Changing Their Minds With Time: A Comparison of Hypothetical and Actual Reproductive Behaviors in Parents of Children With Cystic Fibrosis

Susan M. Sawyer, MD\textsuperscript{a,h,c,d}, Belinda Cerritelli, BAppSc, BA\textsuperscript{a,h,d}, Lucy S. Carter, MBBS\textsuperscript{a,h,c}, Mary Cooke, PhD\textsuperscript{a}, Judith A. Glazner, MA, RN\textsuperscript{a}, John Massie, MD\textsuperscript{a,d}

\textsuperscript{a}Department of Respiratory Medicine and \textsuperscript{b}Centre for Adolescent Health, Royal Children’s Hospital, Melbourne, Victoria, Australia; \textsuperscript{c}Department of Paediatrics, University of Melbourne, Melbourne, Victoria, Australia; \textsuperscript{d}Murdoch Childrens Research Institute, Melbourne, Victoria, Australia

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ABSTRACT

OBJECTIVE. Newborn screening for cystic fibrosis, with appropriate counseling, enables carrier parents to be informed early about future reproductive choices. Previous studies have assessed attitudes toward reproductive decisions in a hypothetical pregnancy or have measured reproductive behaviors. We aimed to measure parent attitudes to reproductive technologies and to compare prospectively these attitudes with later reproductive behaviors.

METHODS. Parents of children who had cystic fibrosis and were aged 2 to 7 years were surveyed at baseline using a written questionnaire that explored attitudes to prenatal testing and termination of pregnancy in a hypothetical pregnancy. Parent knowledge and access to genetic counseling services also were assessed. Five years later, we compared attitudes with actual reproductive behaviors.

RESULTS. Fifty-six mothers participated at baseline, and 43 were resurveyed 5 years later. Parent knowledge of cystic fibrosis and genetics was very good. A total of 93\% had met a genetic counselor at the time of diagnosis, and more than half had on at least 1 subsequent occasion. At baseline, 82\% reported that they would be likely to have prenatal diagnosis in a subsequent pregnancy, and 56\% reported that they would be likely to terminate an affected pregnancy. Twenty-seven mothers since had been pregnant, with prenatal diagnosis used in 33 of the 55 pregnancies. In 67\%, the hypothetically reported behavior regarding use of prenatal testing was the same as their actual behavior. Five of the 33 tested pregnancies were affected; all ended in termination. Reproductive choices in relationship to the number of children wanted, together with attitudes toward prenatal diagnosis and termination of pregnancy, were dynamic over time, with decisions having changed in both directions.

CONCLUSIONS. This cohort of parents has actively used reproductive technologies since the birth of a child who has cystic fibrosis that was diagnosed by newborn screening.
screening. The dynamic aspect of reproductive choices highlights the importance of ongoing access to genetic counseling beyond the initial period of diagnosis and education, regardless of whether parents report that they expect to use reproductive technologies.

The value of newborn screening (NBS) for cystic fibrosis (CF) continues to be debated. However, compared with a diagnosis that is based on the recognition of clinical features at a mean age of 16 months, NBS facilitates early diagnosis of infants by 6 weeks of age and enables parents to be informed about reproductive choices before they embark on subsequent pregnancies. What is less clear is how parents use this information.

Farrell et al reported a significant difference in the mean age of diagnosis in a screened versus unscreened US population (3 months vs 16 months, respectively), with significant implications for subsequent reproductive risks and choices. More specific, a retrospective study of 68 British families with 2 children with CF suggested that the delay in the clinical diagnosis of CF in the first child led to the birth of the second affected child in 22 cases. By contrast, in a screened French population, 39 (34%) of 115 families who were identified by NBS opted for subsequent prenatal diagnosis at least once. Twelve couples had prenatal testing while their first child was still symptom-free.

Significant advances in reproductive technologies in the past 20 years have greatly changed the nature of the reproductive choices that are offered to parents of children with CF. Before prenatal diagnosis was available, parents faced the choice between having no additional children and risking a 1-in-4 chance of CF affecting each subsequent pregnancy. Now parents of children who have CF diagnosed by NBS have access to a range of reproductive technologies that include prenatal diagnosis (by 10–14 weeks’ gestation), preimplantation genetic diagnosis, or other in vitro technologies that use donor gametes.

Various studies have explored particular aspects of parent reproductive choices. There are, for example, studies of parent attitudes toward prenatal diagnosis or termination of an affected pregnancy in both screened and unscreened populations. Other studies have explored reproductive outcomes or behaviors, such as rates of subsequent pregnancy, use of prenatal diagnosis, and termination of pregnancy. Only 1 study has compared hypothetical versus actual reproductive behaviors but in an unscreened cohort. The reproductive attitudes and choices of parents whose children’s CF has been diagnosed clinically cannot necessarily be extrapolated to contemporary parents whose children’s CF has been diagnosed by NBS because of the healthy appearance of most newborn-screened infants compared with those who later receive a clinical diagnosis.

There are few studies of reproductive decisions in screened populations, although the available studies show widely varying behaviors. For example, 66% of Australian women who had a subsequent pregnancy used prenatal diagnosis, with 10 of the 12 affected pregnancies resulting in termination. Thirty-four percent of French couples opted for prenatal diagnosis in a subsequent pregnancy, of which 100% of affected pregnancies ended in termination. In contrast, 21% of couples in a study from the United States used prenatal diagnosis, 100% of which were carried to term. These studies did not report in detail parent knowledge of reproductive technologies or access to genetic counseling. Because use of reproductive technologies will be affected by attitudes toward reproductive technologies, knowledge of services, and access to services, parent knowledge about reproductive technologies and genetic counseling services is required to interpret study results.

The aim of this study was to assess the attitudes of parents with a child whose CF was diagnosed by NBS toward prenatal diagnosis and termination of pregnancy in a subsequent pregnancy. At the same time, we determined parent knowledge of CF, including genetics, and their use of genetic counseling services. To explore how attitudes and behaviors change over time, we compared prospectively the attitudes about a hypothetical pregnancy with their actual reproductive behaviors during the subsequent 5 years.

METHODS

Setting

NBS for CF first was introduced in Australia in 1981. Mutation analysis for the common cystic fibrosis transmembrane conductance regulator gene mutation, AF508, has been incorporated as part of NBS in Victoria since 1991. In Victoria, the screening laboratory is part of the same service that is responsible for genetic counseling (Genetic Health Services Victoria). These services lie within the Royal Children’s Hospital (RCH), a tertiary hospital that has a specialist CF clinic of ~300 infants, children, and adolescents and serves the Victorian population of 4.5 million.

The CF genetic counselor is involved in the notification of the initial screening result to families and in arranging a confirmatory sweat test. After a CF diagnosis (at ~6 weeks of age), genetic counseling is provided to parents as part of our integrated approach to CF family education. Genetic counseling specifically includes information about prenatal testing in subsequent pregnancies, options to terminate an affected pregnancy, in vitro fertilization with donor ova or sperm, and preimplantation genetic diagnosis (once it became available). For the purposes of this article, these interventions are all
included under the term “reproductive technologies.” These technologies are complex and take time to explain (and understand), which is why our service provides a trained genetic counselor to supplement the physician’s role. In addition to genetic education, both parents are offered carrier testing, and the wider family is involved in cascade family testing at their discretion.

Participants
Participating parents were recruited in 1997 (baseline study) and studied again in 2002 (follow-up study). All parents had children who had CF and had undergone NBS in Victoria, Australia. Both studies were approved by the RCH Ethics in Human Research Committee.

For the baseline study, parents of children who were aged 2 to 7 years and attended the RCH CF Clinic were invited to participate. This age group was chosen because the parents were past the initial stage of diagnosis and still were likely to be considering reproductive choices. We assessed parent attitudes to prenatal testing in a hypothetical pregnancy, regardless of whether they had plans for a future pregnancy.

The same cohort of parents was approached 5 years later to determine whether their thoughts had changed about various reproductive attitudes and which reproductive choices they had made. Parents were ineligible when their child with CF no longer attended the RCH CF Clinic or was no longer alive.

Questionnaire
A structured questionnaire was developed specifically for the study. It included questions about CF knowledge, the health of the child with CF, plans for future pregnancies, attitudes toward prenatal testing and termination of pregnancy, and knowledge and use of genetic counseling services that are available to the parents and their wider families. It took ~20 minutes to complete. The same questionnaire was administered at both time points. The follow-up interview contained a set of additional questions about reproductive behaviors since the initial interview. Given the sensitivity of the questionnaire themes, particular attention was paid to the wording of every question to ensure that it was neutral and nonjudgmental. The structured questionnaire was administered by an experienced research assistant in person when possible and otherwise by telephone. Because of the poor response from fathers in the baseline study (results not reported here), only mothers were surveyed in the follow-up study.

RESULTS
Demographics
The study outline and subject inclusions are presented in Fig 1. The baseline demographic details are presented in Table 1. All mothers had a single child with CF (age range: 2–7 years; mean age: 5.5 years). Forty-six of these (82%) children were either the first or the second born in their family. Although all children were screened at birth, 43 (77%) had CF diagnosed only by NBS, 6 (11%) because of meconium ileus, and 6 (11%) because of an older sibling with CF. One (2%) was missed by screening and presented with respiratory symptoms at 13 weeks of age.

![Diagram of study recruitment (baseline and follow-up).](image-url)
age. The median age of these diagnoses was 6 weeks (range: 3 days to 13 weeks).

Parent Knowledge of CF
At baseline, mothers reported that their knowledge about CF was either “very good” (32%) or “quite good” (68%). A good understanding of CF was confirmed by the questionnaire: all mothers understood that both parents need to be carriers to have a child with CF, that formal medical testing is essential to establish whether someone has CF, and that a carrier does not develop CF. However, 3 mothers believed that CF was contagious. At baseline, 27 (48%) mothers correctly reported the average life expectancy in CF to be between 30 and 35 years, and 6 (10%) believed that it was between 25 and 29 years, and 6 (10%) thought that it was lower (1 in 5500), and 7 (13%) did not know.

Forty-three (77%) mothers correctly identified that the frequency with which infants are born with CF in Australia is 1 in 2500. Thirty-one (55%) mothers knew that the frequency of CF was either “very good” (32%) or “quite good” (68%). A good understanding of CF was confirmed by the questionnaire: all mothers understood that both parents need to be carriers to have a child with CF, that formal medical testing is essential to establish whether someone has CF, and that a carrier does not develop CF. However, 3 mothers believed that CF was contagious. At baseline, 27 (48%) mothers correctly reported the average life expectancy in CF to be between 30 and 35 years, 8 (14%) thought it was <25 years, 13 (23%) believed that it was between 25 and 29 years, and 6 (10%) believed that it was >35 years. Two did not know.

Forty-five (98%) mothers reported that they were aware of the availability of genetic counseling services. When their child first received the diagnosis, 52 (93%) mothers reported that they had met with a counselor. Fifty-five (98%) mothers also reported subsequent consultations, ranging in number from 1 to 11. One third of partners also had consulted a genetic counselor since diagnosis. The majority (72%) of mothers rated these consultations as either “extremely useful” or “very useful.”

Thoughts About More Children
Nineteen (34%) mothers reported having changed their plans about the number of children that they intended to have as a result of the diagnosis of CF; 6 wished to have more children, whereas 13 wanted fewer children. Thirty-three (59%) mothers reported that having a child with CF had not caused them to change their reproductive plans. Four mothers indicated that they had had no firm plans about the number of children that they wished to have. From the group of parents who wanted fewer children and the group of parents who had not changed their mind (they believed that they had completed their families regardless) were 27 mothers who reported not wanting any more children after the birth of their child with CF.

The follow-up study indicated that 16 (59%) of the 27 mothers who at baseline reported not wanting more children after the diagnosis of their child with CF had changed their mind. The main reasons for wanting more children than originally thought was that they were coping with their child with CF who remained in good health or that they felt more comfortable about the diagnosis of CF. Four of the 6 mothers who originally wanted more children also had changed their minds (they no longer wanted more children) because of concerns about the health of their child with CF.

Intention to Use Prenatal Diagnosis
At baseline, 46 (82%) mothers reported that they would “definitely” or “probably” use prenatal diagnosis in a subsequent (hypothetical) pregnancy. Of the 46 mothers, 16 (37%) wanted to know to prepare for an ill child, 18 (39%) to decide whether to terminate the pregnancy, and 12 (26%) to terminate the pregnancy. Of the 12 who wished to terminate the pregnancy, 9 indicated that it would be because of the (poor) quality of life of the child and the family.

Nine (16%) of the 56 mothers reported that they “definitely” or “probably” would not use prenatal diagnosis, and 1 mother did not respond. Of the 9, 2 considered that CF was not sufficiently severe to warrant prenatal diagnosis, 2 would rather trust to chance, 1 was opposed to termination of pregnancy outright, and 1 believed that termination would devalue the life of their existing child with CF.
Twenty-five (45%) mothers reported that their views on prenatal diagnosis had changed since the diagnosis of CF. Table 2 contains a summary of the most important benefits and problems of prenatal diagnosis as reported by mothers at baseline and at follow-up.

Preparedness to Terminate an Affected Pregnancy
At baseline, 13 (23%) mothers reported that they previously had a termination of pregnancy. Six of these were because of a CF-affected pregnancy. Mothers were asked whether they would consider termination if, in a future pregnancy, prenatal diagnosis confirmed that the fetus had CF. Twenty-nine (52%) mothers reported that they “definitely” or “probably” would terminate, whereas 16 (28%) mothers reported that they “probably” or “definitely” would not terminate. Ten (18%) mothers were unsure, and 1 (2%) mother did not answer. Considerations about termination included the quality of life of the child (12), the quality of life of the family (6), or that they could not cope with another child with CF (8). The main reasons reported against termination were that CF was not sufficiently serious to warrant termination (10), they do not wish to abort (4), they do not want to interfere (3), and for religious reasons (2). Of those mothers with a partner, 79% indicated that they thought that their partner would agree with their decision regarding termination.

Change in Attitude Toward Termination of Pregnancy
At baseline, 14 (25%) mothers reported that their views on termination of pregnancy had changed since having a child with CF. Half (7) of these mothers reported that the main change was toward consideration of termination of pregnancy, which previously would not have been considered. One mother reported that she previously was in favor of termination but would no longer consider it. The follow-up study indicated that even more mothers (37%) reported that their views on termination had changed since having a child with CF.

Follow-up Study: Mothers’ Use of Prenatal Diagnosis and Termination of Pregnancy
Mothers’ actual reproductive behavior since the birth of their child with CF is presented in Fig 2. Twenty-seven (63%) mothers had been pregnant since the index child with CF, resulting in 55 pregnancies. Of the mothers who subsequently had become pregnant, two thirds (67%) had used prenatal diagnosis for at least 1 subsequent pregnancy. Of these, 61% had used prenatal diagnosis because they wanted to know whether the fetus had CF, 33% because they wanted to terminate if it were positive, and 6% because of the impact on the quality of life of their other children (without CF) should they have another affected child. The most important reason cited for having used prenatal diagnosis was that it provided the option to terminate (39%), that they would know for sure (28%), that they could not cope with another child with CF (28%), and that they would have time to adjust if the result were positive (22%).

Five of the 33 pregnancies in which prenatal diagnosis was used were positive for CF. All 5 pregnancies resulted in termination. Twenty-five (89%) of the 28 mothers whose prenatal diagnosis result was negative for CF said that they would have considered termination of pregnancy if the result had been positive. There were no false-negative diagnoses of CF.

Comparison Between Hypothetical (Baseline) and Actual (Follow-up) Behavior
A comparison of mothers’ hypothetical behavior (baseline study) and actual behavior (follow-up study) is shown in Table 3. In two thirds (67%), the hypothetically reported behavior regarding use of prenatal diagnosis was the same as their actual behavior. However,

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>Most Important Advantages and Disadvantages of Prenatal Diagnosis at Baseline (N = 56) and Follow-up (N = 43)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Most important benefit or advantage of prenatal diagnosis</strong></td>
<td><strong>Baseline, n (%)</strong></td>
</tr>
<tr>
<td>Knowing for sure</td>
<td>24 (43)</td>
</tr>
<tr>
<td>Provides an option to terminate</td>
<td>17 (30)</td>
</tr>
<tr>
<td>Can relax for the remainder of the pregnancy</td>
<td>5 (9)</td>
</tr>
<tr>
<td>Can prepare or adjust to another affected child</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Could not cope with another child with CF</td>
<td>2 (4)</td>
</tr>
<tr>
<td>Not applicable</td>
<td>5 (9)</td>
</tr>
<tr>
<td><strong>Most important problem or disadvantage of prenatal diagnosis</strong></td>
<td><strong>Baseline, n (%)</strong></td>
</tr>
<tr>
<td>Against termination for any reason</td>
<td>4 (7)</td>
</tr>
<tr>
<td>CF not sufficiently severe to consider termination</td>
<td>8 (14)</td>
</tr>
<tr>
<td>Lack of agreement with partner</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Anxiety about the test</td>
<td>12 (21)</td>
</tr>
<tr>
<td>Risks associated with the test</td>
<td>13 (23)</td>
</tr>
<tr>
<td>Too hard to make a decision if the test were positive</td>
<td>12 (21)</td>
</tr>
<tr>
<td>Not applicable</td>
<td>4 (7)</td>
</tr>
</tbody>
</table>
mothers not uncommonly changed their minds, and in both directions. In relationship to those who had terminated an affected fetus, 4 of the 5 mothers had reported at baseline that they would terminate if prenatal diagnosis indicated CF (1 had been unsure).

DISCUSSION

This study confirms that mothers whose children’s CF was diagnosed through NBS can achieve timely access to reproductive technologies. This cohort reveals high use of genetic counseling services and high use of reproductive technologies. Pleasingly, these high rates of use do not result from unplanned pregnancies in poorly informed families. Rather, these mothers are very well informed about CF in general and about genetic and reproductive technologies in particular. This may reflect our standardized and intensive approach to education at the time of diagnosis, including genetic counseling, and the quality of ongoing care, which includes ongoing access to specialized genetic counseling services.

A striking finding of this study is the extent to which mothers changed their minds about one or other reproductive decision after the birth of a child with CF, a finding that cross-sectional studies have not previously described. For example, one third of mothers had changed their plans about the number of children that they wanted as a result of having a child with CF, nearly half had changed their views on prenatal diagnosis, and one third had changed their views on termination of pregnancy (for or against). These views continued to change with time. For example, whereas 25% of mothers at baseline reported that their attitudes toward termination of pregnancy had changed since having a child...
with CF, this had increased to 37% 5 years later. This emphasizes the importance of continued availability of genetic counseling beyond the period of initial diagnosis and education, regardless of whether families report that they expect to use reproductive technologies.

A wide variety of reasons were presented both in favor of and against prenatal diagnosis. Only 1 parent reported that the reason not to use prenatal diagnosis was because of the perception that it would devalue the life of her existing child with CF. This particular attitude may be influenced by a variety of factors, such as culture and religion. Our findings differ from those of a qualitative British study in which this concern was described by 26% and 33% of families, respectively. Access to genetic counseling was not described in detail in these studies. “Quality genetic counseling” is described as an important component of NBS programs. We believe that the capacity of parents to differentiate decisions about future pregnancies from beliefs about the value of their existing child with CF is one outcome of quality genetic counseling.

It is disappointing how few studies of CF reproductive decision-making describe any aspect of genetic counseling. Those that do, report significant deficiencies. For example, only 40% of US families reported having received any genetic counseling, usually from their CF doctor, with only 17% having seen a genetic counselor. In the United States, referral to genetic counselors is recommended after NBS, although access to ongoing counseling is not described. In the United States, the compliance rate for referral varied between 32% and 90% in the CF centers linked to the New England NBS program. A recent study from New South Wales (Australia) reported that only 52% had ever seen a genetic counselor. In contrast, more than half of the families in our study had seen a genetic counselor more than once. We previously reported that at the time of diagnosis of CF, parents rate receiving general CF information and reassurance of the prognosis as more important than obtaining genetic information or genetic counseling. Given the changing reproductive attitudes and behaviors identified in this study, access to genetic counseling after the initial diagnosis phase could be viewed as just as important.

Before NBS, the diagnosis of CF commonly was reported to end the reproductive lives of many families, because of the fear of having more children with CF. For example, 86% of US families, 75% of French families, and 54% of Belgian families reported wanting no more children after having a child with CF. In a US screened cohort, 52% of parents did not conceive more children. These authors postulated that in this cohort, in which only 22% subsequently used prenatal diagnosis, a range of factors may have influenced parent reproductive choices, including their counseling methods, that families know that the prognosis for CF has improved, and their experiences of caring for a child with CF. In contrast, the majority (63%) of women in our study subsequently conceived. Given that our families are well informed about CF and its prognosis and have equally experienced caring for a child with CF, greater access to reproductive technologies may have contributed to the higher conception rate.

Attitudes toward reproductive technologies were very positive: our figures are among some of the highest reported hypothetical and actual rates of both prenatal diagnosis and termination of pregnancy. In addition to a high level of knowledge and access to reproductive technologies, these high rates are likely to reflect a more accepting attitude toward reproductive technologies in Australia than in the United States. In contrast to the only previous study in this area, the change between their hypothetical and actual behaviors was mostly toward greater use of reproductive technologies.

Despite the sensitivity of this topic, we achieved an excellent participation rate of mothers. We believe that this study has the highest participation rate of any study of CF reproductive decisions, making it the most representative. The study numbers are limited because of the tight age range of children with CF (2–7 years) at inclusion, and, to some extent, this has reduced the number of subgroup analyses that could be performed. It is reassuring that recent studies have shown that even in highly sensitive areas, such as pediatric cancer and palliative care, research generally is not viewed negatively as long as it is undertaken with consideration and sensitivity. We believe that the continued high participation in our follow-up study, together with the high response rate for especially sensitive questions, suggests this was the case in our study. For example, only 1 mother did not answer a question about termination of pregnancy in comparison with 12% in another study.

Most studies of reproductive decision-making in CF have determined maternal perspectives. We set out to capture both maternal and paternal perspectives, but, like others, were unable to recruit sufficient fathers in the baseline study to report their views adequately. The value of engaging fathers in clinical care (and research) is underscored by the fact that 21% of mothers reported that they believed that their partner would have a different opinion on termination of pregnancy.

How do parents balance these technologic advances with the reality that the prognosis for CF has greatly improved? It might be thought that improving survival in CF would lead to a lesser perception of disease severity. Notwithstanding accurate assessment of median survival, the reproductive outcomes reported here reinforce the notion that parents continue to perceive CF as a severe disorder. In contrast to previous reports that NBS does not significantly affect parent reproductive attitudes and behaviors, the high level of engagement with
reproductive technologies reported here suggests otherwise, emphasizing the value of NBS in ensuring that parents are informed appropriately about future reproductive options at the earliest possible time.

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