency of Patients Seen by Major Areas of Clinical Practice



SOURCE: Office of Technology Assessment, 1992.

pregnant women receiving followup counseling for abnormal MSAFP results often (27 percent) or very often (31 percent) are apart of their clientele (figure 2-6). Individuals seeking carrier screening for a variety of genetic disorders, such as those described in table 2-5, seldom (22 percent) or sometimes (50 percent) comprise the clientele in genetics clinics (figure 2-6). Cystic fibrosis was reported most frequently as the disease for which carrier screening or testing is offered (table 2-5), and a majority of respondents (62 percent) report they have seen more than 100 clients for CF-related reasons in 1990 (figure 2-7).

FEES AND THIRD-PARTY COVERAGE

How expensive are genetic services and will insurers pay for them? How do third-party payers decide what is medically indicated and, therefore, should be covered? Many of these issues are addressed in the full OTA report (10) as well as the Background Paper, *Genetic Tests and Health Insurance-Results of a Survey* (11). In this survey of genetic counselors and nurses, OTA obtained information about the fees charged by providers for a variety of genetic services, including those related to CF and their experiences with third-party coverage. Costs of services and the availability of third-party coverage will be crucial to the rate and magnitude at which services will be used. This is particularly relevant to the debate about CF carrier screening as the procedure is relatively new, is counter to most insurers' policies against paying for screening, and could involve potentially large numbers of people.

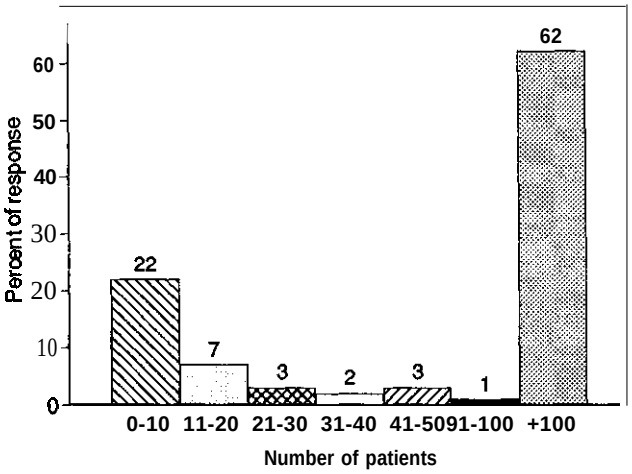
For many years, genetic counselors have faced the problem that few third-party insurers will reimburse for counseling services unless performed by a physician. The costs of counseling are reimbursed as general medical consultation fees or absorbed as part of costs on research grants (9).

Table 2-5-Most Common Diseases for Which Carrier Screening/Testing Is Offered

(Ranked by frequency of response)
1. Cystic fibrosis
2. Tay Sachs disease
3. Sickle cell anemia
4. Duchenne muscular dystrophy
5. Thalassemia
6. Hemophilia
7. Hemoglobinopathies
8. Fragile X syndrome

SOURCE: Office of Technology Assessment, 1992.

Figure 2-7—Number of Cystic Fibrosis Patients or Families Seen in Genetics Units in 1990



SOURCE: Office of Technology Assessment, 1992.

Fees for Genetic Services

Genetic counseling can be provided alone or in conjunction with diagnostic procedures. Most survey respondents work in large university or private medical centers where billing departments are often quite separate and distinct from the various clinical departments. Fees are coded and processed independently. This might explain why a majority of respondents did not know whether certain genetic services were reimbursable and, in some cases, did not even know the fee schedule for basic genetic services (table 2-6). For those who knew the fee schedule for genetic services, general genetic counseling averaged $80 per session. The range was $0

Table 2-6-Average Fees and Knowledge of Fees for Genetic Services

Service	Fee	Percent respondents uncertain of fee
General genetic counseling	$80	45
Genetic counseling for CF with a positive family history	$112	54
Genetic counseling for CF with a negative family history	$105	68
Routine metabolic screen	$157	70
Routine cytogenetic analysis	$425	50
DNA analysis for CF	$235	66

SOURCE: Office of Technology Assessment, 1992.

Table 2-7—Fees for General Counseling

Fee	Percent response
$0 to 50	
$51 to loo	31
$101 to 150	25
$151 to 200	2
$201 to 250	7
$251 to 300	
$301 to 350	38

SOURCE:Office of TechnologyAssessmentj 1992.

to $350 (table 2-7). The fee for genetic counseling for individuals with a family history of CF was not significantly different from the fee that would be charged to individuals requesting the same services with a negative history for CF($112 versus $105). In the summer of 1991, the average fee for DNA analysis for CF was $235 although spring 1992 data collected separately by OTA found an average cost of $170 per sample.

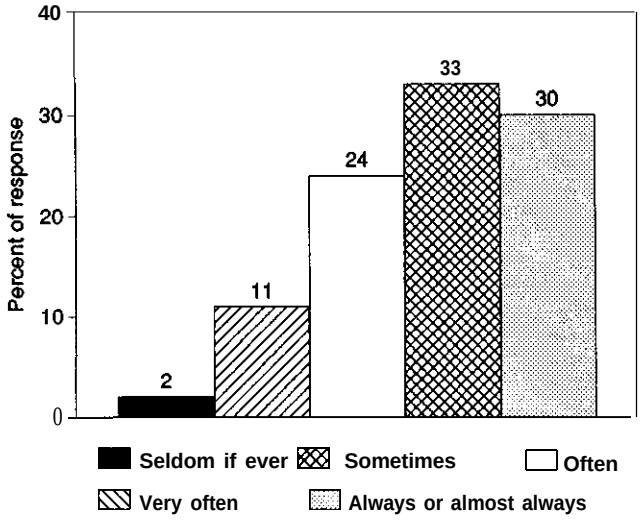
Third-Party Coverage

Respondents reported that most of their clients are covered by some type of health insurance. Two percent said that their patients seldom if ever have health care coverage, whereas 63 percent reported that their clients very often or always have coverage (figure 2-8). Commercial insurance, health maintenance organizations, or managed care programs comprise over half of the coverage (figure 2-9). Medicaid (21 percent) and Blue Cross/Blue Shield plans (17 percent) also cover genetics clients. Four percent of clients have no insurance and 3 percent are indigent.

With regard to coverage of genetic counseling services accompanying DNA-based tests to determine CF carrier status, respondents reported a higher likelihood of coverage if there is a family history of CF than if there is no family history (figure 2-10). This result was confirmed by OTA's survey of health insurers, which found health insurers rarely reimburse individuals for CF carrier tests in the absence of a family history (11).

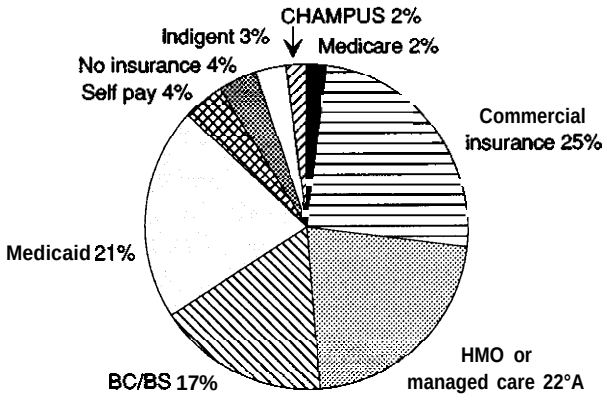
OTA attempted to ascertain whether individuals who avail themselves of genetic tests subsequently have difficulty obtaining or retaining health insurance. The survey asked for reported occurrences for genetic tests, generally, not just carrier tests for CF or other disorders.[2] OTA asked:

Figure 2-8-Health Care Coverage for Genetics Clientele



SOURCE: Office of Technology Assessment, 1992.

Figure 2-9-General Types of Health Care Coverage for Genetics Clientele



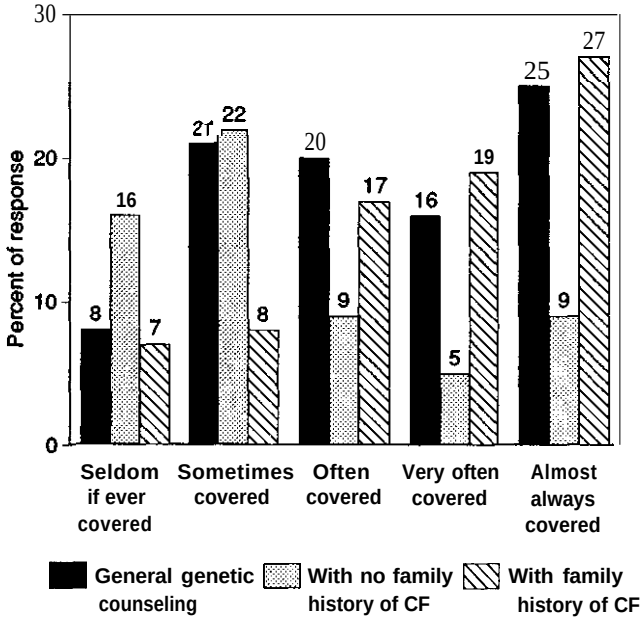
SOURCE: Office of Technology Assessment, 1992.

Have any of your patients experienced difficulties in obtaining or retaining health insurance coverage as a result of genetic testing? If yes, please provide details.

Approximately four-fifths (347) of the 431 respondents to OTA's inquiry currently perform genetic counseling. Fifty respondents (14 percent) reported they had clients who had experienced difficulties obtaining or retaining health care cover-

2 In a separate survey of health insurers, OTA asked respondents to speculate about accepting applicants with certain genetic conditions (11).

Figure 2-10-Third-Part y Reimbursement for General Genetic Counseling and Counseling Specifically for Cystic Fibrosis



SOURCE: Office of Technology Assessment, 1992.

age as a result of genetic testing (table 2-8). Because some respondents described more than one case, the number of affirmative answers understates the actual number of cases. Examination of the qualitative responses, some of which are presented in table 2-9, reveals affirmative responses represent, at minimum, 68 individual cases. (Where the term ''patients" was used with specifics not described, a single event was recorded.)

It is important to emphasize that most of the cases revealed through the OTA survey do not involve recessive disorders and carrier screening for conditions like CF And while one assumption might have been that health care coverage for CF carriers would not be an issue because the individuals have no symptoms of the disorder, OTA's survey of health insurers reveals that a few respondents would require a waiting period or deny coverage for CF carriers (10,1 1).

Test results for some conditions where positive results led to reported difficulties-such as for Huntington disease, adult polycystic kidney disease, and Marfan syndrome-were cited by more than one respondent. In addition to affirmative answers, several respondents reported that although they had no direct experience with a patient's difficulty in

Table 2-8-Difficulties in Obtaining or Retaining Health Insurance After Genetic Tests

Question: Have any of your patients experienced difficulties in obtaining or retaining health insurance coverage as a result of genetic testing?

	Number	(percent)
No	281	81
Yes	50	14
No answer	16	5

SOURCE: Office of Technology Assessment, 1992.

obtaining or retaining health care coverage, they had clients who feared their coverage would be dropped if they requested payment for tests from insurers. One respondent commented that greater than 80 percent of her clients who test for Huntington disease self-pay. Similarly, others with no direct experience said they often advise patients not to request reimbursement for a test so that an insurer would not learn that testing had occurred. One counselor offered the information that a patient had refused testing for adult polycystic kidney disease because of concern over health insurance. Another respondent reported that a patient with a CF-affected child had been dropped by one insurance company and would not consider prenatal testing in the future for fear her current insurer would not cover the child should she decide to continue the pregnancy.

The data collected through this question permit neither extrapolation about the total number of cases that have occurred in the United States nor speculation about any trends. OTA also did not attempt to ascertain whether patients had challenged-or were challenging-insurers' rulings. Thus, OTA cannot determine whether some of the disputes reported in table 2-9 were resolved fully in favor of the consumer because the initial judgment was deemed improper or illegal. Some cases, for example, reported a fetus or newborn had tested positive and the policy cancelled. In all 50 States and the District of Columbia, insurers must cover (or offer the option to include) a newborn child if a valid insurance contract for the parent exists. However, whether the insurance company can deny specific benefits for the newborn by evoking the preexisting condition clause generally contained in all insurance contracts is unclear.

In presenting table 2-9, OTA does not judge the validity-positively or negatively-of the claim. Some cases might have been settled in favor of the individual. Others might have been cases where an

Table 2-9-Case Descriptions of Genetic Testing and Health Insurance Problems[a]

Positive test for adult polycystic kidney disease resulted in canceled policy or increased rate for company of newly diagnosed individual.
Positive test for Huntington disease resulted in canceled policy or being denied coverage through a health maintenance organization.
Positive test for neurofibromatosis resulted in canceled policy.
Positive test for Marfan syndrome resulted in canceled policy.
Positive test for Down syndrome resulted in canceled policy or increased rate.
Positive test for alpha-1 -antitrypsin defined as preexisting condition; therapy related to rendition not covered.
Positive test for Fabry disease resulted in canceled policy.
Woman with balanced translocation excluded from future maternity coverage.
Positive Fragile X carrier status and subsequent job change resulted in no coverage.
After prenatal diagnosis of hemophilia-affected fetus, coverage denied due to preexisting condition clause.
Denied coverage or encountered difficulty retaining coverage after birth of infant with phenylketonuria.
Woman diagnosed with Turner's syndrome denied coverage for cardiac status based on karyotype. Normal electrocardiogram failed to satisfy company.
Family with previous Meckel-Gruber fetus denied coverage in subsequent applications despite using prenatal diagnosis and therapeutic abortion.
Mother tested positive as carrier for severe hemophilia. Prenatal diagnosis revealed affected boy; not revered as preexisting rendition when pregnancy carried to term.
After a test revealed that a woman was a balanced translocation carrier, she was initially denied coverage under spouse's insurance because of risk of unbalanced conception. Subsequently overturned.
Woman without prior knowledge that she was an obligate carrier for X-linked adrenoleukodystrophy found out she was a carrier. She had two sons, both of whom were healthy, but each at 50 percent risk. Testing was done so they could be put on an experimental diet to prevent problems that can arise from mid- to late childhood or early adulthood. One boy tested positive. The family's private pay policy (Blue Cross/Blue Shield) is attempting to disqualify the family for failing to report the family history under preexisting conditions.
After birth of child with CF unable to insure unaffected siblings or themselves.

[a]1991 OTA survey of genetic counselors and nurses in genetics. Not all cases, or multiple cases involving same disorder, listed.

SOURCE: Office of Technology Assessment, 1992.

applicant attempted to select against an insurer by misrepresenting his or her health history, which would have been resolved against the individual.

In 1991, at least 50 genetic counselors or nurses in clinical practice knew of at least 68 actual incidents where their own patients reported difficulties with health insurance due to genetic tests. OTA estimates, based on the average number of patients directly counseled, that genetic counselors and nurses responding to the survey collectively saw about 110,600 individuals in 1990. However, OTA did not advise respondents to limit descriptions of clients' insurance difficulty to 1990. Thus, it is unlikely that all reported cases occurred in 1990; assuming all cases occurred in 1990 means the 68 cases represent 0.06 percent of patients seen by respondents.

Critics question whether the data-especially the qualitative descriptions—merely represent more anecdotal stories that unfairly present one side of the story and for which no response can be developed. Skeptics point out that some of the cases might fall into the gray area of whether exclusion or increased rates resulted because an adverse medical condition was revealed through a diagnostic test that just happened to be genetic. The border between what conditions are genetic or not is blurred, however, and will become increasingly diffuse. Because genetic-based predictive testing promises to have a profound impact on clinical medicine-and because access to medical care is inextricably linked to private health insurance in this country-these cases underscore certain policy dilemmas arising from the increased availability of genetic assays.

SUMMARY

Although genetic counselors and nurses in genetics work in a variety of settings, they are concentrated in metropolitan medical centers on the West coast or Northeast region. States with a large proportion of rural residents are less likely to be served. The clientele served, in the aggregate, tend to be representative of the national averages for majority and minority groups, although no effort was made by OTA to match racial and ethnic data with regions, cities, or localities.

Most genetic counselors have a master's degree and are either certified or eligible for professional

certification. They spend most of their work week seeing or talking with clients. Less time is spent on administration and research, and even less on professional and public education. Seventy percent of the genetics clientele is comprised of adults of reproductive age suggesting the strong influence of prenatal diagnosis as a primary genetics service. Respondents report that their counseling services are frequently not covered by third parties, even when "medically indicated.'

OTA's survey reports consumers can experience difficulties in obtaining or retaining health care coverage after genetic tests. Because genetic-based predictive testing promises to have a profound impact on clinical medicine-and because access to medical care is inextricably linked to private health insurance in this country-these cases underscore certain policy dilemmas arising from the increased availability of genetic assays.

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Chapter 3

Cystic Fibrosis Carrier Screening: Policies and Practices

Prospects of routine cystic fibrosis CF carrier screening polarize people. Everyone agrees that persons with a family history of CF should have the opportunity to avail themselves of CF mutation analysis, yet controversy swirls around using the same test in the general population. This polarization is illustrated in the written comments of two survey participants.

> NO to widespread screening! Must be close to 100 percent detection for all CF mutations before it can even be considered.
>
> **Let's go with screening!** I can't believe we are not halfday through a pilot program by mid 1991.

As described in the full OTA report (18), proponents of a measured approach to CF carrier screening express concern about several issues that might be raised if CF carrier screening becomes routine, such as the use of genetic information by insurance companies to set rates or deny coverage, and concerns that market pressures will drive widespread use of tests before the potential for discrimination or stigmatization by other individuals or institutions is assessed. Also expressed are questions about the adequacy of quality assurance for DNA diagnostic facilities, personnel, and the tests themselves. Still others also wonder whether the current number of health care professionals in genetics can handle a swell of CF carrier screening cases, let alone cases of other genetic conditions arising from increased knowledge from the Human Genome Project. Finally, the extraordinary tensions in the United States about abortion affect discussions about CF carrier testing and screening.

In summer 1991, OTA asked genetic counselors and nurses in genetics to provide data regarding their experiences concerning CF carrier screening as a means to judge the validity of these concerns. The questionnaire was designed to gather data on the frequency of DNA analysis for CF carrier status and trends over time, clinic policies regarding CF carrier screening, counseling and clinical practices regarding CF carrier testing and screening, and sources influencing the development of, and policies and procedures related to, CF mutation analysis. Survey participants were also asked their opinions about who should conduct carrier screening, in what settings, and on what target population(s). Respondents were encouraged to rank the most important issues to be addressed before embarking on a large-scale screening program.

The data in this chapter are specific to CF carrier screening. Data regarding third-party reimbursement for DNA-based tests are presented in chapter 2, along with general demographic data concerning the survey respondents and their clientele and clinical settings.

POLICIES AND PRACTICES, SUMMER 1991

Survey participants were asked to consider three issues. First, what is their opinion or the policy of their institution about the appropriateness of CF carrier screening at this time? Second, what are the current logistics of providing DNA-based tests for CF carrier status-i.e., once a decision had been made to offer CF mutation analysis, which mutations are analyzed, and how are those individuals to be tested identified or contacted? Third, survey participants were asked to estimate whether requests for DNA-based tests for CF had changed since the tests' development in 1989.

Policies on Cystic Fibrosis Carrier Screening

Currently, it is standard practice to offer CF carrier tests to individuals who have a positive family history of CF (6,16,18). An unaffected sibling of an individual with CF has a 2 in 3 likelihood of being a CF carrier. A consanguineous uncle or aunt of an individual with CF has a 1 in 2 likelihood of being a carrier. A first cousin of an individual with CF has a 1 in 4 likelihood of being a carrier (table 3-l).

As of the summer of 1991, most genetic counselors and nurses in genetics did not offer unsolicited CF mutation assays to individuals with a negative family history. A large majority of survey respondents use medical journals and other professional sources to obtain information regarding new advances in human genetics (table 3-2), and the American Society of Human Genetics (ASHG) and the National Institutes of Health (NIH) published policy documents in 1990 discouraging CF carrier

Table 3-I—A Priori Carrier Risks for Cystic Fibrosis

Negative family history	
Caucasian	1 in 25 (4%)
African American	1 in 60 to 65 (1.5 to 1.7%)
Asian American	1 in 150 (0.7%)
Hispanic American	1 in 46 (2.2%)
Positive family history	
Parent of child with CF	1 in 1 (100%)
Sibling with CF	2 in 3 (67%)
Aunt or uncle with CF[a]	1 in 3 (33%)
First cousin with CF	1 in 4 (25%)
Niece/nephew with CF	1 in *2 (50%)*

[a]Consanguineous.

SOURCE: Office of Technology Assessment, 1992.

Table 3-2-Sources of Information About New Advances in Human Genetics

Human genetics	Percent indicating yes
Medical journals	96
Professional colleagues	94
National inferences	83
American Society of Human Genetics	82
National Society of Genetic Counselors	80
State or regional conferences	71
Grand rounds	44
Lay press	37
Continuing education courses	35
Literature from biotechnology companies or commercial firms	35
Other	8

SOURCE: Office of Technology Assessment, 1992.

screening (6,16).[1] Seventy-six percent of respondents stated that they were familiar with the 1990 ASHG statement. Thirty-five percent were familiar with the NIH statement.

OTA's survey of genetic counselors and nurses revealed that 53 percent of respondents believe that CF carrier tests should only be offered to individuals with a positive family history of CF and not to those with a negative family history. Twenty-one percent felt that CF carrier tests should be offered to individuals with no family history. The most frequently cited reasons for making tests available to individuals regardless of family history were to reduce anxiety or increase patient autonomy. In the words of one counselor, ''DNA screening is a personal issue, different in every case. What one person or family feels may be quite different from that of another person or family in any given genetic disorder with any given family history.' Twenty-six percent of respondents were uncertain as to whether they should provide CF carrier screening where family history is negative.

When asked about their likelihood of introducing the topic of CF carrier tests during a counseling session, 82 percent of respondents stated that they would seldom, if ever, do so to all patients or families (table 3-3). Seventy-three percent would seldom, if ever, discuss it with pregnant women seeking prenatal diagnosis unless there was a family history of CF in which case, 90 percent would almost always bring it up during counseling.

When asked whether their institution or clinic had a specific policy regarding CF carrier screening, 33 percent of genetic counselors and nurses responded in the affirmative. Of those responses, 70 percent stated that it is the policy of their clinic or organization to offer CF carrier tests only to those with a positive family history (table 3-4).

The overall lack of policies for CF carrier screening apparently stems from the fact that, in general, explicit and official policies for clinical practices were not routine at the majority of facilities. When asked whether their group or unit had

Table 3-3-Likelihood of Introducing the Topic of DNA Testing for Cystic Fibrosis

Patient population	Predominant response	(Percent)
All patients/families	Seldom if ever	(82)
Pregnant women seeking prenatal diagnosis	Seldom if ever	(73)
Coupies/individuals with a family history of CF	Almost always	(90)
Caucasian coupies/individuals with a negative history of CF	Seldom if ever	(65)
individuals/famiiies who inquire about CF	Almost always	(80)
Selected coupies/individuals	Seldom if ever	(72)

SOURCE: Office of Technology Assessment, 1992.

Table 3-4-Specific Policies Regarding DNA Testing for Cystic Fibrosis

Policy	Percent
Offer to all regardless of family history	14
Offer only to those with a positive family history	70
Provide to those with no family history upon request if informed consent is obtained	16

SOURCE: Office of Technology Assessment, 1992,

[1] In 1992, ASHG's leadership issued a revised statement that CF mutation analysis ' 'is not recommended' fOr those without a family history of CF, but it has not yet been published (1,18).

official policies and procedures for other issues in genetics, 21 percent reported they have policies regarding DNA storage, 42 percent have policies in place concerning prenatal diagnosis for sex selection, 37 percent have policies regarding cases of nonpaternity, and 28 percent adhere to policies regarding confidentiality and Huntington disease testing.

Criteria for Cystic Fibrosis Carrier Screening

Sixty-five percent of survey participants felt strongly that there is an optimum rate of detection that should be reached before they would feel comfortable offering CF carrier screening, as compared to 14 percent who felt there is not and 21 percent who were uncertain. Of those who felt there is an optimum rate of detection, nearly half (46 percent) said that 95 percent test sensitivity should be required before proceeding with widespread screening. Twenty-five percent believe test sensitivity should be even higher, with 4 percent stating that it should be 100 percent (figure 3-l).

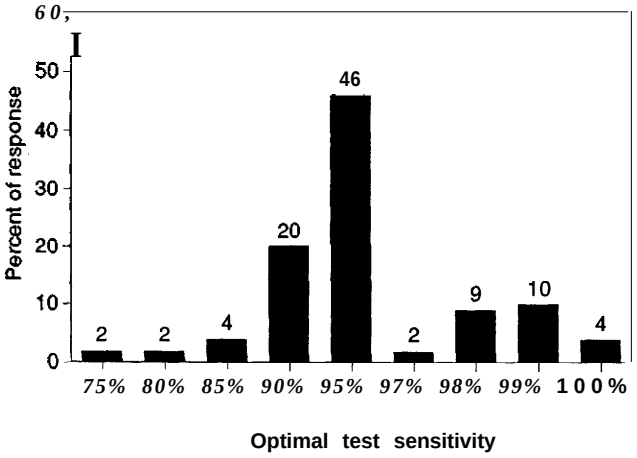
However, survey respondents ranked the availability of adequate counseling and an adequate system of referral for individuals who test positive as slightly more important criteria for CF carrier screening than test sensitivity (table 3-5). Guarantee of informed consent also was mentioned as necessary for implementation of large-scale CF carrier screening.

Perhaps the point on which there was greatest consensus among the respondents is on the issue of autonomy and choice in screening. There are no mandatory genetic screening programs of adult populations in the United States. Ninety-nine percent of survey participants responded that CF carrier screening should be voluntary and never mandatory.

Practices Regarding DNA-Based Cystic Fibrosis Carrier Tests

When asked about the frequency of requests for DNA testing or screening for CF carrier status during the 6-month period from January to June 1991, most respondents reported occasional requests (figure 3-2). When asked to compare this time period with the previous 2 years, nearly half indicated a small increase in the number of requests and a quarter noted a large increase in requests (figure 3-3). The survey did not distinguish whether the requests were carrier tests for individuals known to be at risk by virtue of family history or carrier screens for individuals with no known family history of CF

Figure 3-l—Opinions on Optimal Rate of Detection



SOURCE: Office of Technology Assessment, 1992.

Table 3-5-Minimal Criteria for Cystic Fibrosis Carrier Screening Protocol

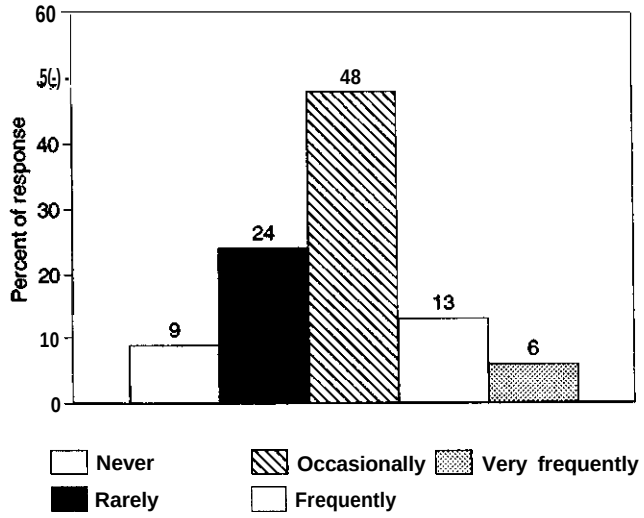
Question: What do you feel should be the minimum criteria for CF carrier screening protocol)?	
Criteria	**Percent[a]**
Provision of adequate counseling	40
Adequate system of referral in place	37
Improved test sensitivity.	35
Guarantee of informed consent	32
Availability of educational materials.	18
Only offer to families with a positive history of CF	15
Must be voluntary.	14
Reasonable cost or payment	12
Protection of confidentiality	12

[a]Percentages do not add to 100; respondents could reply with multiple answers.

SOURCE: Office of Technology Assessment, 1992.

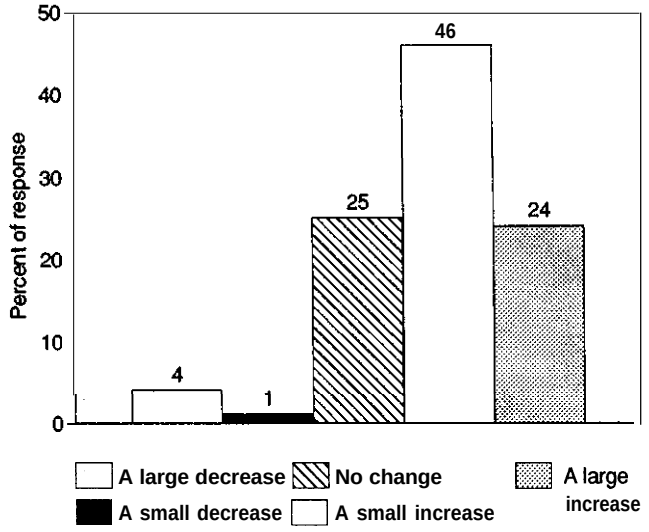
Although 55 percent of survey participants responded that a CF treatment center exists at their institution, 86 percent reported that they do not provide genetic counseling through that facility. Several respondents noted that this is the choice of the CF treatment provider, not necessarily the genetics unit. Because OTA did not survey CF treatment centers, it is not known to what extent CF families are informed of, offered, or request carrier testing. The data do show, however, that most families who have a child with CF are not routinely

Figure 3-2—Frequency of Requests for Cystic Fibrosis Carrier Screening/Testing, January-June 1991



SOURCE: Office of Technology Assessment, 1992.

Figure 3-3-Comparison of Requests for cystic Fibrosis Carrier Screening/Testing Between January-June 1991 and Past 2 Years



SOURCE: Office of Technology Assessment, 1992.

seen in genetics service settings, and few counselors have routine contact with CF families.

Encouraging known carriers to notify consanguineous relatives (e.g., siblings and first cousins) provides economic and pragmatic benefits because it can detect a larger percentage of at-risk couples (18); testing those known to be at higher risk because of family history is more effective than screening those with unknown risk. In reality, complex psychological factors enter when family members of individuals with CF contemplate screening, and it cannot be assumed that all will want to be tested.

For this type of carrier identification to work, those providing health care and counseling to CF families will have to actively participate in referrals of relatives to genetics centers, an uncommon practice, according to OTA's data. Fewer than 10 percent of respondents reported contacting previously identified CF families with whom they had had contact about the availability of CF mutation analysis.

For those respondents whose institutions are engaged in CF carrier testing or screening, direct DNA mutation analysis is the most common approach (table 3-6). In the recent past, the sensitivity of the carrier test was limited to the DF508 mutation. All respondents involved in analyzing CF carrier status assay for the DF508 mutation. But roughly 74 percent indicated that they also test for at least one other mutation, most commonly four others, G551D, R553X, G542X, and N1303K (table 3-7). At the time the survey was done, the mutation that accounts for 60 percent of CF mutations in Jewish persons of

Table 3-6—Types of Genetic Analyses Provided for Cystic Fibrosis Screening/Testing

Procedure	Percent response
Direct mutation analysis	67
Prenatal DNA analysis	63
DNA linkage analysis	61
DNA haplotyping	56
Staging of studies	37
DNA banking	31
Fetal intestinal enzyme analysis	28

SOURCE: Office of Technology Assessment, 1992.

Table 3-7-Cystic Fibrosis Mutations Routinely Analyzed

Mutation	Percent response
DF508	100
G551D	77
R553X	76
G542X	71
N1303K	70
Other	79

SOURCE: Office of Technology Assessment, 1992.

Central and Eastern European descent (Ashkenazic Jews), W1282X, had not been found.[2]

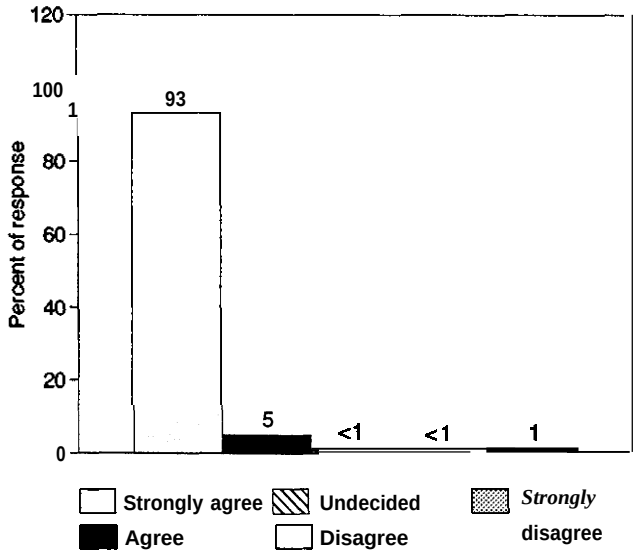
Respondents report an almost even split between commercial and university-based laboratories as the facility performing their CF mutation assays (45 percent and 48 percent, respectively). Most centers send the sample offsite (76 percent), frequently to a laboratory greater than 150 miles away.

Finally, although the need for professional and public education was cited as critical for the implementation of widespread carrier screening, few genetic counselors and nurses in genetics reported spending professional time engaged in either activity. For those respondents who do, an average of 3 hours per week devoted to educating health professionals and 1 hour per week on educating the general public was reported (ch. 2). For CF carrier screening, specifically, 8 percent of genetic counselors and nurses had developed, or were in the process of developing, educational materials relevant to DNA tests for CF mutation.

PREFERRED STRATEGIES AND PROTOCOLS

The importance of informed consent, careful presentation of counseling, and confidentiality have long been recognized as essential components of genetic testing and screening (9). Respondents strongly agreed that genetic counseling should precede DNA tests for CF carrier status regardless of family history (figures 3-4 and 3-5). Geneticists, perhaps more than any other medical specialty, have advocated a nondirective approach to counseling and have a strong commitment to patient autonomy (3). Further, a history of concern exists about the delivery of genetic information by health professionals used to a more directive approach (7). This concern has been played out in the debate over maternal serum alpha-fetoprotein (MSAFP) screening and is a factor in the reluctance of the clinical genetics community to rush toward widespread screening for any disease (18). For example, as part of the debates surrounding MSAFP and CF carrier screening, concern has been voiced about informed consent—in particular, that tests would be available to primary care practitioners who might incorporate

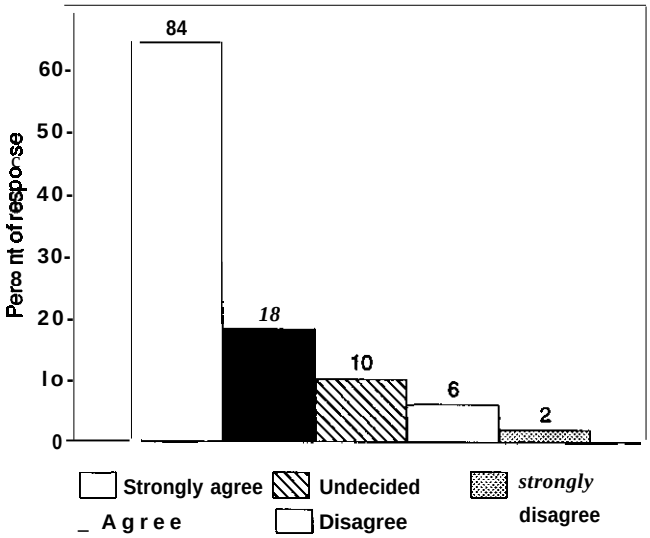
Figure 3-4-Opinions Regarding Genetic Counseling of Individuals with a Positive Family History



Genetic counseling should precede DNA testing for CF when there is a positive family history.

SOURCE: Office of Technology Assessment, 1992.

Figure 3-5-Opinions Regarding Genetic Counseling of Individuals with a Negative Family History



Genetic counseling should precede DNA testing for CF when there is a negative family history.

SOURCE: Office of Technology Assessment, 1992.

2 When the survey was fielded, test sensitivity was 75 to 85 percent, depending on race and ethnicity. Today, most commercial and university laboratories examine DF508 and 6 to 12 additional mutations, and taken together these mutations comprise 85 to 90 percent of CF mutations in U.S. Caucasians (95 percent in Ashkenazic Jews).

the assay into their practice without considering the informed consent requirements usually adhered to in genetics practices. Seventy-nine percent strongly agree that informed consent prior to CF carrier screening is a necessity (figure 3-6).

In addition to informed consent, prescreening education for clients is imperative. Information regarding an individual's a priori risk, types of tests available, and uncertainties in risk assessment based on screening results are important for potential screenees to understand. When asked if educational materials can provide adequate information about CF carrier screening, 44 percent disagreed or strongly disagreed with that concept (figure 3-7).

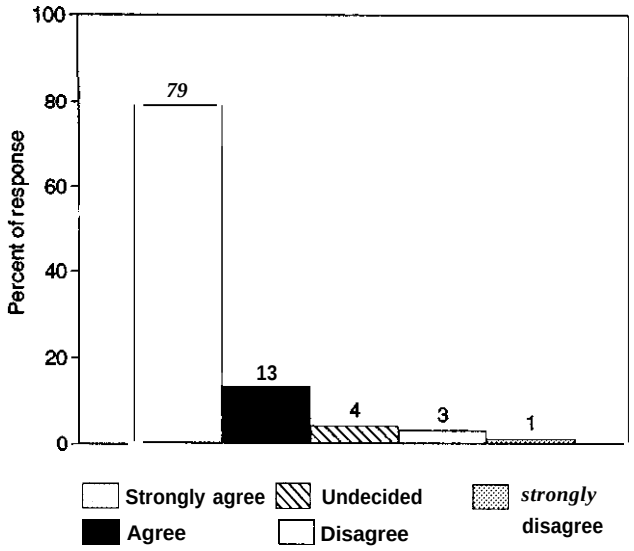
Who Should Provide Cystic Fibrosis Carrier Screening?

Concern about the complex nature of some genetic information and the need in some cases for post-test counseling leads many human genetics professionals to advocate restricting CF carrier screening primarily to the human genetics community. Pretest education, felt many respondents, can be offered by a wide range of professionals (figure 3-8), but organizing CF carrier screening should be provided by genetic specialists (table 3-8). Nearly 82 percent of the respondents surveyed by OTA said the human genetics community should be the primary organizer of CF carrier screening programs (table 3-8). Also mentioned were State or local health departments (59 percent) and primary caregivers (27 percent). Over 89 percent believed CF population screening should be provided in genetics centers, but 59 percent thought CF carrier screening could also be provided in the primary care setting or organized, community-wide programs (53 percent) (table 3-9). Concern about the sometimes difficult nature of communicating risk information regarding CF even for experienced genetic centers—has led some in the clinical genetics community to caution against rapid movement to routine CF carrier screening (2). In the words of one respondent:

> Counseling should not be left to hurried family practitioners or OB's [obstetrician/gynecologists], who routinely spend less than 15 minutes with each patient.

As noted in chapter 2, most counselors and nurses spend little to no time on professional education or general public education in schools and communities. Thus, the majority of people will rely on their primary care provider for preliminary, if not most,

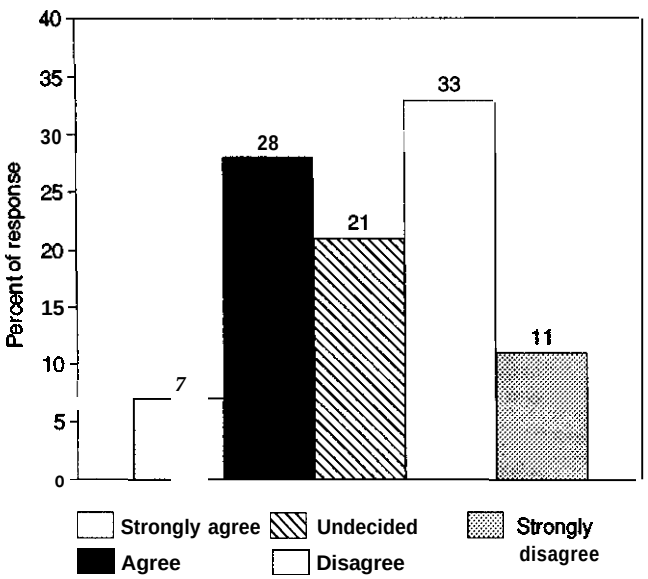
Figure 3-6—Opinions Regarding the Need for Informed Consent Prior to Cystic Fibrosis Carrier Screening



Informed consent prior to CF carrier screening is a necessity.

SOURCE: Office of Technology Assessment, 1992.

Figure 3-7-Opinions Regarding the Use of Educational Materials as a Source of Information About Cystic Fibrosis Carrier Screening



Educational materials (culturally sensitive and understandable) can provide adequate information about CF carrier screening.

SOURCE: Office of Technology Assessment, 1992.

Table 3-8—Preferred Organizations for Implementation of Voluntary Cystic Fibrosis Carrier Screening

Organization	Yes	No[a]
	(percent)	
Human genetics community	82	15
State or local health department	59	39
Voluntary health organizations	30	67
Primary caregivers	27	71
Medical societies	17	81
Federal Government	15	82

[a]3 percent gave no response

SOURCE: Office of Technology Assessment, 1992.

Table 3-9-Preferred Sites for Cystic Fibrosis Carrier Screening Programs

Site	Yes	No[a]
	(percent)	
Genetics centers	89	7
Primary care setting	59	37
Community-wide	53	43
Public health department	48	49
Public schools	14	83
Workplace	9	87

[a]3.5 percent gave no response

SOURCE: Office of Technology Assessment, 1992.

genetic information (18), and many survey respondents said primary care providers and public health departments should play an active role in educating the public about DNA tests for CF carrier status (figure 3-8). Health care provider and community-wide genetics education will become increasingly important, as will the interaction of genetic specialists with other health professionals and the public.

Who Should Pay for Cystic Fibrosis Carrier Screening?

When asked who should pay for screening, 80 percent of respondents ranked third parties as the primary source of payment (table 3-10). Self pay was ranked second, and employers ranked last. Additionally, some participants noted that if screening ever became mandatory, as in many State newborn screening programs, the State or Federal Government should be responsible for payment.

Strategies for Screening Various Populations

Two key considerations in deciding how routine CF carrier screening is best implemented are the clinical settings in which it will take place and the target populations. Delineation of a target group (or groups) determines other elements such as location, educational approach and tools, time, format, types of counseling, facilities, and publicity.

The NIH statement on CF carrier screening emphasized the importance of preconceptional screening (16). Most pilot projects in the United Kingdom are directed at preconceptional populations (18). One program in Canada targets high school students (11).

Newborn Screening

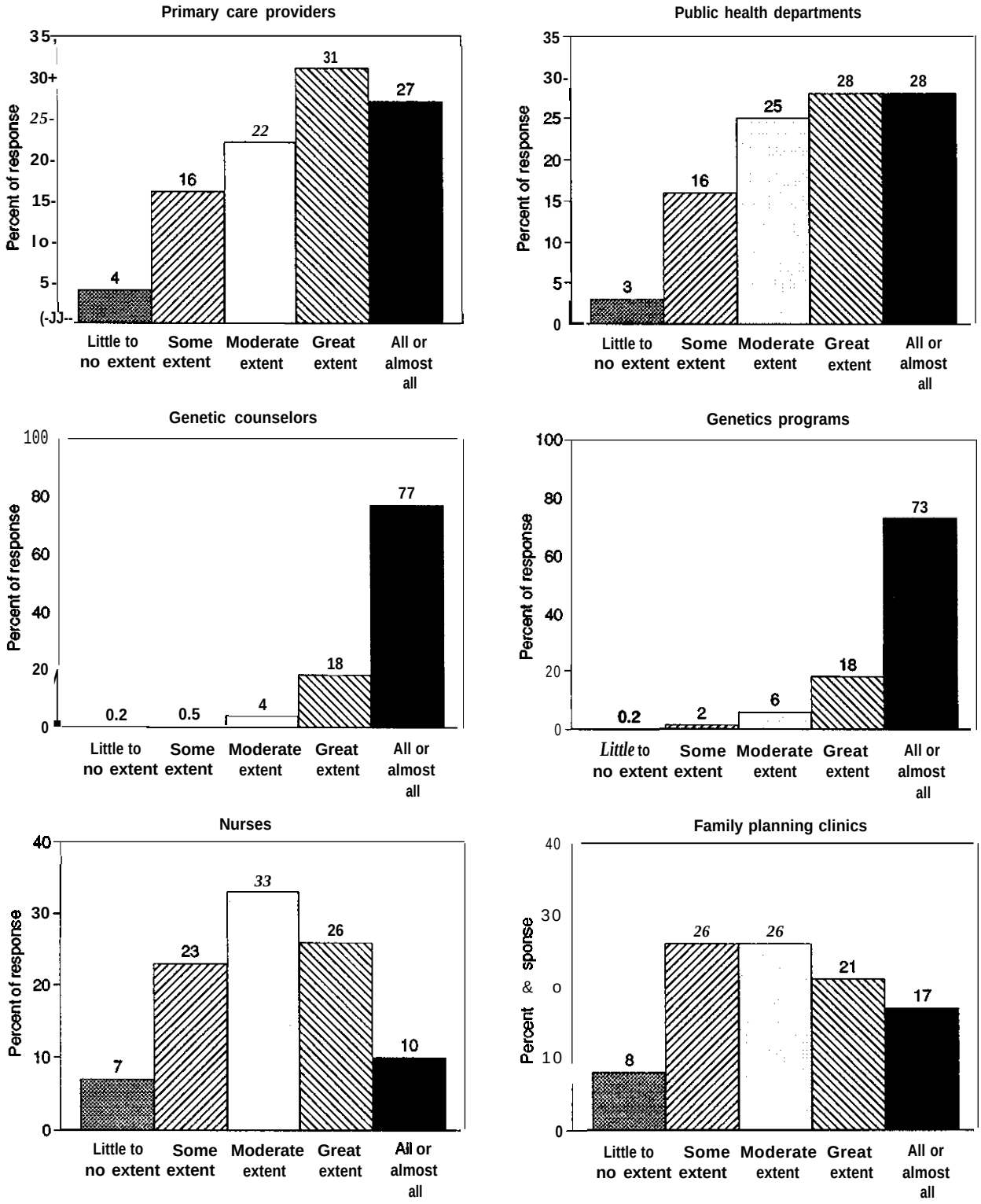
Numerous newborn screening programs exist for genetic disorders such as sickle cell anemia and phenylketonuria. These are programs intended to screen for the presence of disease, although some can also detect the carrier status of the newborn. Using the immunoreactive trypsin assay, Wisconsin has performed statewide neonatal screening for CF disease since 1985, and primary care physicians have been cooperative in referring screened patients to designated CF centers for followup (14). But even newborn screening for CF disease is not without controversy. Evidence of heightened anxiety and disrupted maternal-infant bonding have been reported in cases of false-positive diagnoses (4).

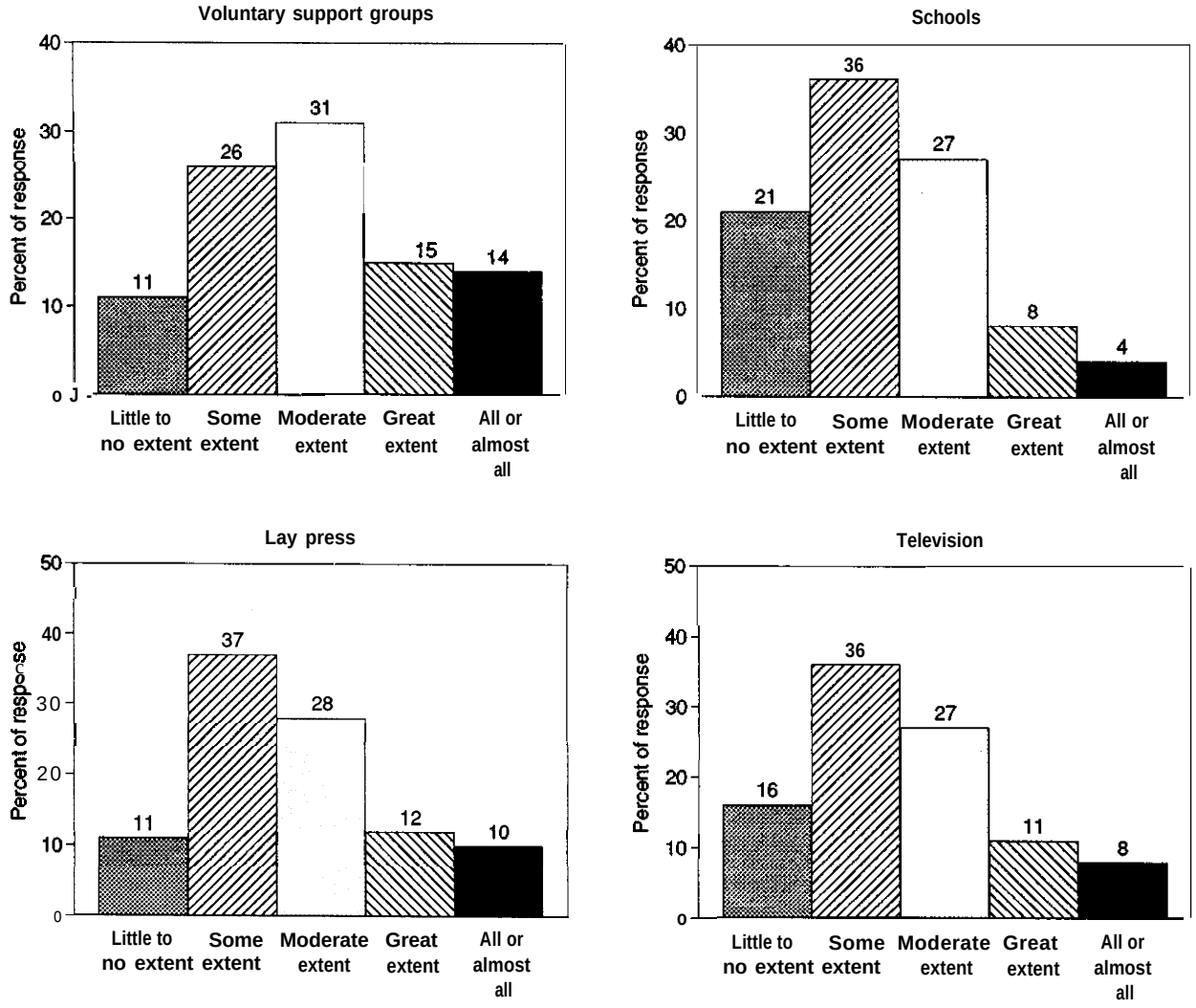
For at least two reasons, many believe that newborn screening is an inappropriate and inefficient mechanism for carrier detection. First, newborns determined to be carriers must be tracked through their reproductive years to ensure they are aware of their carrier status. Second, detection of newborn carriers might unnecessarily raise the anxiety level of parents. Thus, newborn screening for CF carrier status is not generally viewed as acceptable (15). This survey revealed that 33 percent of genetic counselors and nurses in genetics believed the newborn population would be an appropriate target group for widespread CF carrier screening (table 3-11).

Adolescent Preconceptional Screening

Some geneticists advocate carrier screening at the high-school level (11). A recent nationwide survey of American attitudes about, and knowledge of, genetic tests showed better knowledge and more positive attitudes in younger populations (17). Studies of pregnant women known to be carriers of a hemoglobinopathy gene have shown that age is a predictor of postcounseling knowledge-younger women (and adolescents as young as 12 years old) are more likely to understand genetic information (13). While not routinely done in the United States,

Figure 3-8-Extent to Which Various Groups Should Be Involved with Cystic Fibrosis Pretest Education





SOURCE: Office of Technology Assessment, 1992.

high-school screening programs have been conducted in Montreal, Canada for some time. For any disease where screening is done in childhood or adolescence, however, the benefits of such screening, including savings in resources or anxiety, must be balanced against the potential problems, such as the possibility that an adolescent will be falsely assigned to a low-risk group because of poor test sensitivity (thereby obviating further screening), or the possibility of psychosocial harm to the child as a result of identified carrier status (9).

Adolescents were not considered an appropriate target by the genetic counselors and nurses surveyed by OTA (table 3-11). Less than one-fifth felt individuals ages 13 to 18 years should be screened; only 6 percent responded that children ages 2 through 12 years should be screened.

Adults—Preconceptional or Prenatal?

One debate surrounding CF carrier screening focuses on whether the goals are best accomplished by targeting preconceptional adults or pregnant women. These approaches are not necessarily mutually exclusive. Many believe, however, that the receipt of troubling information during pregnancy is not desirable, and that it would be better for

Table 3-10-Who Should Pay for Cystic Fibrosis Carrier Screening?

Rank order
1. Third parties
2. Self pay
3. State, city, or county
4. Federal Government
5. Employers

SOURCE: Office of Technology Assessment, 1992.

Table 3-1 l—Target Populations for Cystic Fibrosis Carrier Screening

Population	Yes	No[a]
	(percent)	
Adults in reproductive years.	88	8
Prenatal	75	22
Pregnant women or "couples"	66	31
Newborns	33	63
Children ages 13 to 18	19	78
Children ages 2 to 12	6	91
Adults in post reproductive years.	3	94

a3percent had no response in each category.

SOURCE: Office of Technology Assessment, 1992.

individuals to know their risks before getting pregnant (12). Others argue that individuals not facing a pregnancy are not motivated to seek or use information on their carrier status, but will wait until they are either planning a family or starting a family before viewing such information as useful (5).

CF carrier screening offered as part of primary health care rather than prenatal care is likely to encourage preconceptional CF carrier screening. For most individuals, however, the first real opportunity for carrier screening takes place postconception (8). In the future, the primary responsibility for providing CF carrier screening might reside with the obstetrician, as has happened with MSAFP screening. Sixty-six percent of respondents to OTA's survey identified pregnant women or couples as the appropriate target population for CF carrier screening, yet 88 percent more generally identified adults in their reproductive years as the appropriate target group (table 3-11). While most respondents state that the *ideal* target population for carrier screening is the preconceptional adult, in reality, the first target population is likely to be the prenatal population because it has been the traditional entry point into genetic services for many people and comprises the largest population served by genetics centers (table 3-12).

Table 3-1 2—Frequency of Patients Seen by Major Areas of Clinical Practice

Area	Predominant response
Prenatal genetics.	Very often
Pediatric genetics	Sometimes
Adult genetics	Sometimes
Teratogen exposure	Sometimes
Reproductive loss	Sometimes
Specialty disease(s) clinics	Sometimes
Newborn screening	Seldom if ever
MSAFP screening followup.	Often
Carrier screening	Sometimes

SOURCE: Office of Technology Assessment, 1992.

PROFESSIONAL CAPACITY

Another issue in considering widespread carrier screening for CF is whether there are enough adequately trained health professionals to handle the volume of tests. One study estimated that a minimumof651,000 counseling hours would be required annually if the maximum estimate of 6 to 8 million preconceptional couples are screened for CF carrier status (19). Considering the current number of practicing genetic counselors in the United States today, this translates to 17 weeks per year from each genetic counselor to serve solely CF-related clients. On the other hand, another estimate suggests the supply of genetic specialists could absorb routine carrier screening for CF sickle cell anemia, hemophilia, and Duchenne muscular dystrophy, assuming that obstetricians or other primary care physicians perform the screening on pregnant women, with referral of those with positive results to genetics professionals (10).

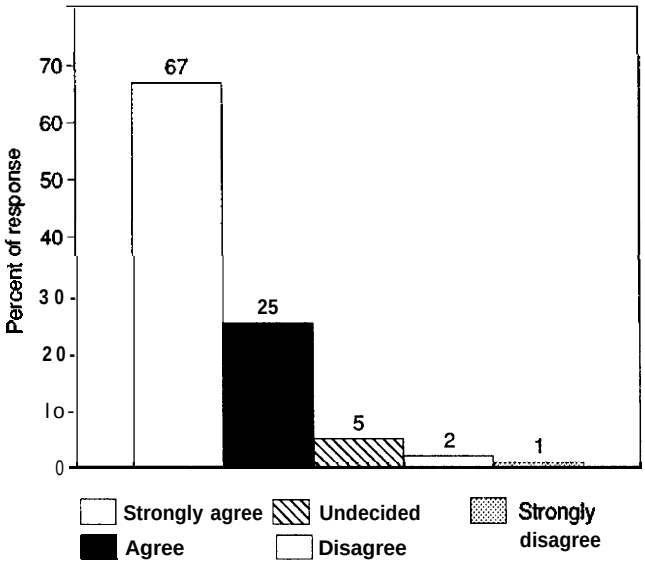
The counselors and nurses surveyed by OTA estimate pretest counseling time for CF carrier status would range from about 45 minutes to over 1 hour, depending on family history (table 3-13). It is unclear to what extent increased demand for CF carrier screening would strain the current system. Current estimates undercount the number of health care professionals who practice genetic counseling and assume that counseling would always be provided in a clinical genetics setting by board-certified or board-eligible counselors. Such estimates also ignore the role that aggressive public education can play in improving pretest knowledge. Improvements in public education could result in dramatically less time required in formal counseling, as could reliance on health professionals not formally trained in genetics.

Table 3-1 3-Time Required for Genetic Counseling for Various Conditions

Condition	Time (minutes/visit)	Number visits
Prenatal counseling for advanced maternal age	54	1
Positive family history for neural tube defects	57	1
Elevated MSAFP screen	55	1
Couple with newly diagnosed (Tri21) Down syndrome child	78	2
Couple with 14/21 translocation Down syndrome child	73	2
Carrier testing for Duchenne muscular dystrophy	75	2
Newly diagnosed case of neurofibromatosis	70	2
Newly diagnosed CF family	59	2
Carrier testing for CF with a positive family history	70	2
Carrier testing for CF with a negative family history	44	1

SOURCE: Office of Technology Assessment, 1992.

Figure 3-9—Opinions Regarding the Need for More Genetic Counselors



A need for more genetic counselors exists.

SOURCE: Office of Technology Assessment, 1992.

Table 3-14-Strategies for Implementation of Widespread Cystic Fibrosis Carrier Screening

Question: What strategies have you considered implementing if widespread screening for CF becomes a reality?[a]

Strategy	Percent
Plan professional education activities	40
Develop videotapes for patient education	21
Conduct public education	15
Arrange for group counseling sessions	14
Administrative changes in clinics to handle patient load.	13

a237 of the 43 I respondents gave no response.

SOURCE: Office of Technology Assessment, 1992.

Two-thirds of respondents strongly agreed that a need for more genetic counselors exists (figure 3-9). A few respondents raised the possibility of training ''single-gene' counselors to assist in the increased workload, although others expressed concern about this prospect, as taking a family history can reveal other genetic conditions that might not be detected by an individual trained to handle one genetic disorder (18). Still other respondents mentioned the need for more professional education of health care providers who might be in the position of administering such tests, and many survey participants noted that all groups of health care providers should be involved after appropriate training and education. Noted one genetic counselor, "Once screening is close to 100 percent sensitive, doctors and nurses could easily be trained to provide the necessary counseling.

When asked what strategies would be considered to alleviate the projected increase in workload should widespread CF carrier screening occur, 55 percent gave either no response or reported that they had not yet developed any. Of those who had considered or developed strategies, 40 percent said they would plan professional education activities to educate other health professionals, 21 percent would develop videotapes for patient education, 15 percent said they would conduct public education, and 14 percent reported they would arrange for group counseling sessions (table 3-14).

ISSUES TO BE ADDRESSED BEFORE IMPLEMENTATION

When OTA undertook this survey, privately funded pilot projects were under way, but federally funded pilot studies to evaluate CF mutation analysis in the general population had not yet begun, although NIH had begun a grant competition for such projects (18).[3] Thus, OTA asked survey respond-

[3] In October 1991, NIH launched a 3-year research initiative on clinical assessments of alternative approaches to genetic education, testing, and counseling related to CF mutation analysis (18).

Table 3-15-Issues that Need to be Addressed by Pilot Programs in Cystic Fibrosis Carrier Screening

Rank order
1. Access to genetic counseling
2. Education of the public
3. Payment/cost
4. Sensitivity of the test
5. Protection of confidentiality
6. Quality control and assurance
7. Identification of a target group
8. Availability of reproductive options

SOURCE: Office of Technology Assessment, 1992.

ents what issues they viewed as important before widespread screening is embraced. Specifically, survey participants were asked at the conclusion of the questionnaire to list by priority the important issues to be addressed by pilot studies in CF carrier screening.

Interestingly, the sensitivity of the test, which was often cited as the reason not to proceed with screening, was ranked fourth (table 3-15). Access to genetic counseling was listed as the most important issue to be addressed. But with vast geographic inequities in availability of genetic services it is not clear how access could be considered as anything other than a variable in following pretest and post-test consumer behavior. Education of the public was ranked as second in level of importance for evaluation by pilot programs. Payment and cost issues were ranked third.

SUMMARY

A majority (53 percent) of genetic counselors and nurses in genetics do not offer unsolicited CF carrier screening. They are also unlikely to be providing genetic counseling and DNA tests to families followed in CF clinics and have not yet made efforts to contact CF families seen previously to offer carrier testing to family members. Those who advocate CF carrier tests for use beyond affected families argue that individuals should be routinely informed about the assays so they can decide for themselves whether to be voluntarily screened. This population was a minority (21 percent) of respondents.

If carrier screening is to become routine, 99 percent of respondents believe it should be voluntary, and a majority prefer it be offered to preconceptional adults. Given the clientele found in most clinical genetics settings, it is likely that CF carrier screening will be offered as part of family planning or reproductive health, and the medical specialty most likely to offer the test will be obstetrics. This perceived tension over the technology's control likely contributes to the opinions of some in the clinical genetics community that widespread CF carrier screening is premature until greater genetics education of professionals is in place. With regard to CF carrier screening, concern exists that layers of uncertainty will inhibit informed consent, adequate pretest education, and post-test counseling and that, ultimately, more harm than good might be done. Yet respondents recognize the critical role that could be played in pretest education by other health care professionals and some indicated that should the momentum toward CF carrier screening accelerate, they would make efforts to increase their public and professional education activities.

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Chapter 4
Summary

For years, experts theorized about confronting the potential consequences of increased knowledge of human genetics. In the early 1990s, the cystic fibrosis CF mutation test moved the debate from the theoretical to the practical. OTA concludes that the value of the CF carrier testis the information it provides. No one can estimate in common terms what it means to an individual to possess information about his or her genetic status, especially when the value concerns reproductive decisionmaking. On a larger scale, the potential for widespread CF carrier screening raises legal, ethical, economic, and political considerations.

This survey of genetic counselors and nurses working in genetics, conducted in the summer of 1991, reflects the tensions and concerns surrounding dissemination of CF mutation analysis. The survey was conducted to better understand the environment in which the average genetic counselor or nurse in genetics works, to describe the infrastructure and tools available to these professionals, to assess the state of practice in the provision of CF carrier screening, and to evaluate their attitudes regarding CF carrier screening.

In summer 1991, most genetic counselors and nurses in genetics did not offer unsolicited CF carrier screening and expressed concerns about access to health insurance, quality control, public education, discrimination, stigmatization, and the adequacy of trained personnel as reasons why they did not. They are also unlikely to be providing genetic counseling and DNA tests to families followed in CF clinics and have not yet made efforts to contact CF families seen previously to offer carrier testing to family members, although agreement exists that such individuals should be offered CF mutation analysis.

Reasons why survey respondents do not offer CF mutation analysis are varied, but professional guidelines exert some influence. The 1990 policy statement of the American Society of Human Genetics (ASHG) stated that CF carrier screening is ***"NOT*** yet the standard of care," and a majority of survey respondents were aware of that statement. Several stated that it alone was the reason for their refusal to offer CF carrier screening. In mid-1992, after extended discussion, ASHG's leadership approved a revised statement that CF mutation analysis 'is not recommended' for those without a family history of CF Some argue that the subtle change in language of the new statement reflects an evolution of debate within the society-that some believe CF carrier screening *may now be offered* to individuals without a family history of CF although it might not be the "standard of care. " Others argue that ASHG's position is unchanged. The effect of the new statement remains to be seen.

Concern about test sensitivity was another barrier that respondents said should be addressed before routine CF carrier screening. Two-thirds of participants felt that an optimum frequency of detection should be reached before they would feel comfortable offering CF carrier screening to the general population, although nearly a quarter of respondents were uncertain about whether an optimum was necessary. Of those who felt there is an optimal frequency of detection, nearly half felt that 95 percent test sensitivity should be required before proceeding with widespread CF carrier screening. Twenty-five percent believed test sensitivity should be greater than 95 percent, with 4 percent stating that it should be 100 percent. At the time this survey was conducted, test sensitivity was approximately 80 percent. It has increased to 85 to 90 percent as of summer 1992, so opinions might have changed.

Two other factors ranked slightly more important than test sensitivity as criteria to consider before implementing routine CF carrier screening: the availability of adequate counseling and an adequate system of referral for individuals who test positive. Genetic counseling can be labor intensive. Survey respondents indicated that they spend most of their work week seeing or talking with clients; patient loads are frequently heavy. Respondents said that, given the potentially complex or emotional nature of some genetic information, professionals trained in human genetics are essential to insure high quality care and informed consent. Guarantee of informed consent also was mentioned as necessary for implementation of large-scale carrier screening.

Those who advocate CF carrier tests for use beyond affected families are no less concerned about

informed consent and quality of services. Proponents argue that the tests are sensitive enough for current use and that individuals should be routinely informed about the assays so they can decide for themselves whether to be voluntarily screened. These voices believe that failing to inform patients now about the availability of CF carrier assays denies people the opportunity to make personal choices about their reproductive futures. In this survey population, however, advocates of routine CF carrier screening were in the minority.

Perhaps the point on which there was greatest consensus among respondents is on the issue of autonomy and choice in screening. There are no mandatory genetic screening programs of adult populations in the United States. Ninety-nine percent of survey participants responded that CF carrier screening should be voluntary and never mandatory.

Given the existing tensions surrounding CF mutation analysis in the general population, who should serve as gatekeeper of this new technology? *Survey* respondents strongly believe that CF carrier screening should be organized by and provided by the human genetics community. This assumes, however, that large numbers of Americans will learn of their CF carrier status through interaction with the genetic services system.

Based on the client populations reported in this survey, routine CF carrier screening will likely integrate into medicine in the reproductive context first. The prenatal population has been the traditional entry point into genetic services for many people; OTA's survey found 70 percent of the genetics clientele are adults of reproductive age, reinforcing the notion of prenatal diagnosis as an entry point for primary genetics service.

Preconceptional individuals are the ideal population for CF carrier screening, according to survey respondents, but for most individuals the first real opportunity for carrier screening takes place post-conception. Thus, despite survey respondents' desire that information about the availability of assays such as CF mutation analysis should come from genetic specialists, the primary responsibility for providing CF carrier screening is likely to reside with obstetricians, at least initially, and especially if reimbursement for CF mutation analysis and its attendant counseling become part of routine obstetric care. Such a scenario would mirror that which has occurred with maternal serum alpha-fetoprotein screening to detect fetuses with neural tube or abdominal wall defects or Down syndrome-a prospect that concerns some, but not others.

OTA's survey of genetic counselors and nurses also reports some consumers experience difficulties in obtaining or retaining health care coverage after genetic tests, though the large majority were not for carrier status, but were for genetic illness. Nevertheless, because genetic-based predictive testing promises to have a profound impact on clinical medicine-and because access to medical care is inextricably linked to private health insurance in this country—such cases underscore certain policy dilemmas arising from the increased availability of genetic assays.

Critics of widespread CF carrier screening question whether the present genetic counseling system in the United States can handle the swell of cases if CF carrier screening becomes routine. Currently, about 1,000 master' s-level genetic counselors practice in the United States, and an additional 100 nurses in genetics provide similar services. OTA's survey of genetic counselors and nurses in genetics indicates that respondents believe routine CF carrier screening will strain the present genetic services delivery system. Respondents estimated that, on average, 1 hour would be needed to obtain a three-generational family history and to discuss CF carrier screening and genetic risks.

Skeptics of a personnel shortage assert that counseling about CF carrier assays is likely to take place in the general obstetric/prenatal context, however, and believe 1 hour exaggerates the amount of time that suffices for all prenatal tests, let alone only CF carrier screening. Furthermore, counseling related to CF carrier screening is likely to extend beyond genetics professionals to include other physicians and allied health professionals. For example, an unknown number of social workers, psychologists, and other public health professionals perform genetic counseling, often to minority and underserved populations.

ultimately, the issue of adequate services and professional capacity could turn on the extent to which patients receive genetic services through specialized clinical settings, as they largely do now, versus access through primary care, community health, and public health settings. Overall, OTA cannot conclude whether increased numbers of genetic specialists are necessary, but clearly in-

creased genetics education for all health care professionals is desirable. Routine carrier screening for CF-and tests yet to be developed for other genetic conditions-will require adequate training and education of individuals in the broader health care delivery system. Some survey respondents recognize the critical role other health care professionals will play in pretest education and indicated that should the momentum toward CF carrier screening accelerate, they would make efforts to increase their public and professional education activities.

Although genetic counselors and nurses in genetics work in a variety of settings, they are concentrated in metropolitan medical centers on the West coast or in the Northeast. States with large rural populations are less likely to be served. The clientele served, in the aggregate, tend to be representative of the national averages for racial and ethnic populations, although no effort was made by OTA **to** match racial and ethnic data with regions, cities, or localities. This diversity presents great opportunity in terms of professional and public education, yet few counselors report an emphasis on these activities in their weekly routine because patient services comprise two-thirds of their time.

One of the tasks of genetic specialists, however, is to provide the educational and counseling services necessary to successful implementation of new technologies. Diagnostic tools, such as DNA tests, can provide powerful information. Increasingly, genetic counselors and nurses working in genetics will be at the front line on the issues raised by assimilating DNA technologies into clinical practice.

Appendix A
Survey Method

Data for this survey were collected from 431 survey questionnaires mailed to 813 individuals in June and July of 1991. The sample was drawn from the membership list of the National Society of Genetic Counselors (NSGC) and the mailing list of the International Society of Nurses in Genetics (ISONG). Only full members (excluding student, associate, and foreign memberships) of the NSGC were surveyed. The initial mailing list provided by ISONG was screened to remove individuals who were not practicing nurses from the sample (e.g., journalists, vendors).

Questionnaires were not numerically or otherwise coded, and hence were completely anonymous. Respondents were asked to return their questionnaire in a post-paid envelope provided by OTA. Approximately 2 weeks after the initial mailing, a followup letter was sent to all survey respondents. The second wave improved the response rate by about 15 percent.

The content of the instruments was identical for the two populations, but the questionnaires were reproduced on different colored stock for easier tracking. Preliminary analysis revealed no significant difference in question response between the NSGC and ISONG samples, and so all data were combined into one set for the final analyses.

Surveys returned after September 30, 1991 were not included in the final data analyses. A statistical software package was used to provide frequency distributions and cross-tabulations of the data. No weighting was done of the sample, as OTA believes that the sample closely represents the entire population.

Appendix B

Survey Instrument

As part of the 1992 assessment ***Cystic Fibrosis and DNA Tests: Implications of Carrier Screening,*** OTA surveyed the summer 1991 memberships of the International Society of Nurses in Genetics and the National Society of Genetic Counselors. The items for the two questionnaires were identical, and the following is a reproduction of the survey instrument.

Office of Technology Assessment
United States Congress
Washington, D.C. 20510-8025

SURVEY OF GENETIC COUNSELING ATTITUDES AND PRACTICES
REGARDING CYSTIC FIBROSIS SCREENING

Genetic Counselor Demographics

1. **Sex:** a. female b. ___ male

2. **Age:** ___ years

3. **Race:**
   a. Asian
   b. ___ Black
   c. ___ Caucasian
   d. ___ Hispanic
   e. ___ Native American
   f. ___ Other: _____

4. **Marital status:**
   a. married
   b. ___ widowed
   c. never married
   d. ___ divorced/separated

5. **In what State do you work? State a.** _____ **ZIP code b.** _____

6. **Degrees held:** **Year granted:**
   a. MA/MS - Genetic counseling _____
   b. ___ RN/BSN _____
   c. ___ MSN _____
   d. ___ MPH _____
   e. ___ MSW _____
   f. ___ Ph. D.: _____ _____
   g. ___ M.D. _____
   h. J.D. _____
   i. ___ currently in degree program: _____ (type)

7. **How many years of clinical practice as a genetic counselor do you have?** _____

8. **Certification status (American Board of Medical Genetics)**
   a. Board certified (CIRCLE Year): 1982, 1984, 1987, 1990
   b. ___ Board eligible
   not necessary for position
   d: none

9. **Are you fluent in any language other than English?**
   a. no b. yes, I speak English and (specify other): _____

10. **Present employment status:**
   a. full time
   b. part time: _____ hours/week
   c. ___ not working

11. **Which best describes your work setting(s)? Designate a primary (1) and secondary (2) setting, if applicable.**

a. private hospital/medical facility
b. university medical center
c. free standing clinic
d. Health Maintenance Organization (HMO)
e. private group practice
f. solo private practice
g. private industry (specify type): _____
h. State laboratory (specify type): _____
i. regional laboratory (specify type): _____
j. commercial laboratory
k. Public Health department (State, county, or city)
L State government agency
m. Federal government agency
n. voluntary health organization
o. educational institution (K-12)
p. higher educational institution (undergraduate or graduate)
q. other: _____

12. **On average, how many hours a week are you involved in:**

a. direct patient contact (counseling patients)
b. indirect patient activities (review of literature or records, coordinating referrals)
performing administrative/managerial tasks
d: educating health professionals, medical students, GC trainees
educating the general public, schools, undergraduates
f" performing laboratory work
g. research
h. marketing/business
i. other: _____

13. **What sources of information about new advances in the field of human genetics do you rely on? (check all that apply)**

a. professional colleagues
b. medical journals
grand rounds
d : State or regional conferences
national conferences
f " American Society of Human Genetics
g . : National Society of Genetic Counselors
h. continuing education courses
i . literature from biotechnology/commercial firms
j . lay press
k. other: _____

14. **In your current position, how frequently were you asked about DNA testing/screening for CF during the 6-month period from January - June, 1991? Please consider this in the context of your total clinical practice.**

a. never
b. rarely
occasionally
d: frequently
e . very frequently

15. **If you were asked about DNA testing/screening for CF please estimate the number of requests per month (January - June, 1991)? _____ (per month)**

16. **Compared to 2 years ago, would you say the number of requests made between January - June, 1991 represents:**

- **a. a large decrease**
- **b. a small decrease**
- **no change**
- **d : a small increase**
- **e . a large increase**

17. **If you noted an increase, when did you note this? (month/year) _____**

18. **In your current position are you engaged in providing genetic counseling?**

a. ___ yes b.___no

If NO, skip the CLINICAL PRACTICE QUESTIONS and GO TO QUESTION #46

THE NEXT SERIES OF QUESTIONS ARE TO BE ANSWERED BY THOSE INDIVIDUALS WHO CURRENTLY PROVIDE GENETIC COUNSELING SERVICES

(All others please skip to question #46.)

19. **Which best describes the primary service area in which you work?**

- **a. ___ rural**
- **b. ___ suburban**
- **c. ___ metropolitan/urban**
- **d. ___ statewide**
- **e. ___ regional (more than one State)**
- **f. ___ national**
- **g. ___ other: _____**

20. **Current level of staffing (including yourself) in your counseling unit/program (please indicate number).**

	#
a. M.D. geneticists	_____
b. Ph.D. geneticists	_____
c. M.D./Ph.D. geneticists	_____
d. genetic counselors	_____
e. secretaries	_____
f. other: _____	_____

21. Indicate the frequency of patients seen by you for each major area of clinical practice.

1 =seldom if ever; 2=sometimes; 3=often (i.e., majority); 4=very often; 5=all or almost all

a. ___ prenatal genetics
b. ___ pediatric genetics
___ adult genetics
d : ___ teratogen exposure
___ reproductive loss
f " ___ specialty disease(s) clinics (please specify): _____
g. ___ newborn screening
h. ___ MSAFP screening follow-up
i. ___ carrier screening (specify disease): _____

22. Does your institution participate in collecting the CORN data set?
a. ___ yes b. ___ no c. ___ don't know

23. For each of the following categories, indicate the number (or best estimate) of genetics clients/patients served in 1990, either DIRECTLY (i.e., counselor to client relationship; one-on-one genetic counseling) or INDIRECTLY (i.e., involvement such as consultant to primary care physician regarding a patient, telephone consultation).

	TYPE OF PATIENT CONTACT		
	Direct	Indirect	Total
All patients seen in 1990			
a. by your unit:	_____	_____	_____
b. by you individually:	_____	_____	_____
CF patients/families seen in 1990			
c. by your institution:	_____	_____	_____
d. by you individually:	_____	_____	_____

24. With respect to your clinical practice, estimate the percent (%) of your patients who are:

A. RACE/ETHNICITY	Percent (%)
a. Asian/Pacific Islander	_____
b. Black	_____
c. Caucasian	_____
d. Native American	_____
e. Spanish surname	_____
f. unable to estimate	_____

B. AGE DISTRIBUTION	
g. neonatal	_____
h. infants	_____
i. children	_____
j. adolescents	_____
k. adults - reproductive age	_____
l. adults - post reproductive age	_____
m. unable to estimate	_____

24. (cont.) With **respect to your clinical practice, estimate the percent (%) of your patients who are:**

C. LANGUAGE	Percent (%)
n. English speaking	_____
o. Non-English speaking	_____
p. unable to estimate	_____

25. Do your patients have health care coverage?

a. seldom if ever (0-15% of patients seen)
b . – sometimes (about 16-50% of patients)
– often (about 51 -74°A of patients)
d : – very often (about 75-69% of patients)
e. – always or almost always (90-100% of patients)

26. Please estimate the percent of patients by category of coverage.

Coverage Category	Percent(%.
a. commercial insurance	_____
b. Blue Cross/Blue Shield	_____
c. HMO or managed care plan	_____
d. Medicaid	_____
e. Medicare	_____
f. CHAMPUS	_____
g. self pay	_____
h. no insurance	_____
i. indigent	_____
j. unknown	_____

27. For individuals with insurance coverage, what has been your experience with reimbursement of fees for service in each of the following areas? Also, please indicate the average fee amount charged for each service.

1 =seldom if ever covered; 2 =sometimes covered; 3 = often covered; 4 very often covered; 5=almost a/ways covered; 6=uncertain

a. ___ general genetic counseling: Fee $_____
b. ___ genetic counseling for cystic fibrosis with positive family history: Fee $_____
c. ___ genetic counseling for cystic fibrosis with negative family history: Fee $_____
d. ___ routine metabolic screen: Fee $_____
e. routine cytogenetic analysis: Fee $_____
f. — DNA analysis for cystic fibrosis: Fee $_____

28. **Have you had any experience with a patient's insurance claims for DNA testing being rejected?**
a. ___ **no experience** **b.** **yes. Please provide details:**

29. **Have any of your patients experienced difficulties in obtaining or retaining health insurance coverage as a result of genetic testing?**
a. ___ **no experience** **b.** ___ **yes. Please provide details:**

30. **Consider the following reasons for referral for genetic counseling. Please estimate to the best of your ability, the average NUMBER of patients you see per month, total amount of direct COUNSELOR TIME spent (in minutes), and the average number of VISITS needed to provide genetic counseling to individuals and/or families for each of the following scenarios. (Answer for cases appropriate to your practice.)**

	AVG # Pts	Time/ visit	AVG # visits
a. prenatal counseling for advanced maternal age	_____	_____	_____
b. positive family history for neural tube defects concerns for current pregnancy	_____	_____	_____
c. Elevated MSAFP screen	_____	_____	_____
d. Couple with newly diagnosed (Tri 21) Down's Syndrome child	_____	_____	_____
e. Couple with 14/21 translocation Down's Syndrome child	_____	_____	_____
f. Carrier testing for DMD	_____	_____	_____
g Newly diagnosed case of neurofibromatosis	_____	_____	_____
h. Newly diagnosed CF family	_____	_____	_____
i. Carrier testing for CF with a positive family history	_____	_____	_____
j. Carrier testing for CF with a negative family history	_____	_____	_____

31. **If you have not been involved with counseling for CF based on your experience, how much direct counselor time (minutes) would you estimate would be needed to:**

a. obtain 3 generational family pedigree: _____ (minutes)

b. discuss carrier testing and recurrence risks: _____ (minutes)

32. **How would this estimate compare to the direct patient time spent with your typical patient load?**
a. ___ **more time** **b.** **less time** **c.** **about the same**

33. **How frequently do you use each of the following formats to provide genetic counseling?**

1 ***=seldom if ever; 2=sometimes; 3=often; 4=very often; 5=almost always***

a. individual counseling session(s)
b . group counseling
videotape alone
d : videotape with counseling
written educational materials
f " slide-tape
g . interactive computer

34. **Where is the closest CF treatment center to your institution?**

a. at my institution
b . less than or equal to *50* miles
greater than 50 miles
d : not aware of one

35. **Do you personally provide genetic counseling through the CF treatment center in your area?**

a. ___ no b. ___ yes

If yes, please provide the following information for 1990.

1) total # new patients seen by the CF center _____

2) total # return patients seen by the CF center _____

3) # referrals for genetic counseling _____

4) # requests for information on DNA testing _____

5) # undergoing actual DNA testing _____ individuals _____ families

36. Do you or your group/unit have a specific policy regarding DNA testing for CF

a. ___ no, we do not. b. ___ yes; if yes, what is it?

37. **Are individuals/families seeking DNA testing for CF asked to sign an informed consent?**

a. ___ no b. yes

38. **Do you or your group/unit have official policies and procedures for other issues in genetics? (check all that apply)**

a. DNA storage
b . prenatal diagnosis for sex selection
non-paternity
d : confidentiality and Huntington's disease testing
e . other: _____

39. For each of the following patient groups, indicate how often, if at all, you introduce the topic of DNA testing for CF

1=seldom if ever; 2=sometimes; 3=often; 4=very often; 5=almost always

a. all patients\families
b. ___ pregnant women seeking prenatal diagnosis
couples/individuals with a positive family history for CF
d : ___ Caucasian couples/individuals with negative family history for CF
f . ___ individual/families who inquire about CF
e . ___ selected couples/individuals; how selected:

40. Have you made an effort to contact old genetics families as appropriate regarding the availability of CF testing?

a. ___ yes, by (check all that apply):
1) telephone
2) ___ letters/mass mailing
3) ___ at future visits
4) ___ other: _____

b. ___ no, because (check all that apply):
1) not enough time; too busy
2) ___ no mechanism for rapid chart retrieval
3) ___ requires chart by chart analysis
4) ___ plan to do so in future, as time permits
5) ___ other: _____

41. During the last 12 months:

a. Have you referred any patients for DNA testing for CF
1) no
2) ___ yes: how many individuals: _____ # samples _____

b. Have you=referred any patients/families for DNA testing *for* other disorders?
1) no
2) ___ yes: how many individuals: _____ # samples _____
If yes,for which conditions:

42. At your institution, is DNA testing for CF
a. performed at onsite/inhouse lab
b . ___ sent offsite to lab less than or equal to 50 miles away
c . ___ sent offsite to lab between 50 miles and 150 miles away
d. ___ sent offsite to lab greater than 150 miles away

43. Type of laboratory used for CF testing:
a. private/commercial
b . ___ private hospital
university hospital
d : ___ regional laboratory
e . ___ other: _____

44. **If you are-or have been-involved with CF testing, does the laboratory you use provide (check all that apply):**

a. direct mutation analysis
b. DNA linkage analysis
DNA haplotyping
d : staging of studies depending on case
prenatal DNA analysis
f " fetal intestinal enzyme analysis
g . DNA banking

45. **For direct mutation analysis of CF what mutations does the laboratory you use include? (Please list or give number):**

THE FOLLOWING QUESTIONS ARE TO BE ANSWERED BY ALL RESPONDENTS

46. **Are you familiar with the following statements concerning CF screening published by:**

a. 1990 ASHG ad hoc CF Screening Committee: no — yes
b. 1990 NIH panel: no yes

if yes to either one of the above how have you incorporated this into clinical practice?

47. **At this time do you think it is appropriate to provide CF screening in cases where family history is negative?**

a. ___ no b. ___ yes c. ___ uncertain

if yes, why?

48. **Do you feel there is a optimum rate of detection at which widespread CF carrier screening should proceed?**

a. yes, specify: _____ % rate of detection
b . n o
c . no opinion

49. **Are you familiar with the NSGC brochure "Genetic Testing for Cystic Fibrosis: A Handbook for Professionals"?**

a. no b. yes

50. **Have you developed any educational materials relevant to DNA testing specifically for CF**

a. ___ no b. yes (Please send a copy.)

51. **Have you been tested for CF carrier status?**

a. ___ no b. ___ yes

52. **If you have been tested for CF carrier status, why were you tested?**

a. research subject
b . wanted to know
positive family history
d : family planning
e . other:_____

53. **How was your test covered?**

a. by my insurance
b. professional courtesy
c. self pay
d. research subject

54. To what extent, if at all, should each of the following groups be involved with educating the public about DNA testing for CF if it becomes standard practice?

1=to little or no extent; 2=to some extent; 3=to a moderate extent; 4=to a great extent; 5=to a very great extent; 6=no opinion

a. ___ primary care providers
b. ___ public health departments
___ genetic counselors
d: ___ genetics programs
___ nurses
f ___ family planning clinics
g. ___ voluntary support groups
h. ___ schools
___ lay press
j ___ television
k. ___ other: _____

55. If widespread CF carrier screening begins, it should be:

a. ___ mandatory b. ___ voluntary

56. If widespread CF carrier screening begins, what target populations should be screened? (check all that apply)

a. ___ prenatal
b. ___ newborns
c. ___ children ages 2-12
d. children ages 13-18
e. ___ adults in reproductive years
f. ___ adults post reproductive years
g. ___ pregnant women or "couples"

57. **If CF carrier screening is voluntary, who should organize the screening programs? (check all that apply)**

a. voluntary health organizations
b. ___ State or local health department
Federal Government
d : medical societies
the human genetics community
f " primary care givers
g. : others (specify): _____

58. **If CF carrier screening is mandatory, who should organize the screening programs? (check all that apply)**

a. voluntary health organizations
b. State or local health department
c. Federal Government
d. medical societies
the human genetics community
f" primary care givers
g. ___ others (specify): _____

59. **Where should CF population screening programs be provided? (check all that apply)**

a. ___ in public schools
b. ___ in public health departments
___ in organized, community-wide programs
d. ___ in the primary care setting i.e., physicians
___ in genetic centers/programs
f. ___ in the workplace
g. ___ other (specify): _____

60. **Who should pay for screening? (Please rank, but be realistic.)**

a. ___ self pay by patient
b. ___ third party payment
c. ___ employers
d. ___ State/city or county
___ Federal government
f. ___ other (specify): _____

61. **Do you agree or disagree with the following statements?**
1=strongly agree; 2=agree; 3=undecided; 4=disagree; 5=strongly disagree)

a. ___ genetic counseling should precede DNA testing for CF when there is a positive family history.
b. ___ genetic counseling should precede DNA testing for CF when there is a negative family history.
c. ___ educational materials (culturally sensitive and understandable) can provide adequate information about CF screening.
d. ___ a need for more genetic counselors exists.
e. ___ informed consent prior to CF screening is a necessity.

62. **In your opinion, what are the important issues that need to be addressed by pilot programs in CF screening? List in order of priority:**

1.

2.

3.

4.

63. **What strategies have you considered implementing if widespread screening for CF becomes a reality?**

64. **What do you feel the minimum criteria for CF carrier screening should be (protocol)?**

Thank you very much for your cooperation in answering our Questions! On the back of this survey, please feel free to give us as any other options, concerns, or suggestions that you feel our questions did not address. These comments will be anonymous, but may be incorporated in our report to Congress.

Appendix C

Acronyms and Glossary

Acronyms

-/- —negative CF carrier/negative CF carrier (couple)
+/- —positive CF carrier/negative CF carrier (couple)
+/+ —positive CF carrier/positive CF carrier (couple)
ABMG —American Board of Medical Genetics
ASHG —American Society of Human Genetics
BC/BS —Blue Cross and Blue Shield
CF -cystic fibrosis
CFTR -cystic fibrosis transmembrane conductance regulator
DF508 -delta F508 (most prevalent CF mutation)
DF508#i12-delta F508 plus 6 to 12 additional CF mutations
DNA -deoxyribonucleic acid
G542X —a CF mutation
G551D —a CF mutation
Em40 —health maintenance organization
ISONG —International Society of Nurses in Genetics
MSAFP —maternal serum alpha-fetoprotein
N1303K —a CF mutation
NIH —National Institutes of Health (NIH)
NSGC —National Society of Genetic Counselors
OTA -Office of Technology Assessment
R553X —a CF mutation
W1282X —a CF mutation

Glossary of Terms

Allele: Alternative form of a genetic locus (e.g., at a locus for eye color there might be alleles resulting in blue or brown eyes); alleles are inherited separately from each parent.

beta~-thalassemia: An autosomal recessive disorder affecting the red blood cells, resulting in anemia, infections, growth retardation, and other complications. β-thalassemia predominantly occurs among individuals of Mediterranean, Middle Eastern, Asian Indian, Chinese, Southeast Asian, and African descent.

Buccal: Relating to the inside of the cheek. A buccal swab collects cells that can be analyzed for CF mutations.

Carrier: An individual apparently normal, but possessing a single copy of a recessive gene obscured by a dominant allele; a heterozygote.

Chest physical therapy (chest PT): A cornerstone of CF therapy that moves the mucus blocking major air passages out of the lungs. A specific form of chest PT is bronchial drainage during which an individual claps on the chest or back of the patient who is usually lying on a table.

Chromosome: A threadlike structure that carries genetic information arranged in a linear sequence. In humans, it consists of a complex of nucleic acids and proteins.

Confidentiality: A fundamental component of the health care provider-patient relationship in which the professional has the duty to keep private all that is disclosed by the patient.

Consanguineous: Related by blood or origin, rather than by marriage.

Cystic fibrosis CF A life-shortening, autosomal recessive disorder affecting the respiratory, gastrointestinal, reproductive, and skeletal systems, as well as the sweat glands. CF is caused by mutations in the CF gene that affect the CF gene product, cystic fibrosis transmembrane conductance regulator (CFTR). Individuals with CF possess two mutant CF genes.

Cystic fibrosis carrier: An individual who possesses one CF mutation and one normal CF gene. CF carriers manifest no symptoms of the disorder. See ***carrier.***

Cystic fibrosis carrier screening: The performance of tests on persons for whom no family history of CF exists to determine whether they have one aberrant CF gene and one normal CF gene. See ***cystic fibrosis screening.***

Cystic fibrosis screening: The performance of tests to diagnose the presence or absence of the actual disorder, in the absence of medical indications of the disease or a family history of CF This type of diagnostic screening usually involves newborns, but rarely for CF except in Colorado and Wisconsin. See ***cystic fibrosis carrier screening.***

Cystic fibrosis transmembrane conductance regulator (CFTR): The CF gene product, which regulates chloride (Cl-) conductance and might be a Cl^- ion channel, the structure that governs Cl^- entry and exit in the cell. CFTR produced by a mutant CF gene is frequently impaired, resulting in the medical manifestations of CF in affected individuals.

DF508: A three base pair deletion in the CF gene that results in a faulty CF gene product (i.e., a flawed CFTR). This mutation results in the deletion of one amino acid, phenylalamine, at position number 508 in CFTR. DF508 is the most common mutant allele among the greater than 170 identified in the CF gene.

Deoxyribonucleic acid (DNA): The molecule that encodes genetic information. DNA is a double-stranded helix held together by weak bonds between base pairs of nucleotides.

Discrimination: Differential treatment or favor with a prejudiced outlook or action.

Dominant: An allele that exerts its phenotypic effect when present either in homozygous or heterozygous form.

DNA: See *deoxyribonucleic acid.*

DNA analysis: A direct examination of the genetic material, DNA, to reveal whether a individual has mutation(s) for CF or other disorders.

DNA probe: Short segment of DNA labeled with a radioactive or other chemical tag and then used to detect the presence of a particular DNA sequence through hybridization to its complementary sequence.

Gene: The fundamental physical and functional unit of heredity. A gene is an ordered sequence of nucleotide base pairs to which a specific product or function can be assigned.

Gene therapy: The deliberate administration of genetic material into the cells of a patient with the intent of correcting a specific genetic defect.

Genetic counseling: A clinical service involving educational, informational, and psychosocial elements to provide an individual (and sometimes his or her family) with information about heritable conditions. Genetic counseling is performed by genetics specialists, including physicians, Ph.D. clinical geneticists, genetic counselors, nurses, and social workers.

Genetic screening: The analysis of samples from asymptomatic individuals with no family history of a disorder, groups of such individuals, or populations.

Genetic testing: The use of specific assays to determine the genetic status of individuals already suspected to be at high risk (e.g., family history or symptoms) for a particular inherited condition.

Genetics: The study of the patterns of inheritance of Specific traits.

Genome: AU the genetic material in the chromosomes of a particular organism; its size is generally given as its total number of base pairs. The human genome is 3.3 billion base pairs.

Heterozygote: A heterozygous individual, such as a CF carrier.

Heterozygous: Having two different alleles at a particular locus.

Homozygote: A homozygous individual.

Homozygous: Having the same alleles at a particular locus.

Immunoreactive trypsin (IRT) test: An assay that measures levels of pancreatic trypsin, a digestive enzyme. As a protocol for newborn CF screening, a drop of blood is isolated on a card, dried, and chemically analyzed to detect elevated levels of the enzyme. It is not intended to be a diagnostic test.

Mutation: Changes in the composition of DNA.

Nucleotide: The unit of DNA consisting of one of four bases—adenine, guanine, cytosine, or thymine-attached to a phosphate-sugar group. The sugar group is deoxyribose in DNA. In RNA, the sugar group is ribose, and the base uracil substitutes for thymine.

Probe: A short segment of DNA tagged with a reporter molecule, such as radioactive phosphorus (^{32}P), used to detect the presence of that particular complementary DNA sequence.

Protein: A biological molecule whose structure is determined by the sequence of nucleotides in DNA. Proteins are required for the structure, function, and regulation of cells, tissues, and organs in the body.

Recessive: An allele that exerts its phenotypic effect only when present in homozygous form, otherwise being masked by the dominant allele.

Sensitivity: The ability of a test to identify correctly those who have a disease.

Sickle cell anemia: An autosoma1 recessive disorder affecting red blood cell flow through the circulatory system, causing complications in numerous organ systems. Sickle cell anemia predominantly occurs in individuals of African descent.

Sickle cell trait: The heterozygous state of sickle cell anemia; sickle cell carrier status.

Single-gene disorder: Hereditary disorder caused by a single gene (e.g., cystic fibrosis, Tay-Sachs disease, sickle cell anemia).

Specificity: The ability of a test to identify correctly those who do not have the characteristic which is being tested.

Stigmatization: Branding, marking, or discrediting because of a particular characteristic.

Sweat test: An assay used to confirm CF that measures levels of sodium Na^+) and chloride (Cl-) ions. These ions appear in high concentrations in patients with CF Sweating is induced by running a low electric current through a pilocarpine-soaked gauze pad on the individual's arm or back. The amounts of Na^+ and Cl- in the sweat can then be determined to confirm or question a diagnosis of CF

Tay-Sachs disease: A lethal autosomal recessive disorder affecting the central nervous system which results in mental retardation and early death. Tay-Sachs disease predominantly occurs among Jews of Eastern and Central European descent and populations in the United States and Canada descended from French Canadian ancestors.