Why It's Important

Why do research in children

Video transcript –

Victoria Pemberton, RNC: There are a number of reasons why research in children is so crucial. First and foremost, some things only happen in children. Children are developing. Their brains are developing. Their bodies are developing. And so we're administering perhaps medications or treatments to those developing organs and brains. We don't know the long-term outcomes or the long-term impact of some of those drugs and treatments.

Gail Pearson, MD: It is true that maybe 70% or so of medications that we prescribe in children have never been tested in them. For the most part, this seems to work very well.

Renee Jenkins, MD: When youngsters, until they're around 12, we really calculate the dose for a lot of medications based on their weight. And so let's say an adult preparation comes out that is useful for a disease entity that a child has. You can't just guess at the dose. You really have to be able to tell which dose is safe and which dose is effective. You can't just say, "Okay, if this works for an adult, let me just cut it in half and give it to a kid." That's not satisfactory.

Victoria Pemberton, RNC: To continue to do research in children, says to us as a society that our children are important, and that we value them, and that we value their health. And certainly we know that children that start off less healthy, as adults tend to be less healthy. So I think that we need to continue research in children to protect them, to improve outcomes, to enhance quality of life, and to make them ultimately healthier adults.

Sharda: If it does not work for my child, it might be able to work for another child. And somewhere down the line, how many years apart or whatever, by me doing this clinical study

today, last week, somewhere down the line they're going to have some answers as to what happened, how do you get this, how to cure it-somewhere down the line.

"If we can find a way to reverse some of the effects of the disease, we can make it better and maybe parents won't have to worry about it..."
Sawyer, child in Fabry disease study

Medicines, devices and treatments are often not tested in children.

At nearly half of medical visits, children are given a medicine and 70% of those medicines have only been tested in adults.

The simple truth is...**children are not little adults**.

But without research in children themselves, we have no choice but to treat them that way.

Doctors and nurses often give medicines to children even though they have not been studied and approved by the Food and Drug Administration (FDA) for use in children. This is known as "off-label" use. Most of the time, this works well but when the adult dose is adjusted to the weight of a child, there is a chance that the dose used could be ineffective or even harmful.

While it may sound like "guesswork," it's really been more of a 'hand-me-down' approach. Without research in children though, it's all we have. We need to think about how a child's brain and body are developing...as well as the way that medicines and other treatments are handled in a child's body over time.

Children
AND CLINICAL STUDIES

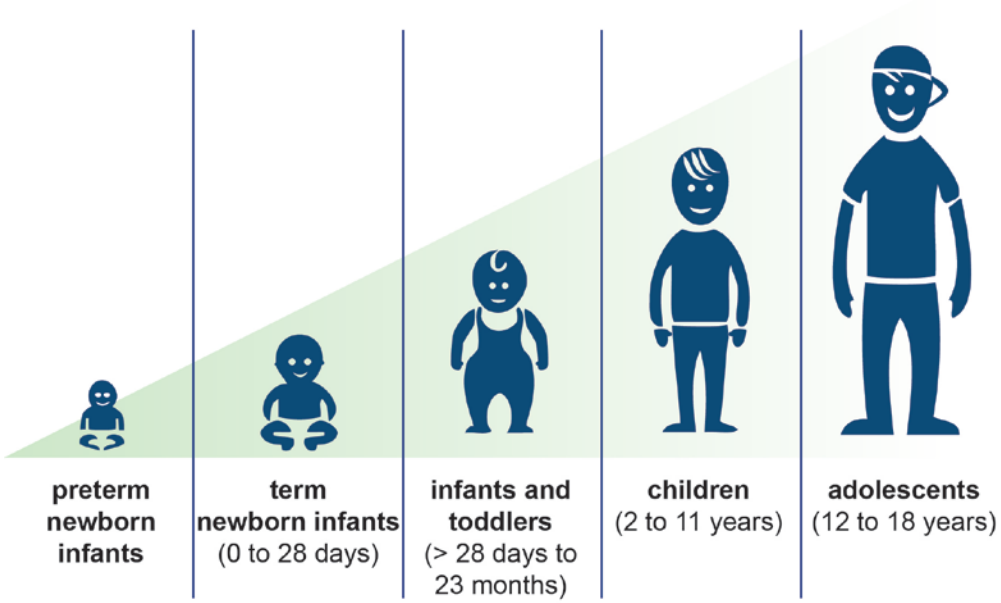
Why Clinical Studies are important

Clinical research in children helps us to treat our children like children, rather than little adults by:

- Finding the best dose of medicines to prevent harmful effects or under-treatment.
- Making chewables, liquids or tablets that are easier for children to take, yet still safe.
- Finding treatments for problems that occur only in children, like prematurity.
- Finding treatments for diseases or conditions that occur in both children and adults but which can act differently in children and adults, like arthritis or heart disease.
- Finding treatments for new or existing diseases to improve the health of children in the future, like vaccine studies that were done years ago help children stay healthier today.
- Understanding how medicines affect children's brains and bodies as they grow and develop.

Stages of Growth

Children are growing. They are changing and maturing all the time. An 8-month-old is completely different from an 8-year-old, who is completely different from an 18-year-old...so even among children, everyone is different. And at each of the stages of growth below, children may need different doses of medicine, different sizes of devices or different types of therapy.



For example, testing of one antibiotic showed that babies needed higher doses than older children to get rid of their infection. Many medicines are filtered out of the body and handled differently by a child's developing liver or kidneys - and because there is limited research, we don't know what the long term effects on these organs may be. So, we need to study them to find out.

"We would not know as much as we know today if people were not brave enough to be in clinical trials. So it helps future generations."
Jackie, mother of child in Fabry disease study

"She's part of a different statistic that's going to help other babies..."
Nicole, mother of child in heart defect study

Research Versus Care

Video transcript –

David Wendler, PhD: Research isn't just taking care of the kids who are in the study. It's also at the same time trying to learn things: how to do better, how to identify better medications, safer medications, for other kids for future medications. Because it's a process of testing medical interventions, treatments, and medications, a lot of times clinical research studies can look a lot like regular medical care. They often take place in hospital; they're often conducted by doctors and nurses, people who wear white coats and have stethoscopes around their necks; and a lot of times, it's hard to know what the difference is between a research study and regular medical care. So a lot of what's very important is getting clear for yourself on what those differences are. Are they going to be shorter procedures, longer procedures? Will the drugs be different? How is what's going to happen to my child, if I enroll them in this study, different than what would happen to them if they just got standard medical care? How are those differences going to affect my child? And how are those differences important for helping other children in the future? And then just deciding whether you want to be part project or not.

"...sometimes I forget that I'm on a study because everything's so routine: I take my medicine in the morning, I take my medicine at night."
Bianca, child in kidney study

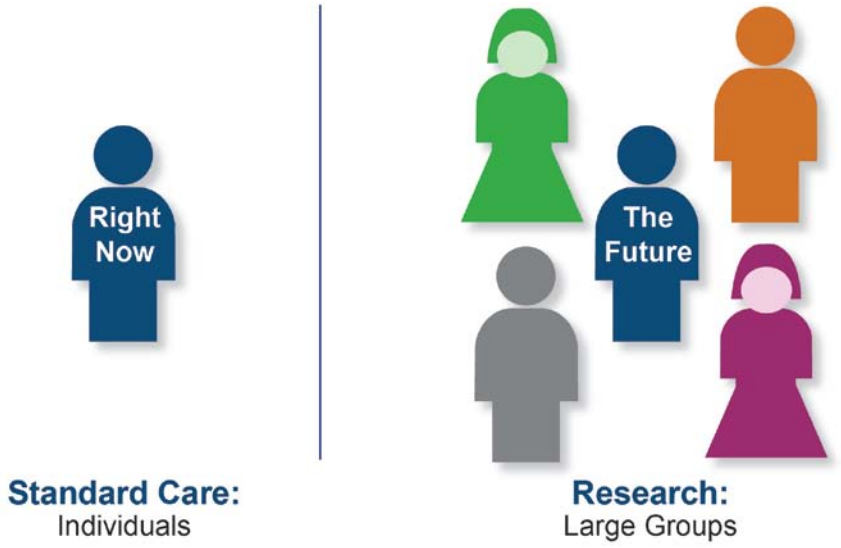
How Research is Different than Care

Clinical research can look a lot like regular, or standard, medical care. Sometimes it is hard to tell the difference.

Here are some of the ways they may be similar:

- The researcher and your healthcare giver can be the same person.
- The setting may be your regular clinic.
- The treatments may seem the same.

Research is done to help find out if a treatment or procedure is good for a large group of people with a certain disease or condition. Research helps to answer questions for the *future* health of those populations. Standard medical care, however, focuses on *individual* needs in the *present*.



When considering enrolling your child in a study, make sure you understand the difference between the regular care your child gets at the doctor and what's involved in research. Even when the place and healthcare providers are the same as your regular healthcare team, find out what makes it a research study.

Make sure you ask: *How is this different from standard care?*

- Will I see different doctors and nurses for the study?
- Will I go to a different hospital or clinic for the study?
- Will the doctors and nurses ask me a lot more questions about my child's condition?
- Will there be more paperwork or additional tests when we are in the study?

- Will there be more rules and deadlines in the study?

Here is an example of how some things in a clinical study are the same as in regular care, while some are different.

	Standard Care	Research
Visit with physician or nurse	✓	✓
Paperwork to enroll (consent)		✓
Eligibility screening		✓
Baseline testing	✓	✓
Medication or procedure	✓	✓
Interim questionnaires or forms		✓
Follow up testing	✓	✓

"...if it does not work for my child, it might be able to work for another child and somewhere down the line...by me doing this clinical study today..."

Sharda, mother of child in kidney disease study

How Children Benefit

Video transcript –

David Wendler, PhD: One of the important things that both parents and children need to ask themselves when they're considering being in a research study, not just whether or not this is the best thing for my child, but they also have to ask themselves: For my child, at this time, in these circumstances, is it appropriate for them to be contributing to a research effort to help others?

Geoffrey: Most of the benefit was not going to be for us now. It was really for other people, for hopefully a future cure.

Gail Pearson, MD: There's the knowledge that you're participating in something that's bigger than you or your child, and has the potential to, even if not benefit your child, or even the other children in the study, to provide some fundamental knowledge about what might be better in the future.

Ned: The study's good, because even if it doesn't help him now, it will in the future. And it might help another kid.

Jill: It's work, but there are also benefits too. Some of them are tangible: We get more information. Some of them are more intangible: We know that we're contributing to science. We know that we could help find a cure for food allergies. We'd be a small part if a cure is found later. And that's a good feeling.

"Oftentimes [parents] will say, 'I thought perhaps it could help my child. But if it didn't help my child, it could help you as researchers...and could help children in the future.'"
Victoria Pemberton RN, Research Nurse

Parents who are asked to enter their child into a study will want to know, "Will being in this study help **MY** child?" It is very important to understand that research is done to gain information about a disease, condition, drug or treatment that will benefit children in the future. It is different from regular medical treatment that is given to help a specific child.

So, while most studies are not done to help a specific child, does this mean there are no benefits to being in a study?

In fact, there can be **potential benefits** when entering a clinical study.

Helping Future Generations

> *"...in exchange for that little vial of blood that may help somebody somewhere, or us..."*
> *Dawn, mother of a child in chronic granulomatous disease study*

One reason that parents say that they join a study is to help other families in similar situations. Today our children have more protection from death, disability and discomfort from many childhood diseases like polio or measles because parents in the past made a decision to allow their child to be in a study to test vaccines.

But still, there are many medicines and procedures that have not been tested in kids. And before they can be accepted for use, they must be tested to see if they are safe and effective.

> *"And I chose to because I wanted to do pretty much anything to help, and also help with the study to help future generations as well."*
> *Sawyer, child in Fabry disease study*

Having Access to New Drugs or Treatments

Researchers test new drugs and treatments because they have reason to believe they might work better or be safer than the standard care. In a study, your child may have access to something that is not available yet. If the drug or treatment is found to be helpful, your child may be among the first to benefit.

"Children who are not able to get the medication [because it wasn't tested in children] are able to get it in a clinical trial."

Jackie, mother of a child in Fabry disease study Britt, parent

Gaining More Information about a Disease or Condition

Sometimes enrolling in a clinical study can give your child a chance to see extra doctors or find out more facts about your child's condition. The study team may be able to tell you about organizations, groups or websites that deal with your child's condition. A clinical study may be able to put you in touch with families going through what you are going through.

"And we wouldn't have known any of that information if we hadn't been in this clinical study. It's just a lot more options that you wouldn't ordinarily know that you had."

Britt, parent of a child in chronic granulomatous disease study

Having Closer Monitoring

A clinical study may offer closer monitoring or additional testing for your child, which may not be part of regular care. Sometimes a study asks parents to keep a diary or to bring a child in to be seen more often, such as weekly visits. Children in a clinical study will be watched closely for side effects and to understand how the treatment is working.

"So, it's actually been good because they've been paying close attention to him..."

Rosaly, mother of a child in aplastic anemia study

Whatever the reason, remember that clinical studies are designed to test if a drug or procedure works and is safe. There may be benefits for your child, but there may not be.

Children AND CLINICAL STUDIES

Terms You Should Know

Video transcript –

Placebo. A placebo is a pill, liquid, or powder that has no active medicine in it. It's a fake.

Randomized. Since researchers don't know which treatment is better, this is a way to determine who gets what, like flipping a coin.

Informed Consent. A parent's guide to learn key facts about a research study.

Protocol. It's a detailed plan that says who can be in a study, for how long, and what will happen. It's like the rules.

IRB. A group of experts who monitor clinical studies to make sure people are safe.

Blinding or Masking. That's when patients-and usually doctors too-don't know which study treatment each child is getting.

Assent. The term used when a child agrees to be in a study.

Clinical studies often include terms that are unfamiliar to you. You should ask your research team to explain each term until you are comfortable that you understand what it means to you. This section discusses some terms very common to clinical studies.

ASSENT:

"The term used when a child agrees to be in a study."

Even though parents and guardians must consent for their child to join a study, children should have a part in making a decision to join a study, if they are capable of doing so. When a child is asked to have a part in the decision, this is called "assent".

Children do want to have a say in what happens to them...and they want to ask questions and have them answered. When children are asked if they want to join a study, it shows respect for them. And they will feel good about being in the study and more committed to doing what the study requires.

If a child is old enough to understand the study, many times assent is required.

> *"You can't [always] just ask a child's parents, do they want to participate. You have to be able to explain it at a level that the child can understand, and get their assent to participate in a project."*
> *Dr. Renee Jenkins, Pediatrician, American Academy of Pediatrics President, 2007-2008*

It has been found that most children from age 7 can understand basic information if it is given at their level. So, in most studies, children are now asked if they agree (assent) to be in a study and are asked to sign an assent form. These forms are usually a simpler version of the consent form that parents sign. They have also been reviewed by the same safety group, the Institutional Review Board, to assure that the forms are accurate and at a child's level. Making sure children have a say is important, but remember - not all studies require assent, and the age when assent is requested can vary depending on the study.

Blinding Or Masking

"That's when patients, and usually doctors too, don't know which study treatment each child is getting."

This study term can sound scary. But it is really pretty simple. In some studies, it is important that certain people do not know (or are blinded to) which study group your child is in. You may be blinded, or your doctor...or the research team itself.

Why? Researchers want to make sure that anything you are filling out, like surveys or diaries - and anything the doctors or research team may be doing, like physical exams or tests - are not affected by knowing which group anyone is in. Let's imagine that your child is in a study of a new medicine. If your doctor knew that your child was taking the new drug, maybe the doctor would go in to the study thinking this is a great drug, and then may, unknowingly, evaluate results based on that

opinion. Or, you may think that because your child is suddenly tired, it has to do with the drug. Researchers want to make sure that the data that is collected is true and not affected by how any one person feels about the treatment.

> *"...the whole point of the study was to not know whether your child was receiving the drug or not. If they were receiving the drug, you might hesitate to give it to them if you saw something else wrong, thinking it might be a side effect from the drug... So the idea is not to have any idea, either way, and keep an open mind."*
> *Jose, father of child in heart defect study*

One important thing to know is that, in every study, there is someone who knows what drug or treatment each participant is taking. In an emergency, the research team and doctors can find out quickly.

Informed Consent

"A parent's guide to learn key facts about a research study."

This is the way that you as a parent are given details about a study so that you can decide if your child should join a study. You are "informed" so that you can give your "consent" or okay. Nothing can happen until you consent to it.

> *"The rules state that you only do research on somebody if you get their informed consent before you enroll them in the research and before you do anything with them."*
> *Dr. David Wendler, Clinical Bioethicist*

Most people think about "informed consent" as a big long document that is given to them when they are asked to be in a study. And while there is a form, the discussion you have with a member of the research team is vital. The study team wants you to know about every detail of the study...you should know everything about what will happen when and what your and your child's involvement will be.

> *"...sit down with the person who gives you the informed consent document and ask them to just explain the study to you in normal terms. "*
> *Tasmeen Singh, Research Coordinator*

Take the time to ask them questions.
Sit down and read the full informed consent document.

After that, if you still have questions, make notes to yourself and go back to the research team.

Take your time! The informed consent form can be long and may have words that are hard to understand. Ask your research team for any help you might need...remember, always ask questions!

IRB

"A group of experts who monitor clinical studies to make sure people are safe."

Most research done in the United States must have what's called "independent review." This means that a group of experts in research on people, who are separate from the research, reviews it. In the US they are usually called Institutional Review Boards (IRB). Outside the US, they can be called Research Ethics Boards or Ethics Committees. They review research studies to decide whether or not to allow the studies to be done at the hospital, doctor's office, clinic or other place for which the IRB is responsible. IRBs are made up of different types of people: doctors, nurses, ethicists, community people, attorneys, patients, pharmacists and others.

The IRB's role is to help ensure that the study is well designed, that the risks are as low as possible and that the rights of study participants are protected. When IRBs review studies in children they take extra care and follow special rules.

> *"So you wouldn't even get invited, the study wouldn't even be proposed to you, unless it had passed all of those hurdles and all of those reviews."*
> *Dr. David Wendler, Clinical Bioethicist*

The IRB continues to monitor the study throughout its duration for safety and to make sure it's continuing to be run properly.

You can usually tell if an IRB has reviewed the study by a stamp on the consent form. If the consent form doesn't contain this information, ask your research team if the IRB has reviewed and approved the study.

Placebo

“Placebo is a pill, liquid or powder that has no active medicine in it. It's a fake."

> *"We did find out that she wasn't on [the study drug]. But even if she was...that's part of a study now...she is already part of a different statistic that's going to help other babies..."*
> *Nicole, mother of child in heart defect study*

There are lots of questions parents have about a placebo. A placebo can be a sugar pill or a look-alike procedure or device that has no curative effects. Parents might worry that their child is going to be denied effective treatment if a placebo is part of a study.

But it is important to know that there are ethical rules that help researchers decide if a placebo is okay to use in a study with children. A placebo must pose little risk to participants and the harms and benefits of being in the placebo group should be similar to those in the treatment group.
A lot of times, studies compare a new treatment to an older treatment. But sometimes it is necessary to see if a new treatment is better than doing nothing. This isn't as silly as it sounds because some treatments have side effects that are harmful. And believe it or not, some patients who get the placebo in studies do improve.

Sometimes there is a standard therapy and researchers want to see what happens if a new therapy is added. This is commonly done in child cancer studies where all children get the standard therapy and half get a new treatment and half get the placebo to see if adding a drug will have more benefits or not.

Most importantly, **risks must be minimal**.

"In any sort of life threatening situation, placebo would be inappropriate and people wouldn't use that."

Dr. Renee Jenkins, Pediatrician, American Academy of Pediatrics President, 2007-2008

Protocol

“A detailed plan that says who can be in a study, for how long, and what will happen. It's like the rules."

The Clinical Study Protocol is the document that describes a study...why the study is being done, how the study will be conducted and how results will be analyzed. If the study is taking place at many different locations, study teams at each site will use the protocol to perform the study in exactly the same way.

The protocol will describe:

- Why the study is being done.
- What types of children can be in the study.
- When the visits, tests and procedures will take place.
- The types of medicines and dosages to be used.
- How long the study will last.
- How children will be kept safe.
- Possible benefits and risks.
- How privacy will be protected.
- How side effects will be monitored and reported.
- Who will monitor the safety of the study participants and how often.
- How the results will be analyzed.

Randomization

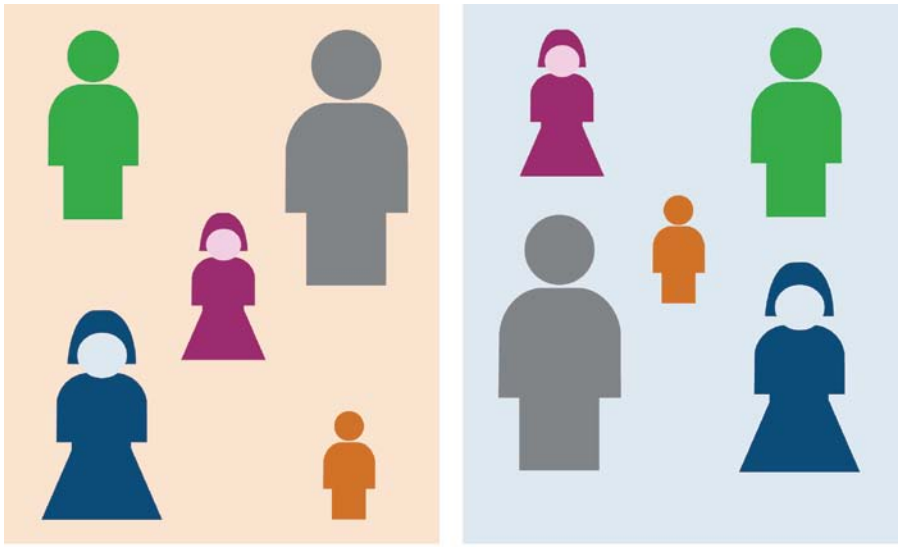
"Since researchers don't know which treatment is better, this is a way to determine who gets what...like flipping a coin."

Randomization is a fancy way of saying "by chance". It's similar to rolling dice or flipping a coin. It is often the best way that researchers have to end up with study groups that will be similar in age, ethnicity and other characteristics in order to better compare the results at the end of a study.

Picture a bowl filled with the same number of green and blue marbles. You cannot see them but you are going to pick one. Green marbles go to DRUG A, and blue to DRUG B. You can't know which color you'll grab before you do it, so there's no determining beforehand which color might get picked at any time. That way, the children selected into treatment groups remains "random".

> *"What you want to do is try to eliminate as much variability or bias in how you sort people into whether you get the treatment or not..."*
> *Dr. Gail Pearson, Pediatric Cardiologist*

If we know who is getting what drug or treatment, we are more likely to make judgments about what is better before we really see the results.



Study Group A Study Group B