Everything You Wanted to Know About Children, for $2.7 Billion

Researchers are planning a major study of mothers and children; after 2 years they've narrowed the possible objectives of the study down to 70

Two years from now, the U.S. government hopes to launch the most ambitious study of American children ever. The plan is remarkable: Researchers aim to enroll 100,000 pregnant women and follow their children from birth to their 21st birthday, measuring many factors along the way—from infections during pregnancy to pollutant exposures to signs of psychosocial growth. It would be a sort of Framingham Heart Study, which tracked men in a Massachusetts town for over 50 years.

Only bigger, like “40 Framinghams across the nation,” says study director Peter Scheidt of the National Institute of Child Health and Human Development (NICHD). And like that famous study, proponents say, the National Children’s Study would yield a gold mine of data on how lifestyle and other exposures contribute to disease.

There is a hitch, though: The project—their children for 21 years.

For example, the study could focus on asthma risk to breast-feeding’s role in obesity—holding them to about 70.

The national longitudinal study of environmental influences (including physical, chemical, biological, and psychosocial) on children’s health and development.

Although popular, the congressional mandate has proved a challenge to put into practice. NICHD began by forming 22 working groups of federal and outside scientists to look at everything from fertility studies to collecting biological samples. Last year, it added an advisory committee that includes community and health activists. The process is “trying to be very democratic,” says Johns Hopkins epidemiologist Jonathan Samet, and is distinctly different from the one that produced Framingham, a narrowly focused study of heart disease proposed by heart experts. The process also differs from the one that led to another big National Institutes of Health (NIH) study, the Women’s Health Initiative, which found last year that hormone replacement therapy doesn’t work as expected. Although the Women’s Health Initiative is also a complex set of overlapping studies, it was planned by NIH staff.

The National Children’s Study, by contrast, is being designed with input from 300 scientists in assorted fields. They have managed to narrow the study’s sweep to five “outcomes” of interest, based largely on the number of people affected by key diseases: Birth defects and preterm birth, neurobehavioral disabilities, injuries, asthma, and obesity and hormonal disorders such as diabetes. (Others, such as childhood cancer, are too rare to study in a sample of 100,000.) But planners have struggled for a year to rethink a balloononing number of proposed hypotheses—from air pollution’s impact on asthma risk to breast-feeding’s role in obesity—holding them to about 70.

Tensions boiled over at last month’s meeting of the study’s advisory committee. In a letter from one working group, epidemiologist Nigel Paneth of Michigan State University in East Lansing and NIH asthma researcher Peter Gergen wrote that planning was at an “impasse.” The problem, they said, is that “no hypotheses or group of hypotheses has emerged as the central driving theme.”

Many of those selected so far “do not seem to justify the… study. Some are highly specific, but not of great significance, while others are broad, but as yet unfocused,” the letter said.

At the meeting, advisory committee members also clashed with federal scientists over how to recruit volunteers—whether through large medical centers or, at the other extreme, use of household addresses to get a diverse, probability-based sample representing the U.S. population. The latter approach, some feel, could compromise the medical aspects of the study. “We don’t want to
The Epidemiologist’s Dream: Denmark

If the planners of a U.S. study of children’s health could work in an ideal world, it might be Denmark. Epidemiologists there finished enrolling a cohort of 100,000 pregnant women into a mother-and-child research project last September and expect to finish collecting data from the children over the next year. The entire survey—which is large for this country of 70,000 annual births—is to be completed in 2005 for about $15 million, a tiny fraction of what the cost would be in the United States.

The Danes didn’t design their Better Health for Mother and Child cohort study to answer specific questions or conduct long-term follow-up, as the Americans plan to do (see main text). Instead, they aim to create a databank that generations of researchers can mine and use as a starting point for studies of how medications, infections, nutrition, and even psychological factors affect pregnancy and child health.

Physicians have recruited volunteers among women making their first pregnancy visit. Participants give two blood samples during pregnancy and cord blood when the baby is born. The samples are saved for later use, including possibly for genetic studies. The mothers also answer a detailed questionnaire concerning nutrition; in an 18-month follow-up, they give information on their health and environmental exposures. The public health system is funding the study, with support from private and public foundations.

“Because the Danish population is probably the world’s best registered, Denmark is the ideal place for such studies,” says epidemiologist Mads Melbye, a steering group member from Statens Serum Institute in Copenhagen. Each citizen has a personal identification number that can be used to track data in centralized health care records, disease registries, and a population registry. Even centralized school records may be used. “It’s an epidemiologist’s dream,” says Mark Klebanoff of the U.S. National Institute of Child Health and Human Development, who says tracking subjects is one of the costliest aspects of long-term U.S. studies.

Norway, which has a system like Denmark’s, is launching a mother-child study that will pool data with the Danish group’s. Both benefit from streamlined management. It’s difficult to get things done with too many decision-makers, says Melbye: “Running such a large study has taught us many things, but the chief lesson is that it is essential to put a very small group of people in charge.”

Results are already beginning to trickle out of the Danish study. For example, one group published an article in The Lancet last November that disproved the existing consensus view that a fever early in pregnancy increases the risk for miscarriage. That’s just the beginning: Denmark’s scientific ethics committee has so far given the green light to more than 70 research protocols based on the mother-child study.

Lone Frank is a science writer in Copenhagen.

—LONE FRANK

Ready subjects. Denmark’s 18-month-long birth cohort survey will collect data from mothers and newborns for a new database.

Okay, you’re probably wondering what Denmark has that the United States does not. For one thing, a national ethics committee, which Melbye describes as “very strong, very independent.”

But beyond that, the Danish approach seems to be based on the idea that there is a single system of data collection, and that one can do studies that are either large or small. The U.S. study planner had to go to a large number of sites to collect the data, and then had to worry about whether the data were going to be used for anything. In Denmark, the data are collected in one place and are available to everyone.

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