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# News from the NHLBI

## Children and Clinical Studies: The National Heart, Lung, and Blood Institute's New Multimedia Resource for Pediatric Research

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In the fall of 2008, the National Heart, Lung, and Blood Institute (NHLBI) launched Children and Clinical Studies (1), a multimedia website (Fig. 1) to educate the public and researchers about children's participation in clinical research. The "no more hand-me-downs" theme emphasizes the importance of research focused on pediatric conditions in improving outcomes and quality of life for children.

Many readers of the *Journal* probably associate the NHLBI with scientific research in diseases that affect adults, with programs like the Framingham Heart Study, the Women's Health Initiative, and the Coronary Artery Surgery Study. In recent years, however, the NHLBI has strongly embraced an expansion of pediatric research in all areas related to its mandate, including sickle-cell anemia and other inherited blood disorders, asthma, neonatal respiratory distress syndrome, sleep disorders, and congenital and acquired heart disease. The NHLBI now supports a robust portfolio of basic, translational, and clinical pediatric research through grants, contracts, networks, and consortia.

Pediatric research has its own checkered history that has shaped current public views regarding the enrollment of children in clinical research. This negative perception held by many is not usually derived from personal knowledge of harmful or exploitative research conducted in children. Rather it comes from "gut feelings" and vague recollection of research harms. Many people are familiar with evidence presented at the Nuremberg trials, which revealed both adult and pediatric "research" gone hideously awry.

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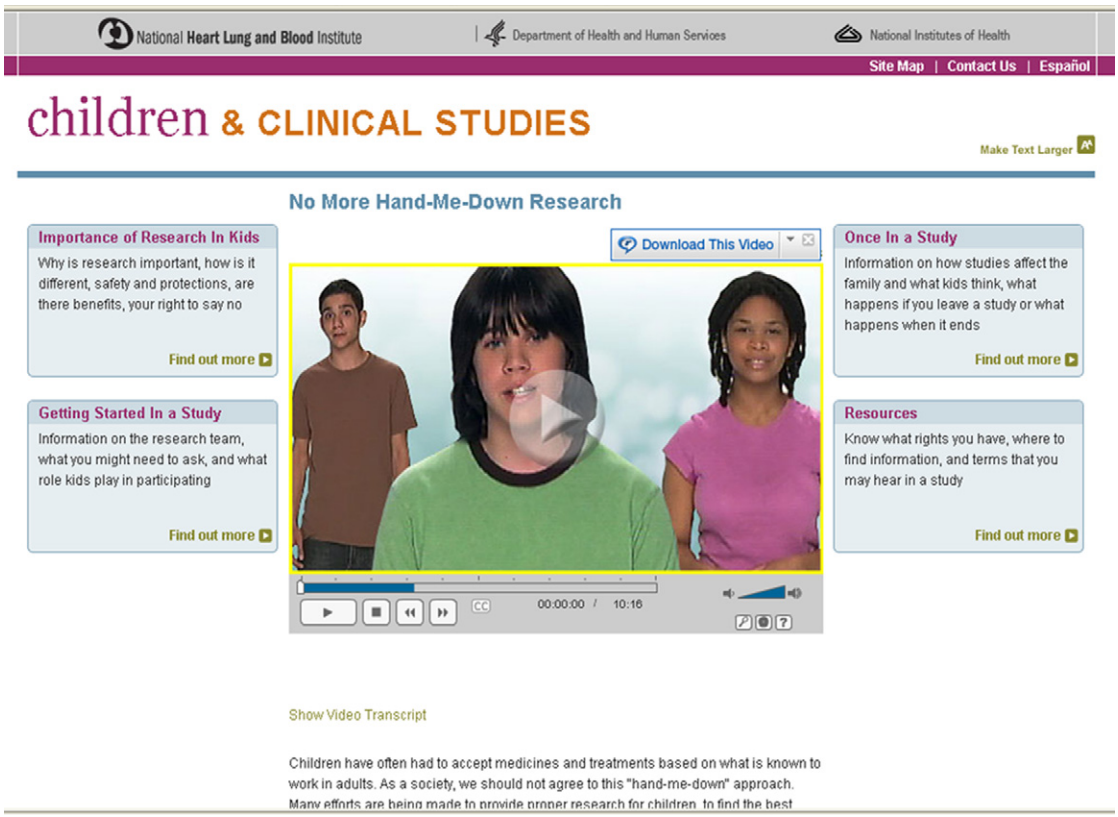
Less familiar is the Willowbrook saga, which made headlines during an investigative television report in 1972 that revealed the horrific care and treatment of the mentally handicapped children living at the Willowbrook State School. Between 1955 and 1970, researchers at the facility deliberately infected children with the hepatitis virus as a purported means of studying the spread and later treatment of the disease in institutional settings. In many cases, parental consent was not obtained for study participation, or children were admitted to the facility only after parents agreed to have their child participate in these studies. It is not surprising, therefore, that in the 1970s, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research found itself grappling with the sensitive and thorny issues of how to extend the benefits of research to children, particularly for diseases that only occur in children, but at the same time ensure that they are protected from harm.

Today, pediatric research remains a challenge for many reasons. There are not always juvenile animal models of pediatric diseases. Assessment tools are often lacking or not suitable for pediatric use. Mainstays of adult research, such as spirometry in pulmonary trials or exercise testing in cardiology studies, are simply not practical for infants and young children. The limited pediatric market translates into few pediatric devices, and many drugs do not have pediatric formulations or are not labeled for pediatric use. The term pediatric covers a broad developmental spectrum, with implications ranging from differential drug metabolism at various ages to concerns about the impact of clinical study interventions on growth. Therefore, pediatric studies need to include children in various phases of development, often

**Figure 1** Screenshot of the Children and Clinical Studies Homepage (1)




following them for extended periods of time, which adds substantially to the costs and time commitment on the part of subjects and research teams (2).

The biggest challenges, however, remain those related to information exchange: informed consent and assent. When asked, 67% of 5,822 adults agreed that pediatric research is needed to advance treatment of diseases that affect children, but only 25% reported that they would consider allowing their child to participate (3). In 2005, a subsequent Harris Poll (4) indicated that only 10% of 2,000 adults surveyed had ever participated in a study. Fewer still have encountered pediatric research. After all, children are usually healthy. Parents who have been approached to enroll a child in clinical research cite several factors that affected their decision-making process, including an evaluation of the risks and benefits, a desire to help others, and an understanding of research processes (4–8). When parents or other family members are not familiar with what happens during a clinical trial, what their rights and responsibilities are, and what they can expect to give and get when entering a study, they are likely to decline enrollment on the basis of uncertainty or fear.

When the Pediatric Heart Network (9) was launched in 2001, we were surprised to find that there were no general, readily accessible resources available for families to consult about pediatric clinical research. This lack was highlighted especially in studies of critically ill infants whose families were preoccupied with their child's desperate medical condition and may have wanted to participate in a trial but had no independent source for information. From this and similar experiences, the NHLBI set about developing those resources.

In 2006, discussions and focus groups began with individuals who were involved with research in children from key institutes of the National Institutes of Health, governmental and private agencies, and academic institutions. As the project evolved, collaborations with various entities such as the National Center for Research Resources Clinical and Translational Science Awards program, the National Marfan Foundation, the Foundation for National Institutes of Health, and New England Research Institutes, to name a few, informed the thinking and approach to creating a valuable resource. The extensive input obtained from parents, children, ethicists, and many others during development of the website ensured that it tackled issues of real importance to parents considering research for their child.

The result is the Children and Clinical Studies website, which addresses how a family may be affected when joining a study, what kids say about being involved in research, and questions and concerns posed by members of minority ethnic groups. Parents and children can learn about safeguards in studies and what happens if they say "no" or want

to leave a study after enrolling. Confusing terms such as placebo, randomization, and blinding are defined, and advice is given about how to locate reliable information on research or medical conditions.

Adults and older children will find the website, written at an average sixth-grade reading level, easy to use and understand. It is organized into short sections so that pertinent information can be accessed quickly but is also designed to encourage the visitor to explore sequentially what happens before entering a study, how to get started in a research protocol, what to expect after enrollment, and how to transition out when a study ends. The site is available in Spanish, and the videos feature families from diverse backgrounds.

Health care providers that are caring for children who may be asked to participate in research might also have questions or concerns related to pediatric clinical studies. Surveys show that nurses, doctors, and ancillary personnel might be unaware of studies for which their patients may be eligible and, although largely supportive of pediatric research, express concern about how informed families are. They also acknowledge that it creates a burden and takes time to talk with parents about research, a topic about which they themselves may know little (10–12).

Recommendations from clinical care providers suggest that research teams need to communicate more effectively with primary health care givers about specific protocols and study procedures, educate clinicians and trainees about pediatric research, and use tools and resources to inform parents about research basics (13,14). The Children and Clinical Studies website can easily serve as an educational resource for medical and nursing school students, health care providers involved in the clinical care of children, as well as families.

The Children and Clinical Studies website is an important resource for the pediatric research community. Directing patients, physicians, trainees, and research teams to the site will foster a better understanding of research in children and help erase the fear and misunderstanding that is often expressed by parents when they say, "I don't want my child to be a guinea pig."

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