RESEARCH INFORMATION SHEET

Name of Study: **TrialNet (Natural History Study)**

Who is Eligible:
- are between the ages of 2.5 and 45 years and have a parent, brother/sister, or child with T1D
- are between the ages of 2.5 and 20 years and have an aunt/ uncle, cousin, grandparent, niece/nephew, or half-brother/sister with T1D
- have not been diagnosed with diabetes

Brief Description: This study will help us learn more about how type 1 diabetes occurs as well as help us to identify people who may be eligible for prevention trials through screening. By ongoing monitoring, we will compare people with and without auto-antibodies to help us better understand differences over time.

Want more information or have a question? Call Heidi at 403-8866 or email Heidi.Virtanen@ahs.ca

Alberta Children's Hospital Diabetes Clinic

Pathway to Prevention Study

Type 1 Diabetes TrialNet

It's families like yours that help TrialNet make important advances in T1D research.

A future without T1D starts with you. Get screened!

Thanks in large part to #T1Dfamily members, we understand T1D as a disease that progresses in three distinct stages. This new definition in conjunction with TrialNet's Pathway to Prevention screening, allows for earlier detection and intervention.

The Stages of T1D

Stage 1	Stage 2	Stage 3
• The immune system has begun its attack on insulin-producing cells • 2 or more autoantibodies are present • Blood sugar is normal; there are no symptoms	• Blood sugar becomes abnormal due to increasing loss of insulin-producing cells • 2 or more autoantibodies are present • No symptoms	• Blood sugar now becomes dangerously high because of continued loss of insulin-producing cells • 2 or more autoantibodies are present • Classic symptoms

Finding T1D in its earliest stage is critical. To find out if you qualify for free screening through the Pathway to Prevention Study, visit **www.trialnet.org/participate**

A future without T1D starts with you. #T1Dfamily

Contact TrialNet for more information about participating near you:
call **1-800-425-8361**, email **info@trialnet.org** or visit **www.trialnet.org**

Quick Facts

What is risk screening?

- A free blood test to detect your risk of T1D years before symptoms appear

Who can get screened?

- People between the age of 2.5 (age 3 in UK) and 45 with a parent, brother, sister, or child with T1D
- People between the age of 2.5 and 20 with a grandparent, aunt/uncle, cousin, niece/nephew, or half-sibling with type 1 diabetes

Why get screened?

- Family members of people with T1D are at a 15x greater risk of developing T1D
- The ability to screen for risk of developing T1D provides an opportunity to participate in research that aims to prevent disease progression
- Participants receive close monitoring—their risk of being diagnosed in diabetic ketoacidosis (DKA) decreases from 30% less than 4%

Pathway to Prevention Study

Type 1 Diabetes TrialNet

Super important. Really easy.

Detecting T1D at its earliest stage is critical. A simple blood test is all it takes to learn your risk. Results are typically available in 4-8 weeks.

1. Get Screened

TrialNet screening is available by appointment at one of our many locations worldwide. Or, we can mail a test kit to you. To learn more, visit **www.trialnet.org**.

Visit Us

Schedule a screening appointment at one of 200 TrialNet locations.

Lab Test Kit

Take it to your local lab or doctor's office for your blood test.

In-Home Kit

Collect your own blood sample with a finger-prick and mail it back to us.

2. Eligibility

If you test positive for two or more T1D autoantibodies, you'll be invited to an eligibility visit. During the visit, you will receive additional testing to confirm your eligibility for a clinical study. If you test positive for one T1D autoantibody, you will be asked in for further testing. If your screening results are negative and you are under 18 years old, you may be offered rescreening opportunities.

3 Enroll in a Trial

TrialNet offers studies for monitoring, prevention, and new-onset. The monitoring study is available to people at increased risk for developing T1D. For people in early stage T1D (stage 1 or stage 2), prevention studies are testing ways to slow down disease progression. Newly diagnosed individuals (stage 3) may be eligible to enroll in new onset studies testing ways to preserve insulin.

Monitoring

Annual or semi-annual monitoring for those at risk.

Prevention

Studies that test specific therapies to maintain insulin production.

New Onset

Studies designed to preserve insulin for the newly diagnosed.

What we learn

When you participate in the Pathway to Prevention Study, you learn your risk of T1D, but we learn so much more! Your blood sample (less than ½ teaspoon) can be used for many other studies to advance our knowledge of T1D.

Autoantibodies

TrialNet screening looks for five auto-antibodies that signal an increased risk for T1D. Two or more autoantibodies signal early stage T1D, and the risk of clinical diagnosis nears 100%. There may be other autoantibodies yet to be discovered. Another reason why your participation is so important!

Beta cells

In people with T1D, the immune system mistakenly attacks healthy insulin-producing cells, called beta cells, and destroys them. Your blood sample, when compared with thousands of others, furthers our understanding of how beta cells react in different stages of T1D. And that's important to finding a way to slow down disease progression.

Immune response

Your blood sample provides greater knowledge of risk factors and events within the immune system that trigger T1D. When you get screened, your sample is compared with thousands of others to help us learn more about why some people go on to develop T1D while others do not.

Our Goal

Your participation today has the potential to lead to life-changing therapies, prevention and the ultimate goal of a cure!

Type 1 Diabetes TrialNet

TrialNet is a network of diabetes centers dedicated to the study, prevention, and early treatment of type 1 diabetes.

To learn more about type 1 diabetes studies or to get a referral to a TrialNet study, call toll free **1-800-HALT-DM1** (1-800-425-8361). You can also learn more about TrialNet on the web: **www.DiabetesTrialNet.org**.

TrialNet Pathway to Prevention

Participant Handbook

Type 1 Diabetes TrialNet

Type 1 Diabetes TrialNet

Researchers in this study are part of a larger group called Type 1 Diabetes TrialNet. TrialNet is an international network of centers dedicated to the study, prevention, and early treatment of type 1 diabetes. We have clinical centers in the United States, Canada, Europe, and Australia.

We are conducting studies to:

- Learn more about the common risk factors among people who get type 1 diabetes.
- Test treatments that could help delay or prevent the start of type 1 diabetes.
- Test treatments that might help people who have recently been diagnosed with diabetes keep producing their own insulin

TrialNet is supported by:

National Institutes of Health

National Institute of Diabetes and Digestive and Kidney Diseases

JDRF IMPROVING LIVES. CURING TYPE 1 DIABETES.

You can learn more about type 1 diabetes studies and get a referral to a TrialNet study or request a screening test kit at: **www.DiabetesTrialNet.org**.

You can also learn more about TrialNet by calling: **1-800-HALT-DM1** (1-800-425-8361).

Clinical Center: _____

Research Physician: _____

Study Coordinator: _____

Tel: _____

Fax: _____

E-mail: _____

TN01March 2019

Participant Handbook

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Pathway to Prevention

Study Overview

We do blood tests on people who have family members with type 1 diabetes to:

* find people who are at higher risk of developing diabetes.
* find people who might be right for TrialNet studies on preventing or delaying diabetes.
* learn more about what happens in the body months and years before a person develops diabetes.

After you read this handbook, we will talk with you about the study and answer your questions. We will ask you to sign a consent form if you want to be in the study. As you make your decision:

* Ask us any questions you have.
* Talk about the study with your family doctor. Your doctor can call us with questions.
* Talk to your family and friends.
* Take the time you need to make your decision.

Background

In type 1 diabetes, the immune system attacks and destroys the cells that produce insulin.

When the immune system attacks the body's own cells, as it does in type 1 diabetes, it makes **autoantibodies**. With a blood test, we can detect diabetes-related **autoantibodies** years before diabetes develops.

When the immune system first starts the attack, the body can still make enough insulin, and blood glucose levels stay in the healthy range. After many of the cells that make insulin have been destroyed, the person's blood glucose levels go up.

The progression of type 1 diabetes

Type 1 diabetes is now understood as a disease that progresses in three stages.

TrialNet screening looks for as many as five diabetes-related autoantibodies that signal an increased risk of T1D. Two or more of these autoantibodies is early stage T1D.

T1D starts with gene(s) that increase risk. T1D occurs in about 1 in 300 people without a family member with T1D. However, T1D occurs in as many as 1 out of 20 people who have a family member with T1D.

The first two stages of T1D can be identified by TrialNet screening prior to symptoms. Our goal is to identify the disease in its earliest stage and to test treatments to stop disease progression by preserving beta cell production.

Stage 1 is the start of type 1 diabetes.

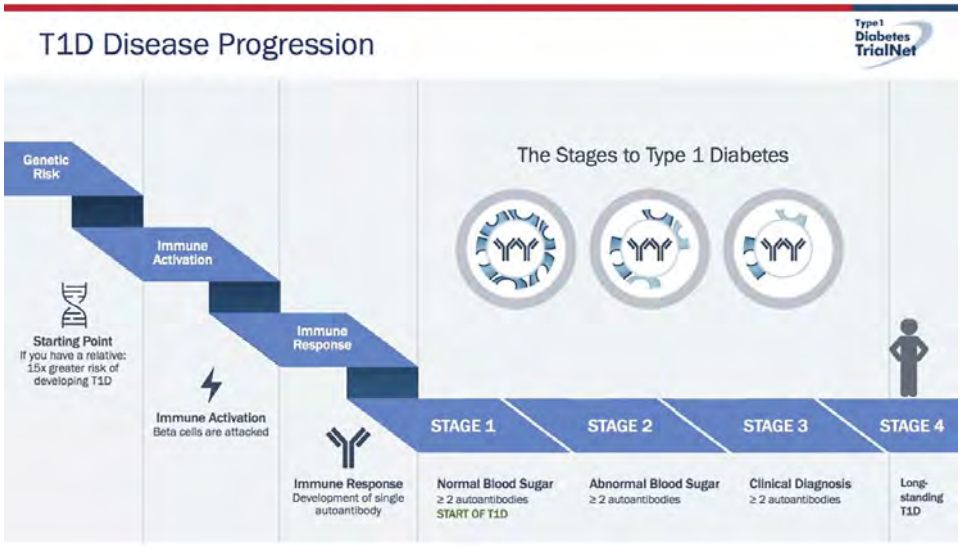
Individuals at Stage 1 have two or more diabetes-related autoantibodies. The immune system has already begun attacking the insulin-producing beta cells, although there are no symptoms and blood sugar remains normal.

Stage 2

Like stage 1, includes individuals who have two or more diabetes-related autoantibodies. But now blood sugar levels have become abnormal due to increasing loss of beta cells. There are still no symptoms.

For both stages 1 and 2, lifetime risk of developing high blood sugars that signal clinical type 1 diabetes approaches 100 percent. However it is not known when this diagnosis will happen. Therefore, monitoring progression of the disease by having periodic blood tests is very important and may help to diagnose the onset of clinical disease before symptoms occur.

Stage 3 is when clinical diagnosis has typically taken place. By this time, there is significant beta cell loss. Symptoms of diabetes, like frequent urination, thirst, weight loss, and fatigue are often present at this stage.



The schedule of visits in this study will let us keep track of your progression.

Participating in Monitoring will help you learn more about your diabetes risk and will provide you with important information about your progression towards type 1 diabetes. If at any point you are eligible for a study testing new treatments to prevent or delay type 1 diabetes, we will tell you about it.

Everything we learn from this study will help researchers in their quest to better understand, how to find a way to prevent or cure type 1 diabetes. As a research volunteer, you are part of this journey.

Who Can Be in This Study?

To be screened in the Pathway to Prevention Study, you must have a close blood relative with type 1 diabetes (defined as diagnosed before age 40 and started to use insulin within one year). You are eligible to be screened if your relative was diagnosed later or started to use insulin later if they were confirmed as having the presence of diabetes autoantibodies at diagnosis).

You can be screened if you are:

[ ] Age 2.5 to 45 and have a sister, brother, child, or parent with type 1 diabetes.

[ ] Age 2.5 to 20 years and have a niece, nephew, aunt, uncle, grandparent, cousin, or half sibling with type 1 diabetes.

Even if you are screened, it is possible you might not be able to be in monitoring or a prevention study if you meet certain criteria or need to take certain medications, such as:

- Medicine to lower blood glucose.
- Medicine that affects your immune system.
- Steroids. (This may include asthma inhalers.)
- Other chronic medical problems

Note: Individuals tested outside of TrialNet and found to be positive for autoantibodies are eligible to be screened. If results are confirmed by TrialNet Screening, these individuals may be eligible for a prevention trial but will not be part of Monitoring in the Pathway to Prevention Study.

Reasons to get Screened:

By being tested, family members provide blood samples that are a precious resource for scientific investigation. Your participation supports the discovery process which will enable researchers to learn more about the causes of diabetes in different people, test ways to delay the progression of the disease in people at risk, and ultimately prevent it. TrialNet screens about 15,000 relatives like you each year. Only ~4-5% of all relatives screened will have autoantibodies. If we find you have one or more autoantibodies, you will be invited to have further testing.

Reasons to be Monitored:

If you have autoantibodies, you are at risk for developing diabetes. During Monitoring, TrialNet can provide you with test results which supply additional information about which stage you are in towards developing the disease.

If you have one autoantibody, you will be re-tested annually to determine if you develop additional autoantibodies which is a sign of increased risk. If you have two or more autoantibodies (stage 1 of diabetes) you will be offered monitoring on a regular basis either once or twice a year and test results will be shared with you after each visit.

While being monitored, TrialNet will tell you about prevention studies for which you may be eligible. If you are diagnosed with diabetes, it is likely to be identified before you develop clinical symptoms. This is important as it can help avoid hospitalization for a potentially life-threatening disease called diabetic ketoacidosis (DKA). Avoiding DKA at diagnosis may help improve glycemic control over time. Early diagnosis may also help preserve residual beta cells, which helps reduce hypoglycemia (blood sugar that is too low) as well as the risk of long-term diabetic complications including eye, nerve, kidney, and heart disease.

There are possible benefits to you when you come in for all your visits.

- **Early diagnosis:** If you develop diabetes, our tests will likely show this before you have symptoms. You can see your doctor and start taking insulin before you feel sick.
- **Chance for another TrialNet study:** Depending on your test results, you may be able to join another TrialNet study.

Screening Visit

To do the test, we need a small sample of your blood (about a tablespoon).

- You can have the blood drawn at a TrialNet site, or by TrialNet staff at a diabetes camp, diabetes walk, or other similar events.
- You can also provide consent to request a test kit at: www.diabetestrialnet.org
- You can take the test kit to your doctor or local lab to have your blood drawn, and then send it back to us.
- You can also request a home blood collection test kit. This requires pricking your fingertip to obtain about 10 drops of blood collected in a tube.
  Note: We may need to repeat the home collection with a regular blood draw if you do not collect enough blood into the tube.)

We test your sample for up to five autoantibodies: GAD65A, mIAA, IA-2A, ZnT8A, and ICA.

We will get the results in 4 to 6 weeks.

Results

Over 95% of the people we test are negative for autoantibodies.

If you are negative for diabetes autoantibodies you are at low risk for developing diabetes at this time. (This does not mean you will never develop autoantibodies or diabetes in the future.) TrialNet will let you know if there may be re-screening opportunities in the future. Please contact us if you are tested outside of TrialNet and learn you have developed autoantibodies. We will let you know if there are any ongoing prevention studies for which you may be eligible.

- It is possible there may be opportunities to re-screen in the future.
- Please let us know if you are diagnosed with diabetes.
- We may call you in the future to ask you to be re-screened or to find out if you have developed diabetes.

Monitoring Visit(s)

Annual Re-Testing for Individuals with One Autoantibody:

If you are positive for one autoantibody at Screening, we will ask you to return in a year for another autoantibody test to monitor you for development of additional autoantibodies. If you develop additional autoantibodies this indicates you have stage 1 diabetes and are increased risk for developing diabetes. We will invite you to an eligibility visit to begin being monitored. The tests done at the eligibility visit determine your monitoring schedule (see below).

Eligibility Visit for Metabolic Monitoring:

If you are **positive** for **two** or more autoantibodies on a Screening test, we will ask you to come to a TrialNet site within 3 months for your Eligibility visit. This visit includes the following tests:

- Autoantibodies
- Oral glucose tolerance test (OGTT), see p. 9
- A1c (see p. 11).

It is possible you will not be eligible if you meet certain criteria or are taking any medications that could affect your test results and our ability to monitor you.

Metabolic Monitoring Visits

Monitoring visits will take place either annually or semi-annually, as determined by results at the Eligibility visit.

Annual Monitoring

Individuals with two or more autoantibodies, **normal glucose tolerance, and HbA1c < 6.0%** will have testing at least once a year including an OGTT, with HbA1c and autoantibodies as needed (to determine eligibility for a prevention study).

Semi-Annual Monitoring

Individuals with two or more autoantibodies and either **abnormal**

glucose tolerance or HbA1c ≥ 6.0% will have testing twice year including an OGTT, with HbA1c and autoantibodies as needed (to determine eligibility for a prevention study).

NOTE: You will need to maintain your visit schedule as determined by your study team. All participants will be asked to complete study visits within four weeks of the required date.

What to Expect at Visits

At every visit, we will draw blood. The volume of blood that we draw will always be safe for your age and weight.

- We will draw blood for tests to see what your risk of diabetes is.
- We may also take blood samples that we will store and use later in other studies to learn more about type 1 diabetes.
- At some visits, we may draw extra blood to make sure the results are accurate.

At some visits, we may ask about your diet and physical activity, and/or do a short physical exam.

	Blood draws for tests that include:	Allow	Need to Fast?	Must be done at TrialNet site?	Can be done at doctor's office, local lab, diabetes camp, diabetes walk?
Screening	Autoantibodies	30 min	No	No	Yes
Annual Re-Testing	Autoantibodies	30 min	No	No	Yes
Eligibility	Autoantibodies, A1c, OGTT	3 hrs	Yes	Yes	No
Annual Monitoring	OGTT, A1c, Autoantibodies as needed	3 hrs	Yes	Yes	No
Semi-Annual Monitoring	OGTT, A1c, Autoantibodies as needed	3 hrs	Yes	Yes	No

Oral Glucose Tolerance Test (OGTT)

This test shows if your body makes enough insulin to use the amount of glucose you would get from a regular meal. If your body can't make enough insulin, it may mean that diabetes is starting to develop.

Test Prep

Most of the time you will undergo an OGTT where we will use a fingerstick to obtain blood samples and one sample taken from a vein in your arm. Sometimes the OGTT test will be done with use of an IV line in a vein in your hand or arm. We will take all the blood samples from this line. This allows us to get additional information from the test.

- You will drink about a cup (less for children) of a sweet drink. You have to drink it all in 5 minutes. Some people feel a little sick to their stomachs (nauseated) when they drink this.
- You will need to sit quietly or rest in bed during the 2 hours after you drink the glucose.

Before Your OGTT

Call us if you're taking any prescription or over-the-counter medicine that you haven't told us about.

Some medicines may change the test results.

Eat plenty of carbohydrate.

Eat at least 150 grams of carbohydrate (starches and sugars) a day for at least **three days** before the test. Most adults and children eat 150 grams or more in a usual day, so this will probably not mean a new diet for you. Eating more than 150 grams of carbohydrate is OK.

Foods with carbohydrate include:

Grains: breads, pasta, crackers, cereals (hot and cold)
Beans
Starchy vegetables: potatoes, peas, corn
Fruit: fresh, canned, dried, juices
Milk: whole, 2%, 1%, non-fat, chocolate, yogurt
Sweets: candy, cookies, cakes, pies, regular sodas

Each of these has about 15 grams of carbohydrate:

- 1 slice of bread
- 6 crackers
- 1/2 cup pasta
- 1/3 cup rice
- 1 cup low-fat milk
- 1 medium apple

Meats and non-starchy vegetables (leafy greens, broccoli) have little or no carbohydrate. You can have these foods in the amounts that you normally eat.

Drink plenty of water the day before and the day of the test.

It will be easier for us to draw blood for the test.

For 10 hours before the OGTT:

Have no food or drink other than water.

This includes:

- No coffee or tea
- No alcohol
- No diet sodas or sugar-free gum. Even though these have no calories, the flavor can prompt your body to make insulin, and this may change the test results.

Don't use tobacco.

Don't smoke or chew tobacco or use nicotine products.

Don't exercise.

Get a good night's sleep.

Don't schedule the test for the morning after you work a night shift.

A1c: The Test with a Memory

An A1c test (also called HbA1c) shows whether or not your average blood glucose level has been within the normal range over the past 2 to 3 months.

Beta cells in your pancreas make insulin. When your body makes enough insulin, your blood glucose levels stay in a healthy range. If your immune system has killed off some of your beta cells, at times your body may not be able to make enough insulin right when you need it. Blood glucose levels are higher than normal for a time. Then the body is able to catch up and blood glucose levels come back down to normal.

When blood glucose levels are high, extra glucose attaches to red blood cells. A blood test done weeks or even two or three months after blood glucose was too high will show that the red blood cells have extra glucose attached. That's why the A1c is called the test with a memory.

In someone who does not have diabetes, the A1c level will be less than 6.5%.

If your A1c is 6% or higher, or if it has increased 0.5% or more from the last time, we need to pay more attention:

- If you were in Annual Metabolic Monitoring, you'll switch to Semi-annual Metabolic Monitoring.
- If your A1c is over 6.5%, we may ask you to come in for more tests.

Risks and Discomforts

You could have discomfort and/or a bruise when you get your blood drawn or pricking your fingertip. When having a regular blood test, some people may faint. It is rare, but some people may get an infection, a small blood clot, swelling of the vein and surrounding tissue, or bleeding at the needle puncture site. If you learn that you are at greater risk for diabetes, it could make you worry. If you are very worried, we will offer a referral for counseling. Money to pay for counseling will not be provided.

Further Studies

Studies to better understand diabetes:

One goal of TrialNet is to learn more about diabetes and autoimmune disease. To do this, we may use your blood samples for studies by TrialNet-approved researchers. These studies may include tests of genes and how they work, as well as tests of the immune system and other cells in the body. You will not routinely be provided with test results from these studies. However, we will notify you if there are any results on routine clinical blood tests that important for your health.

Some samples will be obtained during your scheduled monitoring visits. We may also ask you to come in for extra visits so that we can take additional blood samples. If you don't want to come to these extra tests, you can still come for Monitoring visits. You can say yes to some of the extra visits and no to others. If you agree to these extra tests, you will be helping us learn more about type 1 diabetes. This may help people in the future.

Some samples will be used right away by TrialNet-approved researchers. With your permission, some samples will be stored for future use. While TrialNet is active, you can let us know if you change your mind and want us to remove your stored samples. Once TrialNet is completed, researchers from outside TrialNet can ask for stored samples from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The samples will have only ID numbers. Since there will no longer be any link to you, we would not be able to remove your stored samples.

Watch for Diabetes

Some people in this study will develop diabetes. If you develop diabetes, our tests will likely show this before you have symptoms. Still, be aware of the symptoms:

- often thirsty
- needing to go to the bathroom (urinate) a lot
- getting up at night to go to the bathroom more often
- tired
- losing weight without trying

In addition, in a younger child:

- sleeping more than usual
- more cranky than usual
- wetting the bed when he or she used to stay dry at night
- flu-like symptoms, including fever

If you think you might have diabetes, call us right away.

Don't wait until your next study visit or study phone call to tell us. If you have symptoms of diabetes, we will schedule an extra visit right away. You should also talk with your regular doctor.

* It is better for you to be diagnosed as early as possible.
* It is very important to the success of the study that we do these tests.

If a doctor outside of TrialNet tells you that you have diabetes:

* Tell the doctor that you are in a research study.
* Ask the doctor to call the study site right away. We will want to get as much information as possible about your diagnosis.

If you develop diabetes, we will tell you about other research studies that might be open to you.

Call Us

Call us if you have any questions or concerns about the study.

Please let us know if you don't want to be in the study any longer. You or your child are always free to stop being in the study. Your future medical care will not be affected in any way.

In Case of Emergency: Call 9-1-1

- In the event of a life-threatening emergency, ALWAYS CALL 9-1-1.
- Get medical attention right away rather than calling your study team.

FAQs

Will you tell me if my (my child's) risk changes over time?

Yes, if you have one autoantibody we will tell you if you develop additional autoantibodies as determined by annual re-testing. We will also let you know if there are changes in glucose from the OGTT.

Do I get to choose a prevention study?

We will tell you about any studies that might be right for you. You may have additional tests done to see if you might qualify, or come in more frequently. You can decide if you want to join.

How long will I be in the Pathway to Prevention Study?

Most individuals who are screened for the Pathway to Prevention Study have only one blood test, because the test shows they are not at higher risk. For participants who are children, we may reach out to you about any future re-screening opportunities for your child.

If your Screening test shows that you are at risk with one autoantibody, we will ask you to be re-tested for autoantibodies once a year. If you have two or more autoantibodies, you should come in for either annual or semi-annual metabolic monitoring visits based on the results of your OGTT.

We plan to keep the Pathway to Prevention Study running for years. It is your choice to be in the study. You can stop being in the study at any time.

If I am pregnant, can I be in the study?

You can be screened and re-tested annually if you are single autoantibody positive. You won't come in for Monitoring visits while you are pregnant.

If I start out in the Annual Monitoring group, will I stay on that monitoring schedule?

It depends on your test results. If the results of your OGTT show higher risk (abnormal glucose tolerance), you will most likely go to Semi-Annual Metabolic Monitoring.

If I start out in the Semi-Annual group, is it possible that I will switch to the Annual group if my test results change over time?

No. Once your test results show higher risk, you will most likely stay on the Semi-Annual Monitoring schedule.

What should I do if I develop symptoms of diabetes?

Call us right away. If we don't answer, call your regular doctor. See p. 13.

If I develop type 1 diabetes while I am in the Pathway to Prevention Study, will I be able to join a study for new onset diabetes?

Maybe. If TrialNet has an intervention study that you might be right for, we will tell you.

If I am at higher risk, can you treat me so I don't get diabetes?

There is no proven treatment to prevent diabetes. If you are right for a TrialNet prevention study, we will tell you.

If I have one autoantibody and need to be re-tested, does that mean my risk of getting diabetes is very low?

Your risk may change over time. You may develop additional autoantibodies over time and need to be monitored more frequently (stage 1 or 2). We want to make it easy for you to be checked to see if the risk changes. Visits for people in Annual Re-Testing involve a simple blood draw. You don't have to do any special preparation. You can go to a location convenient to you.

What are the benefits of being in the study?

Early diagnosis: If you develop diabetes, our tests will likely show this before you have symptoms. You can see your doctor and start taking insulin before you feel sick. Early diagnosis may also help you avoid a hospital stay when you are diagnosed.

Chance for another TrialNet study: Depending on your test results, you may be able to join another TrialNet study. TrialNet may have a study that is testing a treatment to see if diabetes can be delayed or prevented (prevention study), or a study to test treatments that might help people keep producing their own insulin after diagnosis (early intervention study).

Natural History Study of the Development of Type 1 Diabetes: A Pathway to Prevention

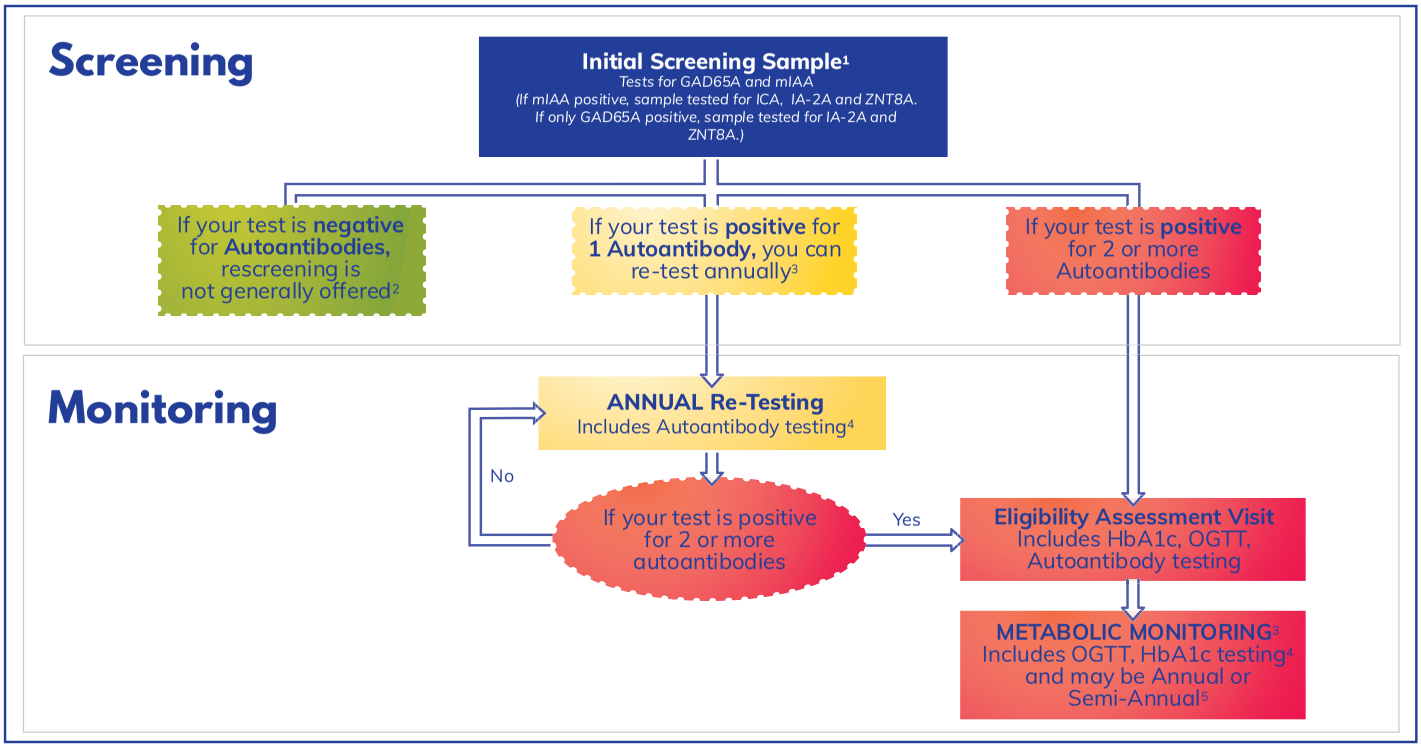


Figure 1: Overview of Study. Emerging data and availability of resources may result in operational changes as noted below.

1. The number, types, and order of antibody screening
2. Limited repeat screening may be offered
3. Metabolic Monitoring may be performed for those with single antibody as needed to assess eligibility for a clinical trial
4. Additional samples for metabolic or mechanistic measures may be collected
5. Frequency of metabolic testing will be semi-annual for those with Abnormal Glucose Tolerance or other high risk of progression. Otherwise, testing will be at least annually.

ASSENT FORM
TrialNet Pathways to Prevention: Monitoring

Based on your blood tests results, you may be at risk of getting diabetes. We want to tell you about the next step which is called Monitoring.

If you have one autoantibody at screening you will be re-tested for autoantibodies once a year.

If you develop two or more autoantibodies you will come for monitoring visits either once or twice a year. We will do a special test called an Oral Glucose Tolerance Test (OGTT) at the first monitoring visit. The results of this test tell us how often you will need to come for study visits. It is possible that, if you start out having annual visits, over time we will ask you to come in twice a year.

The OGTT is done, after an overnight fast (not eating during the night). This test is done to measure the level of glucose (sugar) in the blood after you drink a sweet liquid. Most of the time we will use finger sticks to obtain blood samples and do the last test by drawing blood from your vein. Sometimes we will do the test by placing an intravenous needle and plastic tube (IV) in your arm. We can use a numbing cream, so it shouldn't hurt much. You may feel a small sting when we put the IV in the vein and you could be sore or have a bruise afterwards.

This test will tell us if you need to return to our clinic. The purpose of these visits is to see if your risk for having diabetes changes over time. You will need to come for study visits either once a year (every 12 months) or twice a year (every six months). These visits may also include an OGTT.

We hope this research study will help us better understand how people get diabetes. The study could also help us learn more about preventing diabetes. The decision to continue in this study is your choice. You do not have to continue in this study. If you do, you can change your mind at any time and stop being in the study. The study team will not get mad at you if you do not want to continue in the study.

Sometimes we might also ask you to be in a different kind of research study, but you don't have to do this either if you don't want to.

Please ask any questions you might have.

ASSENT FOR CHILDREN 7-11 YEARS of AGE:

I asked and got answers to my questions. I know that I can ask questions about this study at any time. I want to be in the study at this time.

Child's Printed Name: _____

Child's Signature: _____ Date: _____

I have explained the research at a level that is understandable by the child and believe that the child understands what is expected during this study.

Signature of Person Obtaining Assent: _____

Date: _____

INFORMED CONSENT

Pathway to Prevention Study

MONITORING

PARTICIPANT'S NAME: _____

PRINCIPAL INVESTIGATOR: Dr. Carol Huang

SOURCE OF FUNDING: The National Institutes of Health (NIH), primarily the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Other support is from the Juvenile Diabetes Research Foundation and the American Diabetes Association.

This consent form is only part of the process of informed consent. It should give you (you means you or your child) the basic idea of what the research is about and what your child's participation will involve. If you would like more detail about something mentioned here, or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information. You will receive a copy of this form.

PURPOSE:
You are being asked to continue as a research volunteer in the TrialNet Pathway to Prevention Study. As you know, TrialNet is an international research group dedicated to the study, prevention and early treatment of type 1 diabetes. Type 1 diabetes is now understood as a disease that develops over time in stages. Stage 1 starts with the appearance of two or more autoantibodies. This is followed by Stage 2, which is the development of abnormal blood glucose levels. Stage 3 is the clinical diagnosis of type 1 diabetes. This study will help us learn more about how type 1 diabetes occurs and provides monitoring to individuals at risk. In addition, the study will help us identify people who may be eligible for prevention trials.

You recently participated in Screening in the Pathways to Prevention Study. You were found to have autoantibodies, meaning you may be more likely to develop type 1 diabetes than other people. The monitoring part of the Pathways to Prevention Study offers follow-up visits for people found to have autoantibodies at Screening.

PROCEDURES:

Eligibility Visit:
Based on results of autoantibody testing during screening, qualifying individuals will be invited to return for additional testing as follows:

Annual Re-Testing: Single Autoantibody Positive
Individuals with one autoantibody will be re-tested for autoantibodies once a year to determine if they develop multiple autoantibodies.

If you develop more than one autoantibody you will be asked to come for an Eligibility Visit for Metabolic Monitoring.

Metabolic Monitoring: Multiple Antibody Positive at Screening

Eligibility Visit:
Individuals positive for two or more autoantibodies will undergo an Eligibility Visit to determine:

- If they are eligible to continue in Metabolic Monitoring
- How frequently they will undergo Metabolic Monitoring visits
- If they are eligible for any TrialNet prevention studies that are currently enrolling participants

Annual Metabolic Monitoring:
Individuals with normal glucose tolerance and HbA1c <6.0% will be asked to come in at least once a year.

Semi-Annual Metabolic Monitoring:
Individuals with abnormal glucose tolerance or HbA1c ≥ 6.0% will be asked to come in for visits twice a year.

All Metabolic Monitoring visits include blood tests for an OGTT, HbA1c, and autoantibodies as needed (to determine eligibility for a prevention trial). These tests are described below.

We will also measure your height and weight.

At each visit, we will ask about your health and current medications. We may ask you to come in more frequently for testing if there is a clinical trial that you may be eligible for or to better track your disease progression.

Metabolic Monitoring tests:

- **Oral Glucose Tolerance Test (OGTT)**
  After an overnight fast (not eating during the night), you will have an OGTT. This test is done to measure the level of glucose (sugar) in the blood after you drink a sweet liquid that contains glucose over a 5-minute period. Blood will be drawn before you drink the liquid and then at several times after you have finished drinking it. Most of the time, we will use finger sticks to obtain the blood samples and will take one blood sample from your vein at the end of the test. Other times, we will use an intravenous (IV) needle to place a very small plastic catheter (straw) in a vein in your arm. This IV will stay in your arm until the end of the test. In some cases, we will ask you to return to the study site to do a second test to confirm these results or to see if you may qualify for a clinical trial. The entire test will take about 3 hours.

- **Autoantibody Test**
  This test looks to see if you have diabetes-related autoantibodies in your blood. Autoantibodies are proteins that are made by the body's immune system. They are a sign that the cells in the pancreas that produce insulin could be damaged. These proteins can be found in the blood years before a person develops type 1 diabetes. These tests may be done only as needed to see if you are eligible for a clinical trial.

- **HbA1c Test**
  This blood test measures a person's average blood glucose level for last 2-3 months before the test.

Blood Samples for Understanding Type 1 Diabetes
An important part of this study is to better understand what causes type 1 diabetes, to look for new ways to identify people at risk for disease, and to get ideas about new treatments in the future. While TrialNet is ongoing, these samples will be used only by TrialNet-approved researchers. As such, we may be collecting blood samples including genetic samples for these studies. However, we notify you if there are any results on routine clinical blood tests that are important for your health.

The blood tests for the Annual Re-Testing visits will require about 1 tablespoon of blood and Annual and Semi-Annual Metabolic Monitoring visits will require up to 2 tablespoons of blood in adults. At some visits we may collect about 1/3 cup which includes additional blood for future studies. We will not take more than is safe for your age and weight.

In addition, we may occasionally contact you to ask if you would be willing to give additional blood samples. This will be no more than six times a year and a separate consent form would be provided to you if you choose to give the additional blood samples. We will always tell you what we need and how much blood we expect to draw, and then let you decide if you are able to help us at that time. For adults the maximum

amount of blood drawn for all tests combined will be about 2 cups of blood every 8 weeks. For those under age 18, we will not take more than is safe for your age and weight.

Additional Information

You will be offered the results of your OGTT, HbA1c, and/or autoantibodies testing after each visit. In some cases, we may ask you to repeat certain tests before your next routine study visit to see if you are eligible for a prevention study. If you decide to participate in a prevention trial, you will be asked to sign another consent form. If you were to develop type 1 diabetes, you might qualify for research studies for people with new-onset type 1 diabetes. The data obtained from this study will be combined with data from any other TrialNet or other studies you have participated in which study natural history of type 1 diabetes.

RISKS:
You could have discomfort and/or a bruise when you get your blood drawn. Once in a while, some people may faint. It is rare, but some people may get an infection, a small blood clot, swelling of the vein and surrounding tissue, or bleeding where the needle enters the skin. There are also some risks to the OGTT. Some people may feel nauseous when they have the OGTT. There will be protections in place to keep information about you confidential. If you are at greater risk for diabetes, it could make you worry. If you are very worried, we can offer a referral for counseling. Money to pay for counseling will not be provided

BENEFITS:
There is no guarantee that you will benefit from this study. If you were to develop diabetes, it is possible it would be found sooner and decrease the chance of sickness and hospitalization. This study may also increase knowledge about the prevention of type 1 diabetes.

ALTERNATIVES:
You can choose not to participate in this study.

COST TO SUBJECT:
There will be no cost to you to participate in the study.

SUBJECT PAYMENT:
We will cover your parking, bus or taxi costs up to $13. If this research project results in a product that can be sold, you will not receive a share of money that is made.

PAYMENT FOR INJURY OR HARM:
If you get injured because of this study, the study team will offer medical care. Money to pay for injuries is not normally provided. Money is not available for things like lost wages, disability, or discomfort due to injury.

CONFIDENTIALITY:
Your consent to be in this study gives the TrialNet researchers permission to collect personal information about you and to use it for research purposes. Personal information is information such as your name that directly identifies you. This personal information will be kept in a database at the central TrialNet Coordinating Center at the University of South Florida.

This information may be shared with other TrialNet centers and affiliates and the TrialNet Clinical Hub, as needed and in accordance with country specific guidelines, to help with the study. Your consent also includes permission for the sponsor of this study (NIDDK), the Food and Drug Administration (FDA), or Health Canada to review your records.

If you participate in this study, you will be given a unique study code number. It will identify the information and samples collected from you from study examinations and send to the central TrialNet Coordinating Center.

A Certificate of Confidentiality has been obtained from the National Institutes of Health (NIH). This is intended to further protect the confidentiality of information that we obtain about you. By having a Certificate of Confidentiality, TrialNet researchers are not required to give information that can be used to identify you. For example, we cannot be forced to give information about you to insurance companies. Also, we cannot be forced to give information about you for any civil, criminal, administrative, or legislative proceedings whether at the federal, state or local level. However, the Certificate of Confidentiality does not prevent you from giving this information to others. Please understand that we will maintain the confidentiality of your research record. We cannot guarantee the confidentiality of test results provided to you if you wish to share them.

There are some rare exceptions to the protection offered by the Certificate of Confidentiality. TrialNet researchers are not prevented from telling about matters such as child abuse, certain infectious diseases, or threatened violence to yourself or others.

TrialNet researchers will consider your records private. Rarely, representatives of the United States Department of Health and Human Services (DHHS) or TrialNet may review or ask for a copy of your study records. If this happens, we will provide your records. Also, for auditing purposes, the University of Calgary Conjoint Health Research Ethics Board or its agents could be allowed to see your study records to make sure that the study is being done properly.

The results of this study may be published for scientific purposes. By signing this form, you are agreeing to this. Your records and results will not be identified as belonging to you in any publication.

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION (PHI) FOR RESEARCH PURPOSES

What information may be used and given to others?
The study doctor will collect your personal and medical information such as:

- Past and present medical records with your permission
- Research records and results
- Your contact information
- Records about your study visits and contact with your study team

Who may use and give out information about you?
The study doctor and the study staff may use and share this information.

Who might get this information?
Your PHI may be used by and shared with the following groups of people during the conduct of this research:

- The medical staff that takes care of you and those who are part of this research study;
- TrialNet research sites and study teams involved in this research;
- Any laboratories, pharmacies, or others who are part of this research study;
- The sponsor(s) of this research;
- The data and safety monitoring board or others who monitor the data and safety of the study;
- The TrialNet Clinical Hub at the Benaroya Research Institute in Seattle, Washington;
- The TrialNet Coordinating Center at the University of South Florida

Your information may also be given to:

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to see if the research was done correctly

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
This authorization will not expire.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor, Dr. Huang at Alberta Children's Hospital. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
Once the information is shared with others, it may no longer be protected by the HIPAA Privacy Rule.

STUDY WITHDRAWAL:
Participation in this study is voluntary. You can withdraw your consent at any time. If you choose to stop being in the study, tell a study staff member. Your current or future care will not be any different if you decide not to be in this study or to stop being in this study at any time. Your doctor may choose to take you out of the study at any time, even without your consent. You will be told of any new findings that may affect your being in this study.

INVITATION FOR QUESTIONS:
You are encouraged to ask any questions you may have about the study. In the event of a research related injury, you should contact them immediately:

In case of *emergency 403-955-7211, dial 2 and ask for the Pediatric Endocrinologist on call*
OR
Research Coordinator (403) 955-8866
OR
Dr. Carol Huang (403) 955-7819

If you have any questions concerning your rights as a possible participant in this research, please contact the Director, the Office of Medical Bioethics, University of Calgary at 403-220-7990.

Additional Information:
A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

AUTHORIZATION:

Storage of Samples in NIDDK Repository

When TrialNet is over, we intend to put any remaining samples including genetic samples into the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK) repository for future studies related to type 1 diabetes and its complications. They will be stored there indefinitely without your name or any other identifying information on them, as such, once in the repository you will not be able to have them removed. Researchers must first get permission from the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK) to use samples from the repository.

The following checkbox gives you the choice of allowing us to put any remaining blood samples in the NIDDK repository. Even if you decide not to have your remaining blood samples stored, you can still participate in this study.

Are you willing to allow us to put any remaining blood samples in the NIDDK repository?

☐ YES ☐ NO

Pathway to Prevention Monitoring Study Authorization

By signing this consent form, you agree that you have read this informed consent form and that the study has been explained to you. You also agree that your questions have been answered and that you agree to be in this study. You do not give up any of your legal rights by signing this informed consent form. You will receive a copy of this consent form.

I have read this paper about the study or it was read to me. I know what will happen, both the possible benefits and the possible risks. I choose to be (or to have my child) in this study. I know I can stop being in the study at any time, and I will still get the usual medical care. I will get a copy of this consent form.

Participant

Print Name of participant: _____

Signature of participant (age 12 or older): _____

Date of participant's signature: _____

Parent or guardian (if subject < age 18)

Print Name of parent or guardian: _____

Signature of parent or guardian: _____

Date of parent's or guardian's signature: _____

Consent obtained by:

Print name of researcher: _____

Signature of researcher: _____

Date of researcher's signature: _____

The investigator or a member of the research team will, as appropriate, explain to your child the research and his or her involvement. They will seek your child's ongoing cooperation throughout the study.
The University of Calgary Conjoint Health Research Ethics Board has approved this research study.

ASSENT FORM
TrialNet Pathway to Prevention:
Screening

We want to tell you about a research study. Someone in your family has diabetes. You may have a greater chance of getting diabetes too. Diabetes makes people sick because there is not enough insulin in the body. Insulin is needed so that your body can use the food that you eat which gives you energy to run and play.

We would like to find out more about your risk of getting diabetes. To do this, we will need to stick your arm with a needle to do a blood test. This could sting and you could be sore or have a bruise afterwards.

You may also do the blood test using a test kit at home. Your parent, or the person who cares for you, will assist you with pricking your finger to collect the blood. You could have a bruise from collecting the blood from your fingertip.

Sometimes we need to do the blood test a second time in order to be sure of the results. If we find that you may be at risk of getting diabetes, we will ask you and your parents if you want to continue in this research study.

We hope this research study will help us to understand how people get diabetes. The study could also help us learn more about preventing diabetes. Being in this study is your choice. You do not have to be in this study and if you do, you can change your mind and stop the study. The study team will not get mad at you if you do not want to be in the study.

If we find out that you are not likely to get diabetes now, you still might have a chance of getting it later. We may ask you to come back to repeat the blood test in the future. Please ask any questions you might have.

ASSENT FOR CHILDREN 7-11 YEARS of AGE:

I asked and got answers to my questions. I know that I can ask questions about this study at any time. I want to be in the study at this time.

Child's Printed Name: _____

Child's Signature: _____ Date: _____

I have explained the research at a level that is understandable by the child and believe that the child understands what is expected during this study.

Signature of Person Obtaining Assent: _____

Date: _____

INFORMED CONSENT

Pathway to Prevention Study
Screening

PARTICIPANT'S NAME: _____
PRINCIPAL INVESTIGATOR: Dr. Carol Huang

SOURCE OF FUNDING:
This study is supported by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) of the National Institutes of Health and JDRF.

This consent form is only part of the process of informed consent. It should give you (you means you or your child) the basic idea of what the research is about and what your child's participation will involve. If you would like more detail about something mentioned here, or information not included here, please ask. Take the time to read this carefully and to understand any accompanying information. You will receive a copy of this form.

PURPOSE:
You are being asked to be in a research study called the TrialNet Pathway to Prevention Study. TrialNet is a research group dedicated to the study, prevention, and early treatment of type 1 diabetes. Type 1 diabetes is now understood as a disease that develops over time in stages. Stage 1 starts with the appearance of two or more autoantibodies. This is followed by Stage 2, which is the development of abnormal blood glucose levels. Stage 3 is the diagnosis of type 1 diabetes. This study will help us learn more about how type 1 diabetes occurs and provides monitoring to individuals at risk. In addition, the study will help us identify people who may be eligible for prevention trials.

The study is divided into two parts: Screening and Monitoring. This consent form is only for the Screening part of the study. During screening, you will be tested for diabetes-related autoantibodies in the blood. Autoantibodies are proteins that are made by the body's immune system. If antibodies are present, it could mean that cells in the pancreas which produce insulin are damaged. Certain kinds of autoantibodies can be found in the blood years before type 1 diabetes occurs.

If the screening blood tests show that you have autoantibodies, we will invite you to participate in the Monitoring part of the study. We will then ask you to sign a separate consent form which explains more about this part of the study.

WHAT I HAVE TO DO?
We will ask you to provide information about yourself and your family history of diabetes. You will have a blood test to test for diabetes-related autoantibodies. The blood test can be done by placing a needle into a vein in your arm. We will take up to 1 tablespoon of blood at each screening visit.

You can also be screened by pricking your finger tip to collect about ½ teaspoon of blood (10 drops). If it is not possible to collect enough blood from your fingertip, you may need to repeat the test with a regular blood draw.

If you are positive for autoantibodies you will be contacted by a member of the TrialNet research team and may be invited to participate in the monitoring phase of the study.

If we do not find autoantibodies in your blood (you are negative), you will receive results by letter or secure electronic communication. Testing negative for autoantibodies does not mean you will never get diabetes, but the chances are much lower than if you tested positive. It is still possible that you could develop autoantibodies in the future.

Whether you have autoantibodies or not, we may contact participants younger than 18 in the future to be re-screened, or to ask about your health.

Blood Samples for Understanding Type 1 Diabetes
An important part of this study is to better understand what causes type 1 diabetes, to look for new ways to identify people at risk for disease, and to get ideas about new treatments in the future. While TrialNet is ongoing, your remaining blood samples will be used only by TrialNet-approved researchers. You will not routinely be provided with test results from these studies.

RISKS:
You could have discomfort and/or a bruise when you get your blood drawn from your arm or your fingertip. When having blood drawn, once in a while, some people may faint. It is rare, but some people may get an infection, a small blood clot, swelling of the vein, and surrounding tissue or bleeding where the needle enters the skin.

If the blood sample was collected from your fingertip, it is possible that you will be unable to collect enough blood or that the sample cannot be used for testing. In this case you will need to come to a study site for a regular blood test to obtain blood from your vein.

If you learn that you are at greater risk for diabetes, it could make you worry. If you are very worried, we will offer a referral for counseling. Money to pay for counseling will not be provided

BENEFITS:
There is no guarantee that you will benefit from this study. If you were to develop diabetes, it is possible it would be found sooner and decrease the chance of sickness and hospitalization. This study may also increase knowledge about the prevention of type 1 diabetes.

ALTERNATIVES:
You can choose not to participate in this study.

COST TO SUBJECT:
There will be no cost to you to participate in the study.

SUBJECT PAYMENT:
No payment will be given to you for being in this part of the study. If this research project results in a product that can be sold, you will not receive a share of money that is made.

PAYMENT FOR INJURY OR HARM:
If you get injured because of this study, the study team will offer medical care. Money to pay for injuries is not normally provided. Money is not available for things like lost wages, disability, or discomfort due to injury. No compensation will be provided to you by the University of Calgary, Alberta Health Services or the Researchers. You still have all your legal rights. Nothing said in this consent form alters your right to seek damages.

CONFIDENTIALITY:
Your consent to be in this study gives the TrialNet researchers permission to collect personal information about you and to use it for research purposes. Personal information is information such as your name that directly identified you. This personal information will be kept in a database at the central TrialNet Coordinating Center at the University of South Florida.

This information may be shared with TrialNet centers and affiliates and the TrialNet Clinical Hub, as needed and in accordance with country-specific guidelines, to help with the study. Your consent also includes permission for the sponsor of the study (NIDDK) and the Food and Drug Administration (FDA) to review your study records.

If you participate in this study, you will be given a unique study code number. It will identify the information collected from you from study examinations and procedures and sent to the central TrialNet Coordinating Center.

A Certificate of Confidentiality has been obtained from the National Institutes of Health (NIH). This is intended to further protect the confidentiality of information that we obtain about you. By having a Certificate of Confidentiality, TrialNet researchers are not required to give information that can be used to identify you. For example, we cannot be forced to give information about you to insurance companies. Also, we cannot be forced to give information about you for any civil, criminal, administrative, or legislative proceedings whether at the federal, state or local level. However, the Certificate of Confidentiality does not prevent you from giving this information to others. Please understand that we will maintain the confidentiality of your research record. We cannot guarantee the confidentiality of test results provided to you if you wish to share them.

There are some rare exceptions to the protection offered by the Certificate of Confidentiality. TrialNet researchers are not prevented from telling about matters such as child abuse, certain infectious diseases, or threatened violence to yourself or others.

TrialNet researchers will consider your records private. Rarely, representatives of the United States Department of Health and Human Services (DHHS) or TrialNet may review or ask for a copy of your study records. If this happens, we will provide your records. Also, for auditing purposes, the University of Calgary Conjoint Health Research Ethics Board or its agents could be allowed to see your study records to make sure that the study is being done properly.

The results of this study may be published for scientific purposes. By signing this form, you are agreeing to this. Your records and results will not be identified as belonging to you in any publication.

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION (PHI) FOR RESEARCH PURPOSES

What information may be used and given to others?
The study doctor will collect your personal and medical information such as:

- Past and present medical records with your permission
- Research records and results
- Your contact information
- Records about your study visits and contact with your study team

Who may use and give out information about you?
The study doctor and the study staff may use and share this information.

Who might get this information?
Your PHI may be used by and shared with the following groups of people during the conduct of this research:

- The medical staff that takes care of you and those who are part of this research study;
- TrialNet research sites and study teams involved in this research;
- Any laboratories, pharmacies, or others who are part of this research study;
- The sponsor(s) of this research;
- The data and safety monitoring board or others who monitor the data and safety of the study;
- The TrialNet Clinical Hub at the Benaroya Research Institute in Seattle, Washington;
- The TrialNet Coordinating Center at the University of South Florida

Your information may also be given to:

- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported

Why will this information be used and/or given to others?

- to do the research,
- to study the results, and
- to see if the research was done correctly

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
This authorization will not expire.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor, Dr. Huang at Alberta Children's Hospital. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
Once the information is shared with others, it may no longer be protected by the HIPAA Privacy Rule.

STUDY WITHDRAWAL:
Participation in this study is voluntary. You can withdraw your consent at any time. If you choose to stop being in the study, tell a study staff member. Your current or future care will not be any different if you decide not to be in this study or to stop being in this study at any time. Your doctor may choose to take you out of the study at any time, even without your consent. You will be told of any new findings that may affect your being in this study.

INVITATION FOR QUESTIONS:
You are encouraged to ask any questions you may have about the study. In the event of a research-related injury, you should contact one of the investigators immediately:

In case of emergency 403-955-7211, dial 2 and ask for the Pediatric Endocrinologist on call
OR
Research Coordinator (403) 955-8866
OR
Dr. Carol Huang (403) 955-7819

If you have any questions concerning your rights as a possible participant in this research, please contact the Chair of the Conjoint Health Research Ethics Board, University of Calgary at 403-220-7990.

Additional Information:
A description of this clinical trial will be available on http://www.ClinicalTrials.gov as

required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

PATHWAY to PREVENTION SCREENING AUTHORIZATION:

Storage of Samples in NIDDK Repository

When TrialNet is over, we intend to put any remaining samples into the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK) repository for future studies related to type 1 diabetes and its complications. They will be stored there indefinitely without your name or any other identifying information on them. As such, once in the repository you will not be able to have them removed. Researchers must first get permission from the National Institute of Diabetes & Digestive & Kidney Diseases (NIDDK) to use samples from the repository.

The following checkbox gives you the choice of allowing us to put any remaining blood samples in the NIDDK repository. Even if you decide not to have your remaining blood samples stored, you can still participate in this study.

Are you willing to allow us to put any remaining blood samples in the NIDDK repository?

□ YES □ NO

SIGNATURES:
By signing this consent form, you agree that you have read this informed consent form and that the study has been explained to you. You also agree that your questions have been answered and that you agree to be in this study. You do not give up any of your legal rights by signing this informed consent form. You will receive a copy of this consent form.

I have read this paper about the study or it was read to me. I know what will happen, both the possible benefits and the possible risks. I choose to be (or to have my child) in this study. I know I can stop being in the study at any time, and I will still get the usual medical care. I will get a copy of this consent form.

Participant
Print Name of participant: _____

Signature of participant (age 12 or older): _____

Date of participant's signature: _____

Parent or guardian (if subject < age 18)
Print Name of parent or guardian: _____

Signature of parent or guardian: _____

Date of parent's or guardian's signature: _____

Consent obtained by:
Print name of researcher: _____

Signature of researcher: _____

Date of researcher's signature: __The investigator or a member of the research team will, as appropriate, explain to your child the research and his or her involvement. They will seek your child's ongoing cooperation throughout the study.

The University of Calgary Conjoint Health Research Ethics Board has approved this research study.

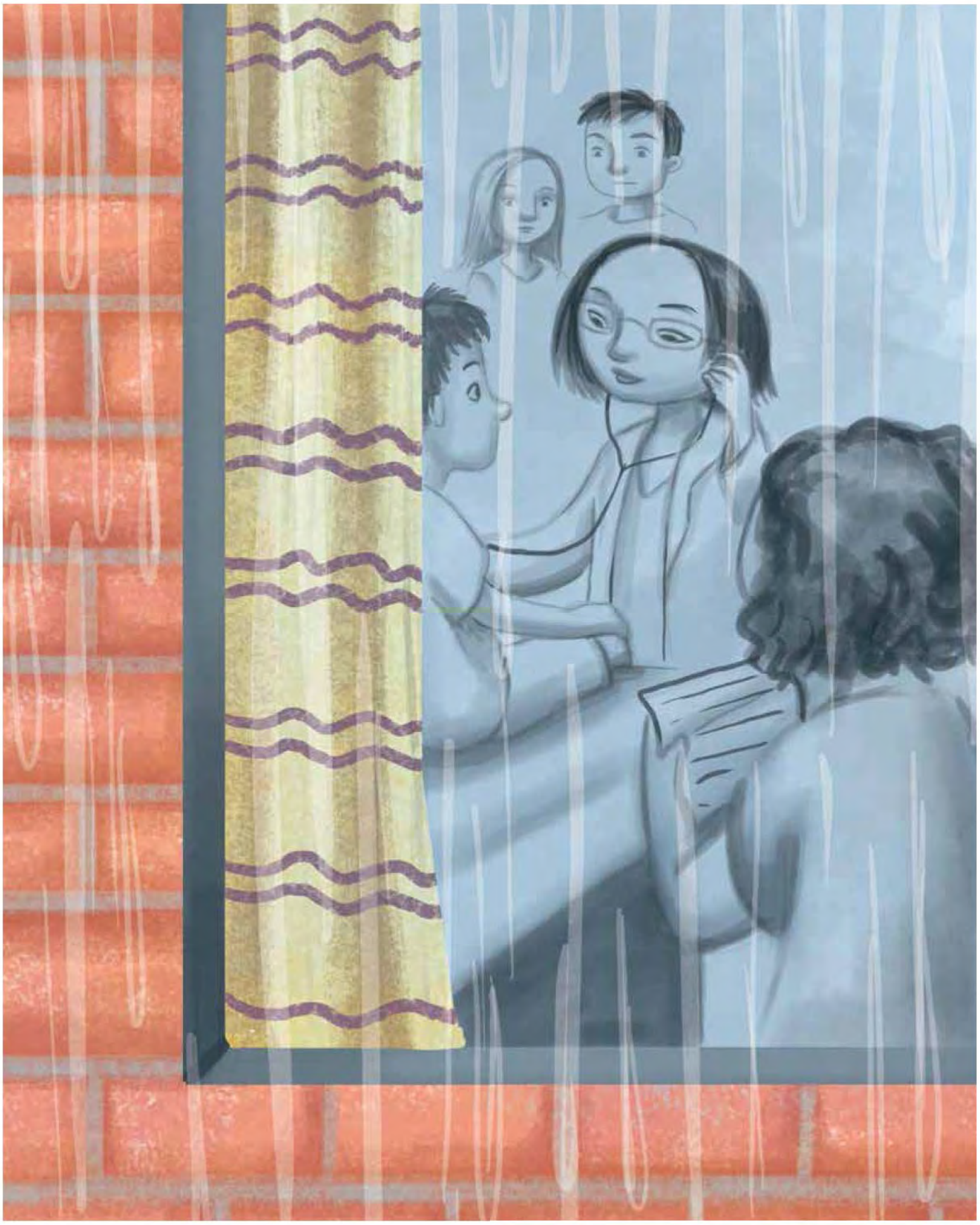
Type 1 Diabetes TrialNet

Be A Hero!

HELP FIND A WAY TO PREVENT DIABETES WITH THE GREAT KATIE KATE

M. Maitland DeLand, M.D.
with illustrations by Jennifer Zivoin

GREENLEAF
BOOK GROUP PRESS



Claire sat on the hard chair in the doctor's office. She was tired and bored. She wanted to play outside. Instead she was stuck waiting for her brother—again.

Ever since Andrew found out he had type 1 diabetes a month ago, it was the same thing. Claire was dragged along to every single one of Andrew's doctor appointments.

No one pays any attention to me anymore, Claire thought. *Why do I have to be here?*


DAY
CAMP

One day the doctor said that she needed to see Claire, instead of Andrew. *How weird!* thought Claire. *I don't have diabetes. Why would she want to talk to me?*

"How would you like to do something really fun?" Andrew's doctor asked Claire.

"Who, me?" Claire said.

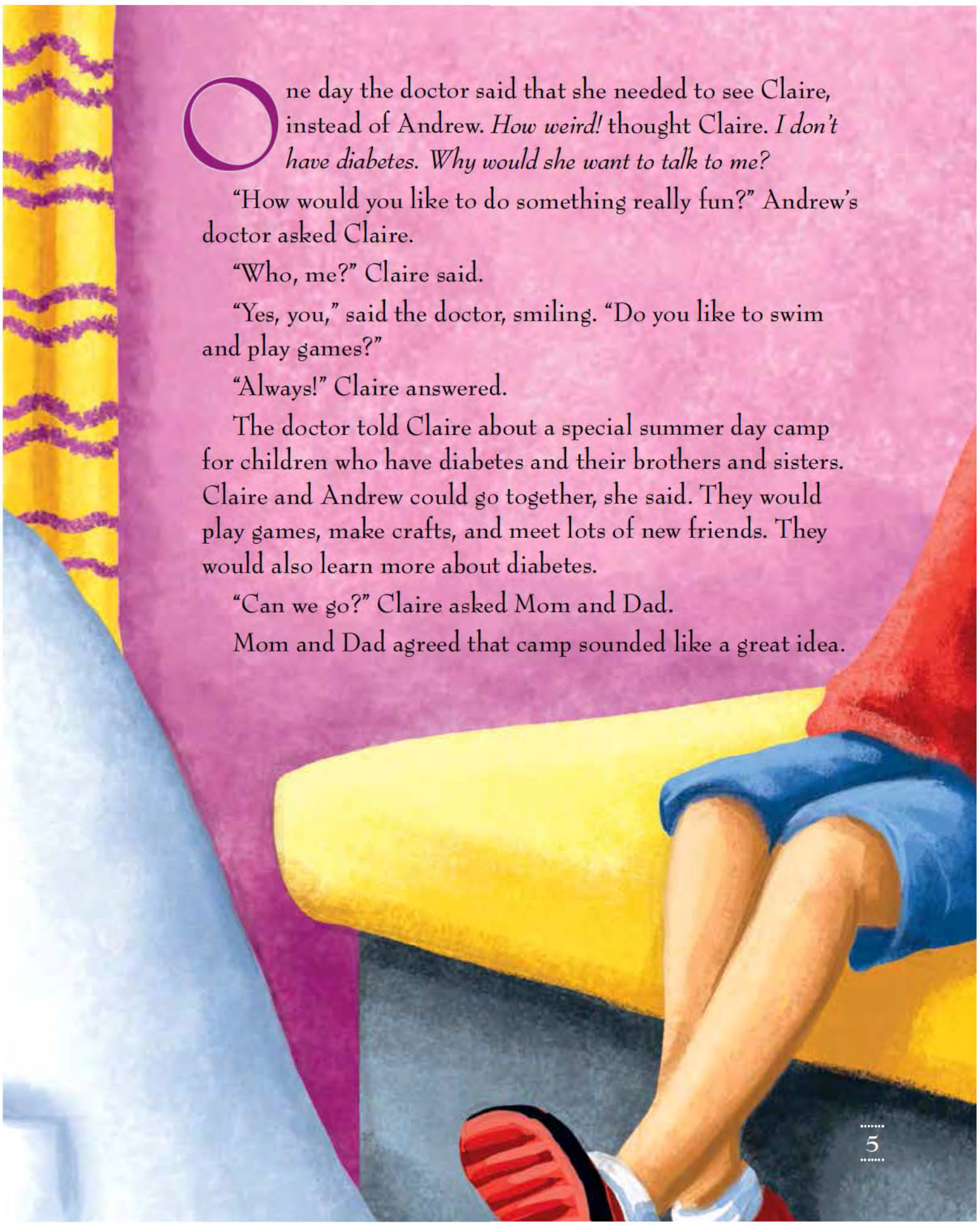
"Yes, you," said the doctor, smiling. "Do you like to swim and play games?"

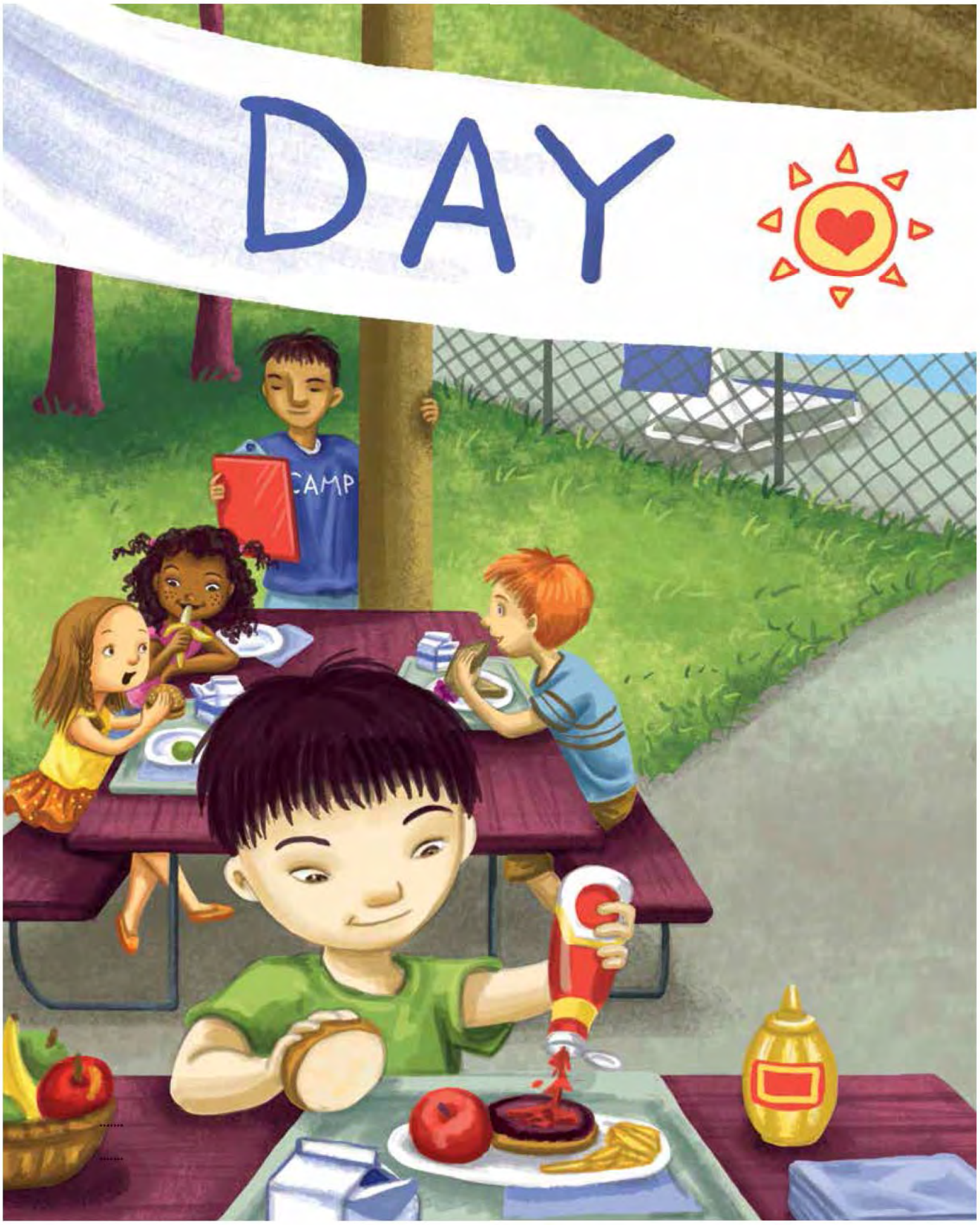
"Always!" Claire answered.

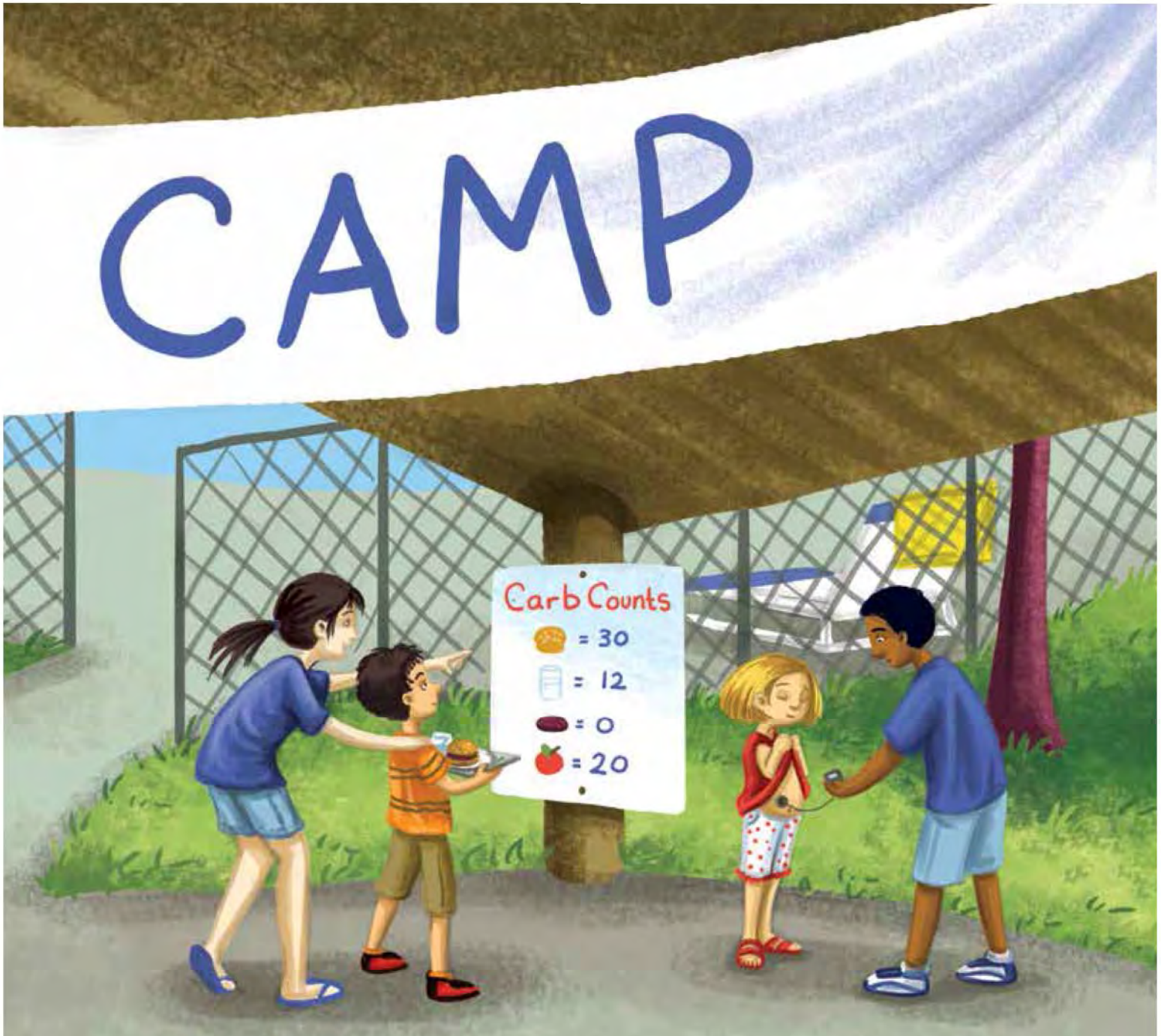
The doctor told Claire about a special summer day camp for children who have diabetes and their brothers and sisters. Claire and Andrew could go together, she said. They would play games, make crafts, and meet lots of new friends. They would also learn more about diabetes.

"Can we go?" Claire asked Mom and Dad.

Mom and Dad agreed that camp sounded like a great idea.




DAY
CAMP



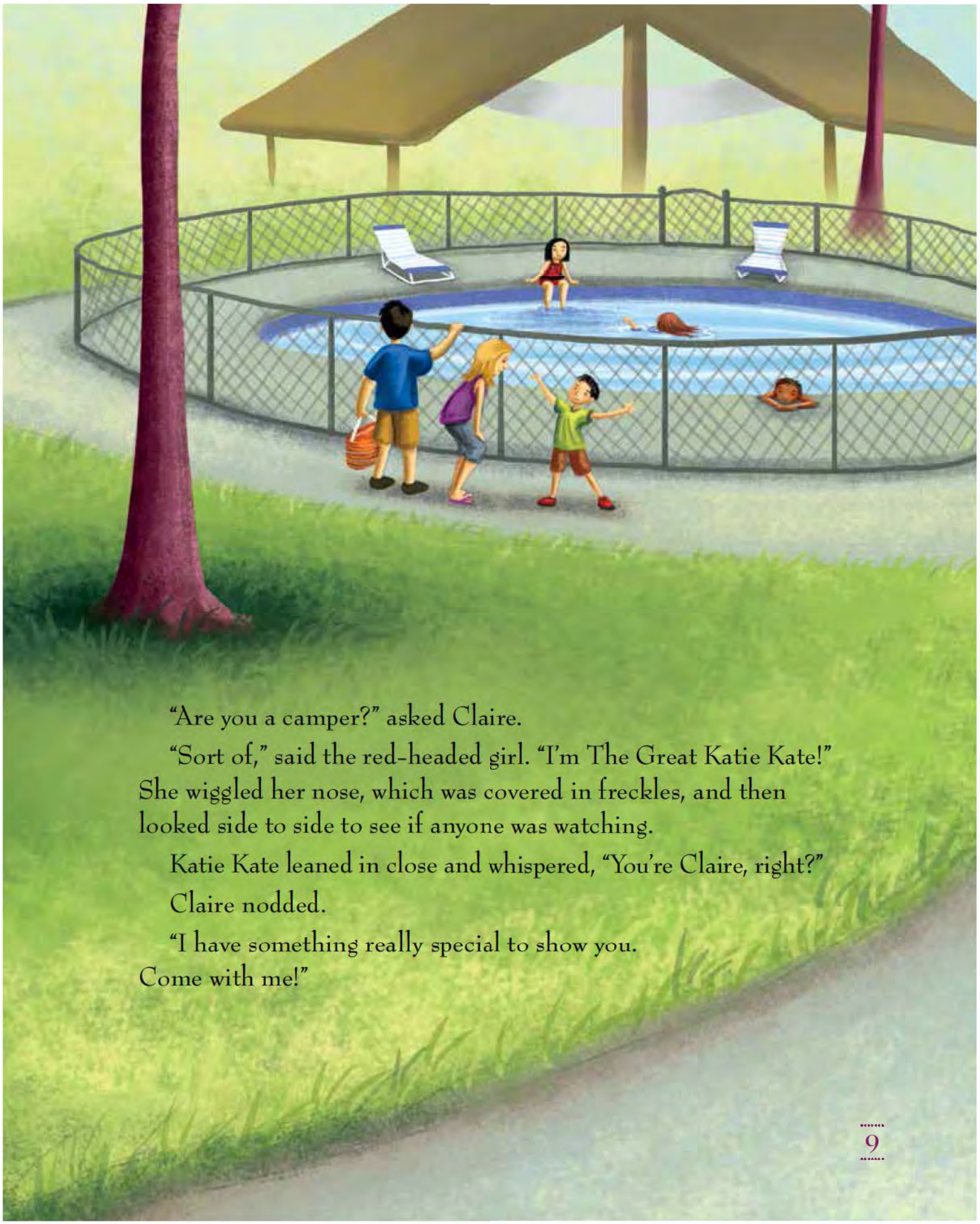
The first day of diabetes camp arrived. Claire and Andrew had so much fun! Andrew met all kinds of kids who also had diabetes. They had to take insulin and count their carbs, just like him.

Claire made new friends, too. Many of them had brothers and sisters who had diabetes, just like Andrew. Claire found out that they did not like waiting in the doctor's office either.

All of the kids had a swimming race, and then they ate hamburgers for lunch. Everyone was excited to be at summer camp!

The next day at camp was a special parents' day. All the parents were invited to spend the day at camp with their children. Claire and Andrew were excited to take Mom and Dad around the camp and show them all the things they had done and made.

They were walking to the swimming pool when suddenly Claire felt a tap-tap-tap on her shoulder. She turned around and there was a girl she'd never seen before. The girl had red hair and wore a long purple cape.



"Are you a camper?" asked Claire.

"Sort of," said the red-headed girl. "I'm The Great Katie Kate!" She wiggled her nose, which was covered in freckles, and then looked side to side to see if anyone was watching.

Katie Kate leaned in close and whispered, "You're Claire, right?"

Claire nodded.

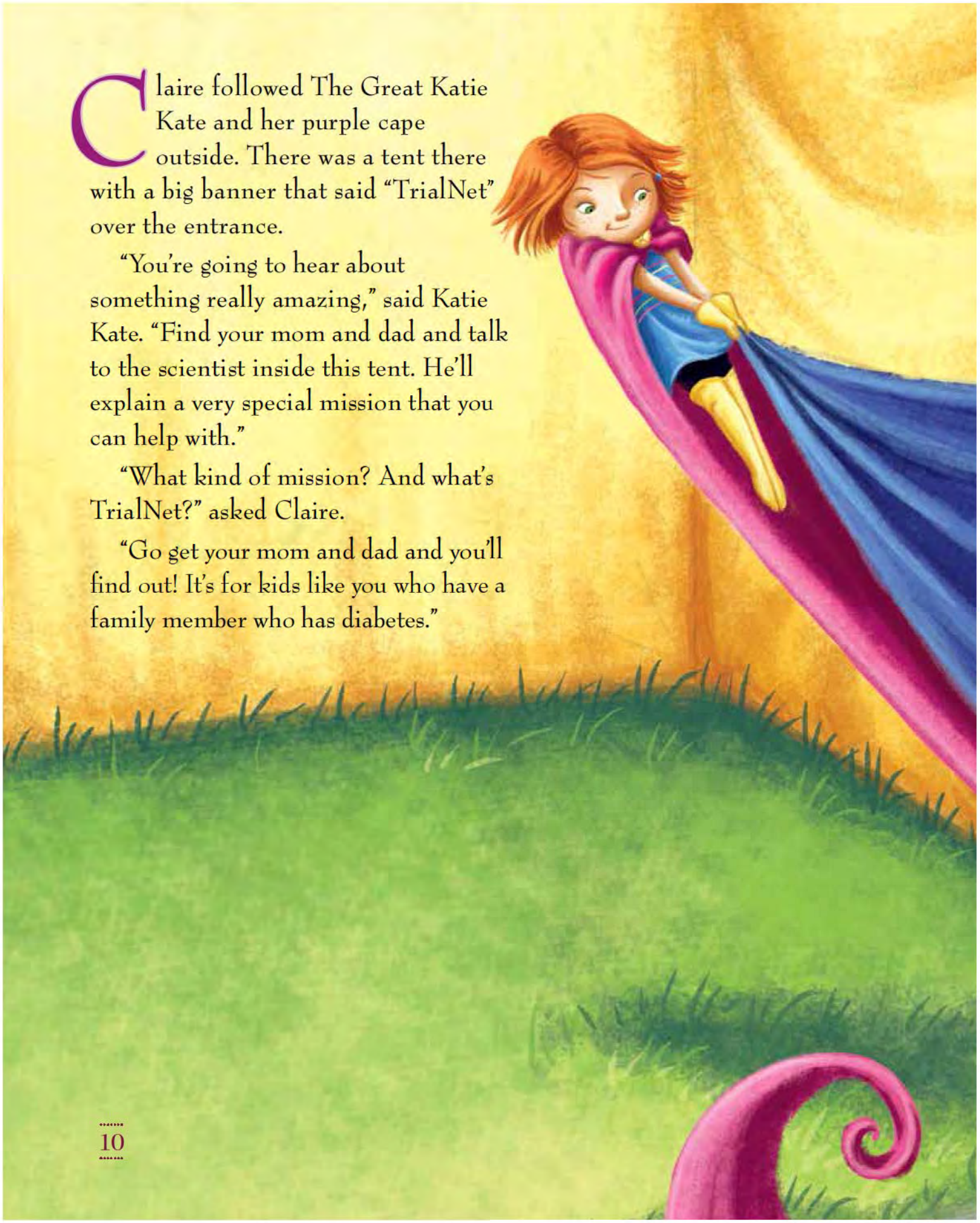
"I have something really special to show you. Come with me!"

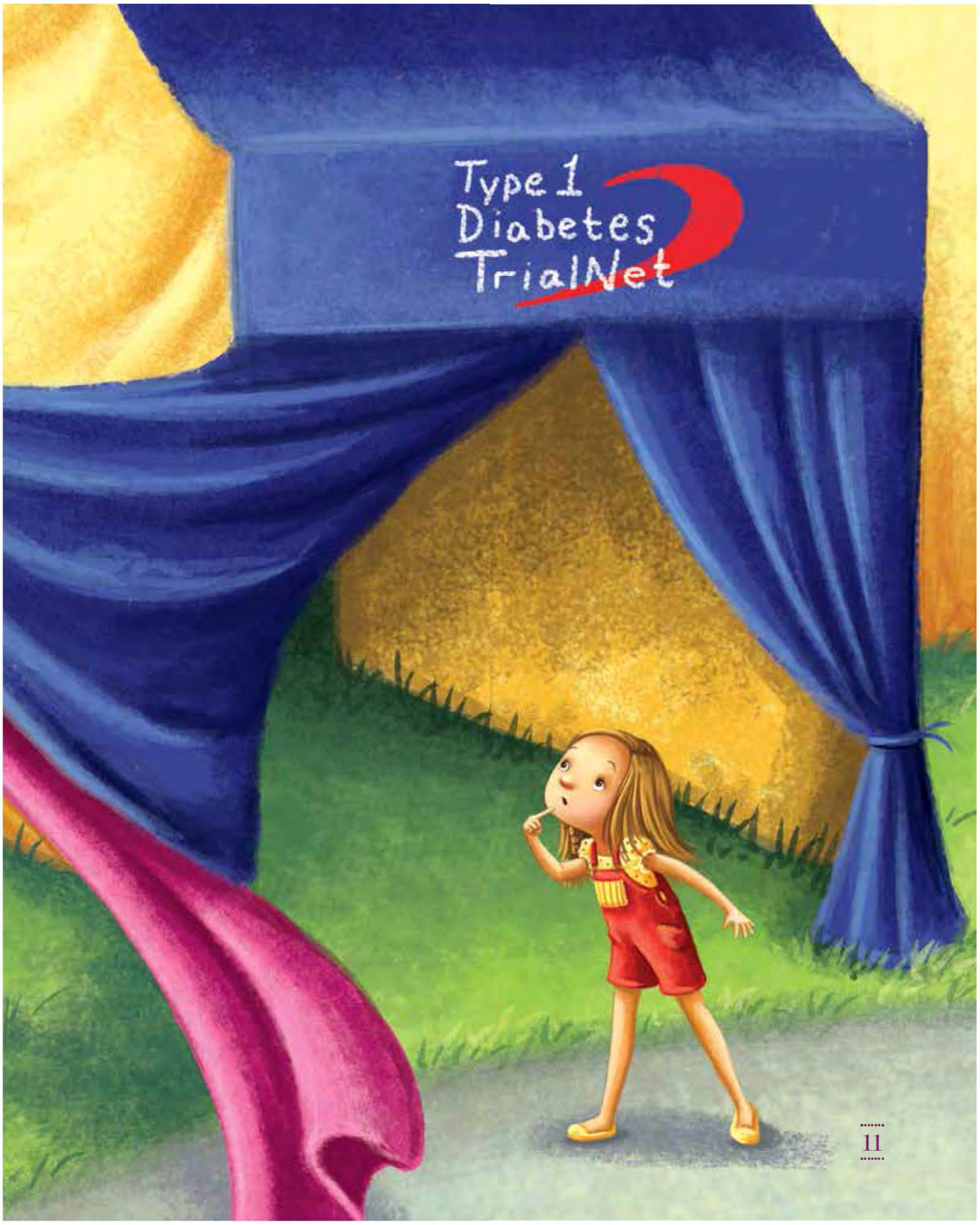
Claire followed The Great Katie Kate and her purple cape outside. There was a tent there with a big banner that said "TrialNet" over the entrance.

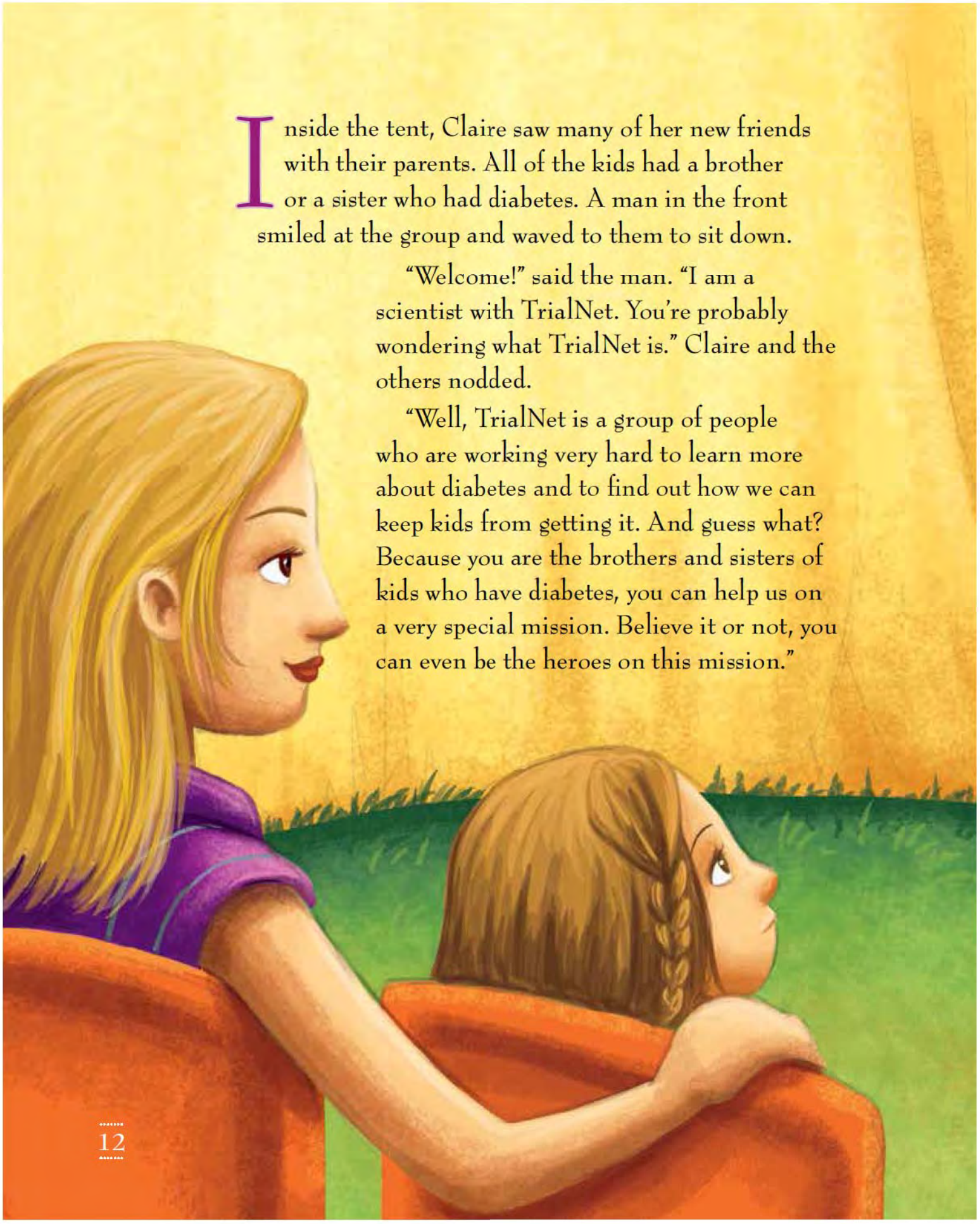
"You're going to hear about something really amazing," said Katie Kate. "Find your mom and dad and talk to the scientist inside this tent. He'll explain a very special mission that you can help with."

"What kind of mission? And what's TrialNet?" asked Claire.

"Go get your mom and dad and you'll find out! It's for kids like you who have a family member who has diabetes."



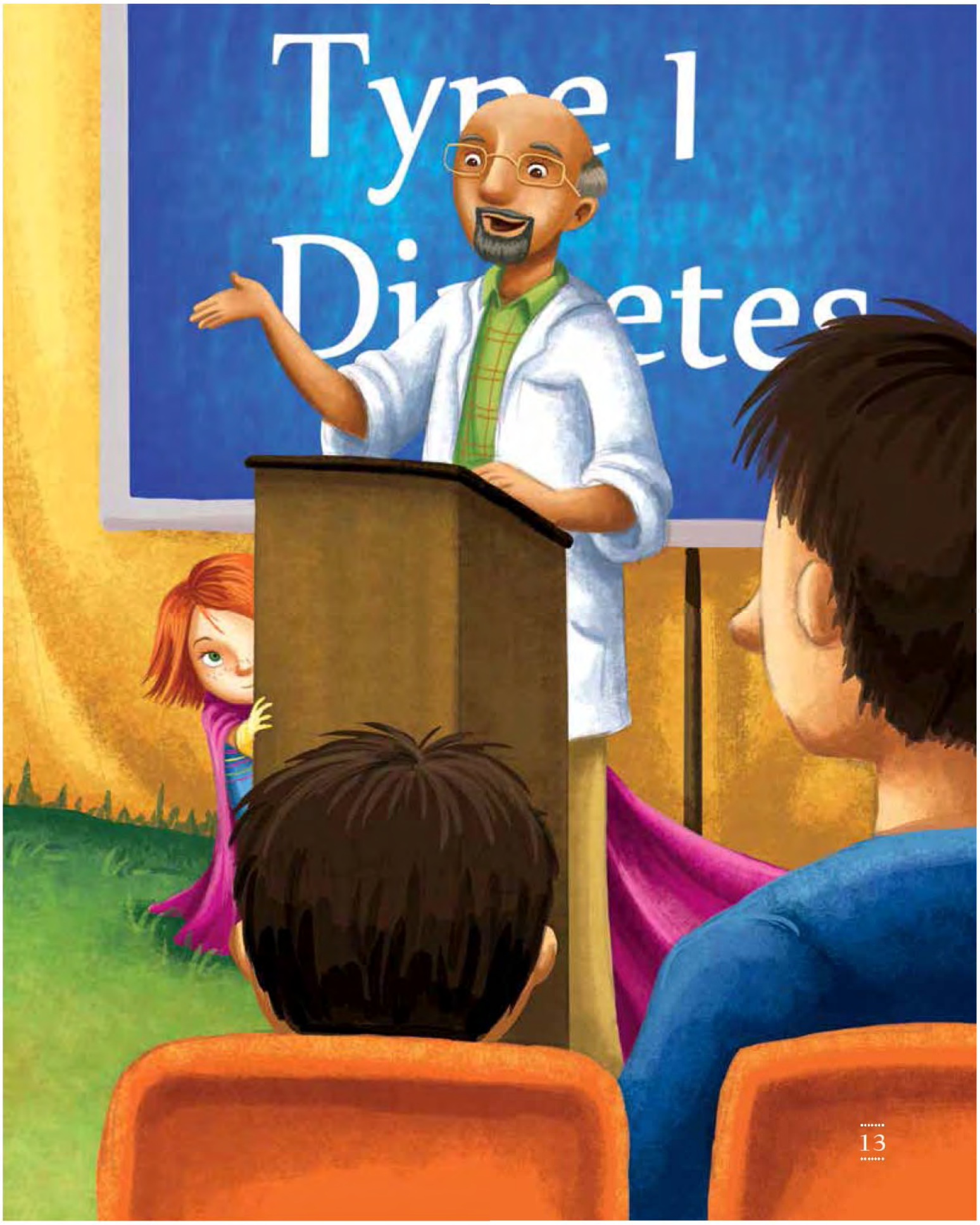

Type 1
Diabetes
TrialNet



Inside the tent, Claire saw many of her new friends with their parents. All of the kids had a brother or a sister who had diabetes. A man in the front smiled at the group and waved to them to sit down.

"Welcome!" said the man. "I am a scientist with TrialNet. You're probably wondering what TrialNet is." Claire and the others nodded.

"Well, TrialNet is a group of people who are working very hard to learn more about diabetes and to find out how we can keep kids from getting it. And guess what? Because you are the brothers and sisters of kids who have diabetes, you can help us on a very special mission. Believe it or not, you can even be the heroes on this mission."


Type 1

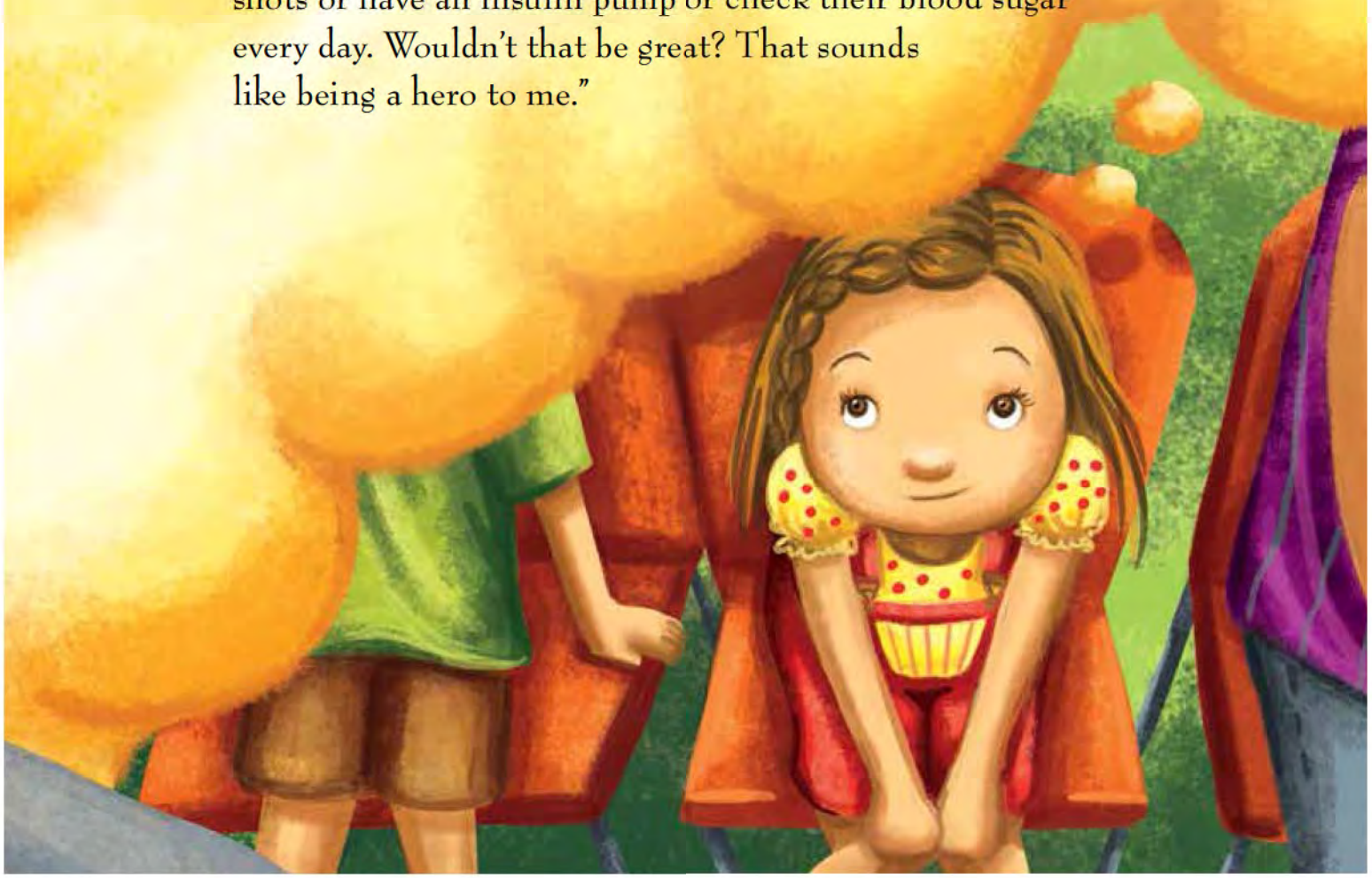
A special hero's mission. How exciting! thought Claire. She looked at Mom and Dad. They were all ears too.

The scientist continued. "You can do something to help us find answers about diabetes. Do you want to know what that something special is?"

"Yes!" all the children in the crowd yelled.

"Well, if it is okay with your parents, you can let us do a test here at camp. When we do the test, we take a small amount of blood from your arm. It is very easy to do. Scientists like me will study your blood. What we find will help us learn about ways to keep kids from getting diabetes.

"Believe it or not, that's all there is to it. Just think: maybe one day kids like your brothers and sisters won't have to give themselves shots or have an insulin pump or check their blood sugar every day. Wouldn't that be great? That sounds like being a hero to me."

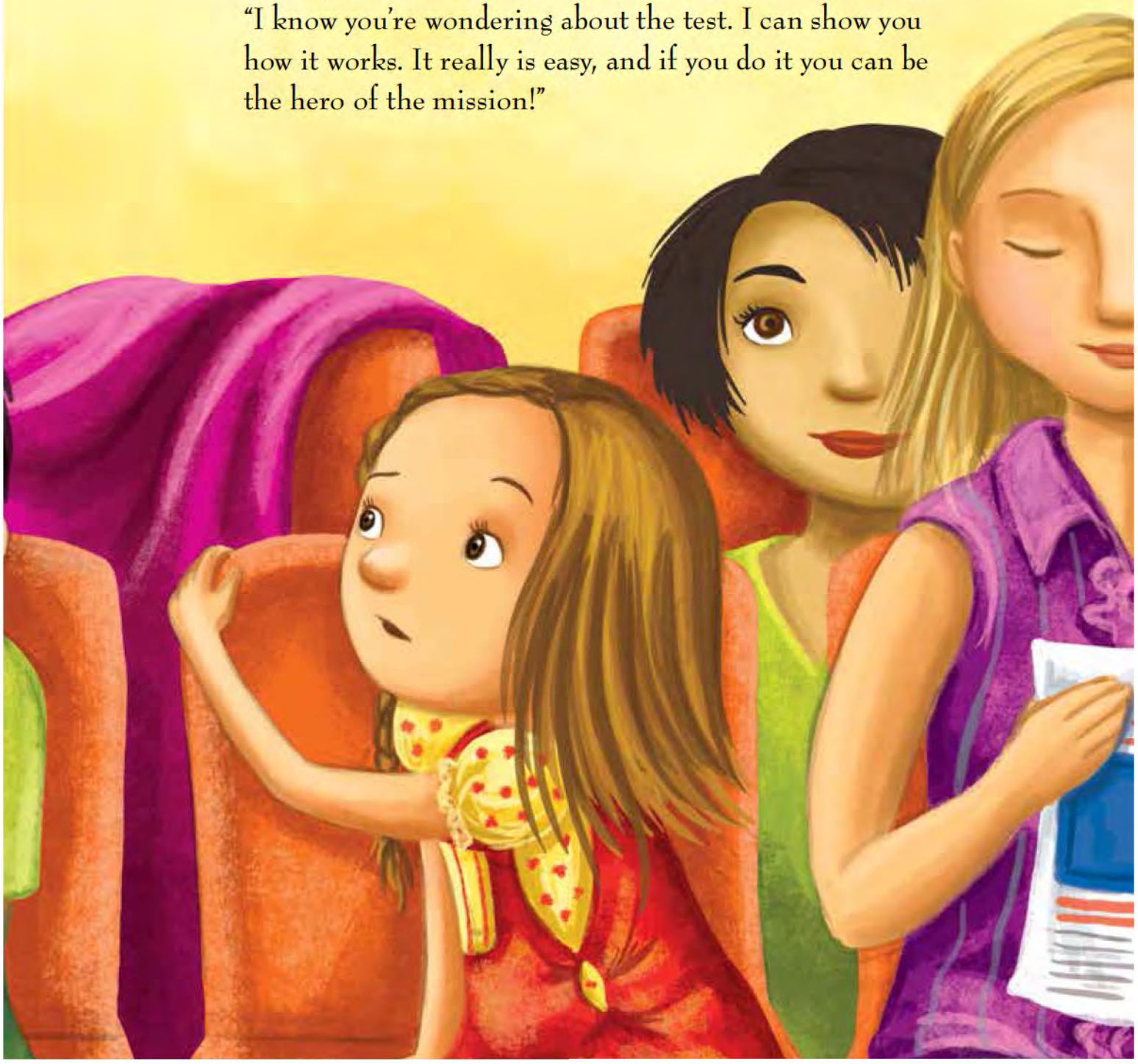


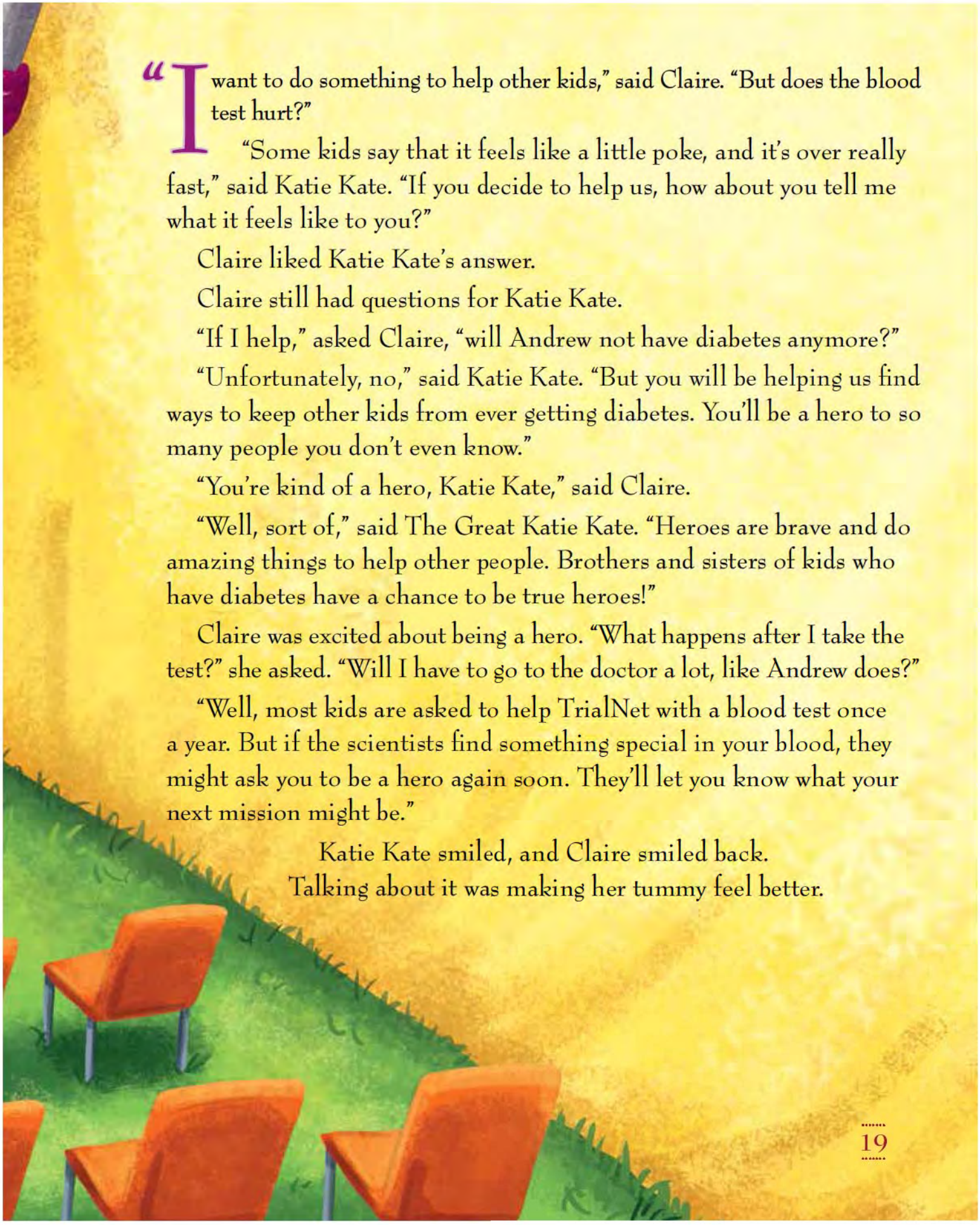
Claire listened carefully to the scientist. She thought it would be really neat to help find a way to keep other kids from getting diabetes.

But Claire suddenly felt a little funny in her tummy. She was worried. She had a lot of questions about the test.

And just like that, she heard a *psssssst* from behind the rows of chairs in the tent.

"Hey, Claire! Over here!" called The Great Katie Kate. "I know you're wondering about the test. I can show you how it works. It really is easy, and if you do it you can be the hero of the mission!"





"I want to do something to help other kids," said Claire. "But does the blood test hurt?"

"Some kids say that it feels like a little poke, and it's over really fast," said Katie Kate. "If you decide to help us, how about you tell me what it feels like to you?"

Claire liked Katie Kate's answer.

Claire still had questions for Katie Kate.

"If I help," asked Claire, "will Andrew not have diabetes anymore?"

"Unfortunately, no," said Katie Kate. "But you will be helping us find ways to keep other kids from ever getting diabetes. You'll be a hero to so many people you don't even know."

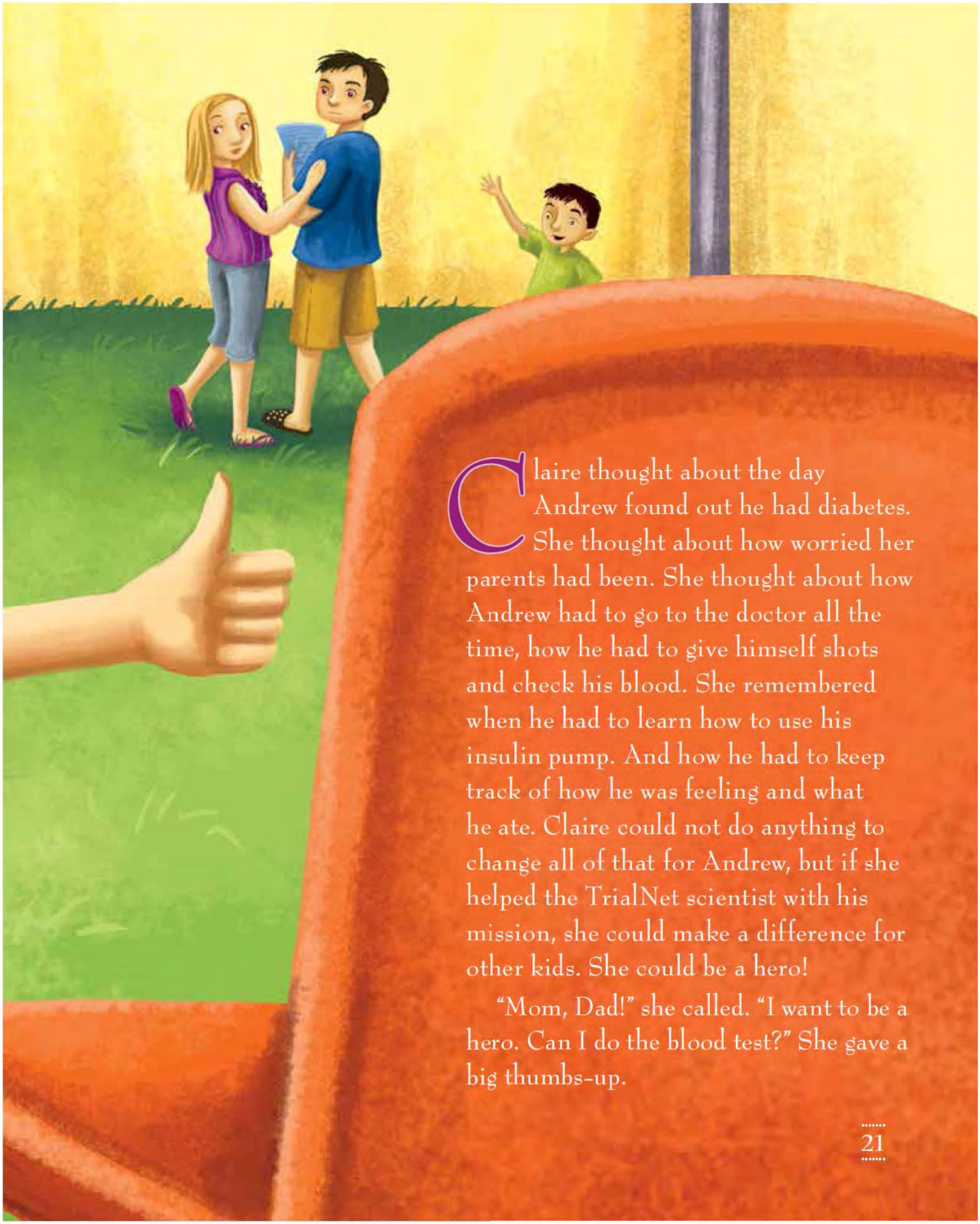
"You're kind of a hero, Katie Kate," said Claire.

"Well, sort of," said The Great Katie Kate. "Heroes are brave and do amazing things to help other people. Brothers and sisters of kids who have diabetes have a chance to be true heroes!"

Claire was excited about being a hero. "What happens after I take the test?" she asked. "Will I have to go to the doctor a lot, like Andrew does?"

"Well, most kids are asked to help TrialNet with a blood test once a year. But if the scientists find something special in your blood, they might ask you to be a hero again soon. They'll let you know what your next mission might be."

Katie Kate smiled, and Claire smiled back.
Talking about it was making her tummy feel better.

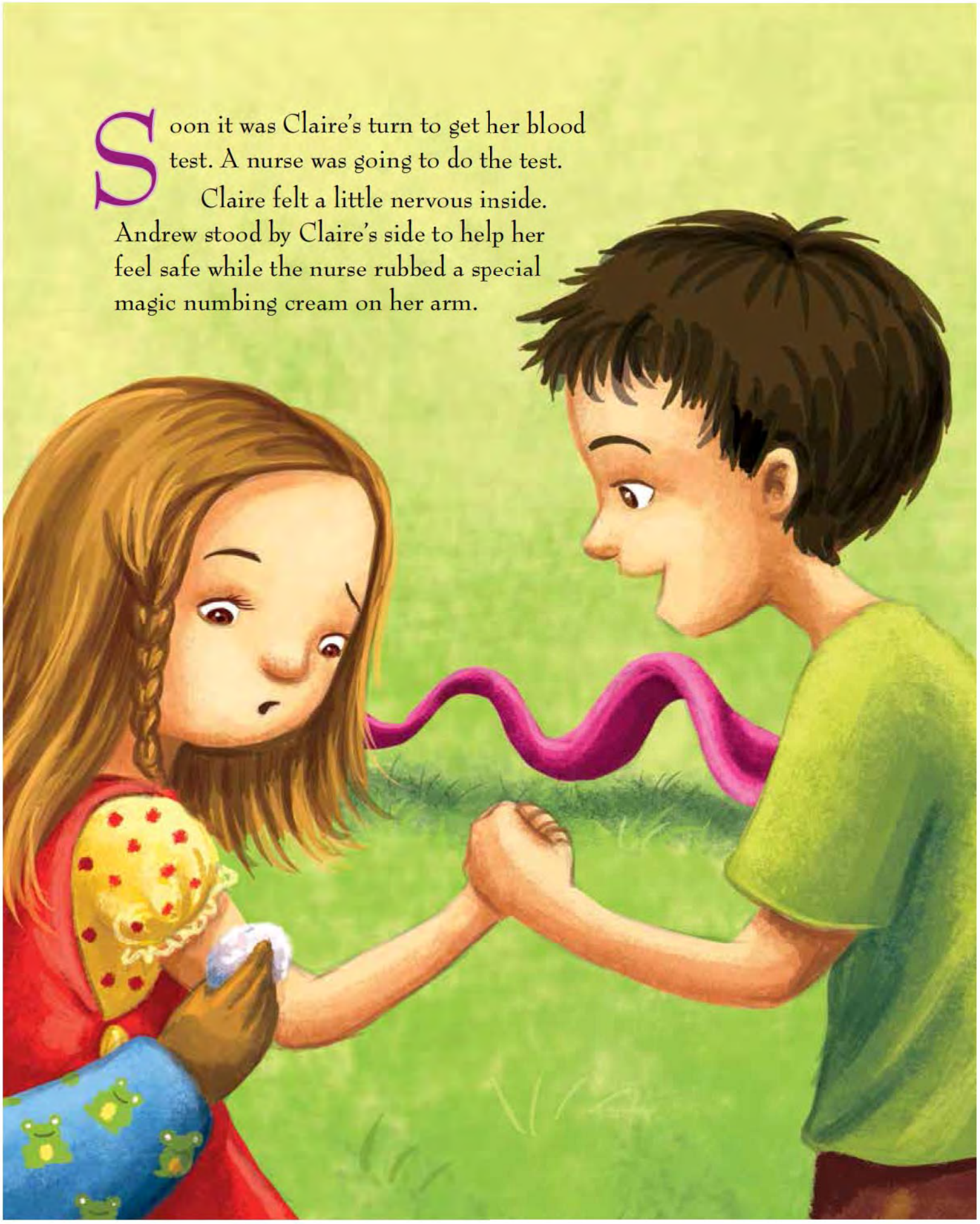


Claire thought about the day Andrew found out he had diabetes. She thought about how worried her parents had been. She thought about how Andrew had to go to the doctor all the time, how he had to give himself shots and check his blood. She remembered when he had to learn how to use his insulin pump. And how he had to keep track of how he was feeling and what he ate. Claire could not do anything to change all of that for Andrew, but if she helped the TrialNet scientist with his mission, she could make a difference for other kids. She could be a hero!

"Mom, Dad!" she called. "I want to be a hero. Can I do the blood test?" She gave a big thumbs-up.

Soon it was Claire's turn to get her blood test. A nurse was going to do the test.

Claire felt a little nervous inside. Andrew stood by Claire's side to help her feel safe while the nurse rubbed a special magic numbing cream on her arm.



"This cream makes it so you don't feel the poke as much," the nurse said. "You're doing a great job. Just keep sitting still and we'll be done before you know it."

"I've had a lot of blood tests, Claire," Andrew said. "I know you can do it! How about we sing a song we learned at camp this week, and Katie Kate can dance to keep your mind off of the test."

"You can see Katie Kate?" exclaimed Claire.

"Sure," said Andrew. "She's a hero to all kids who have to be brave and take tests."

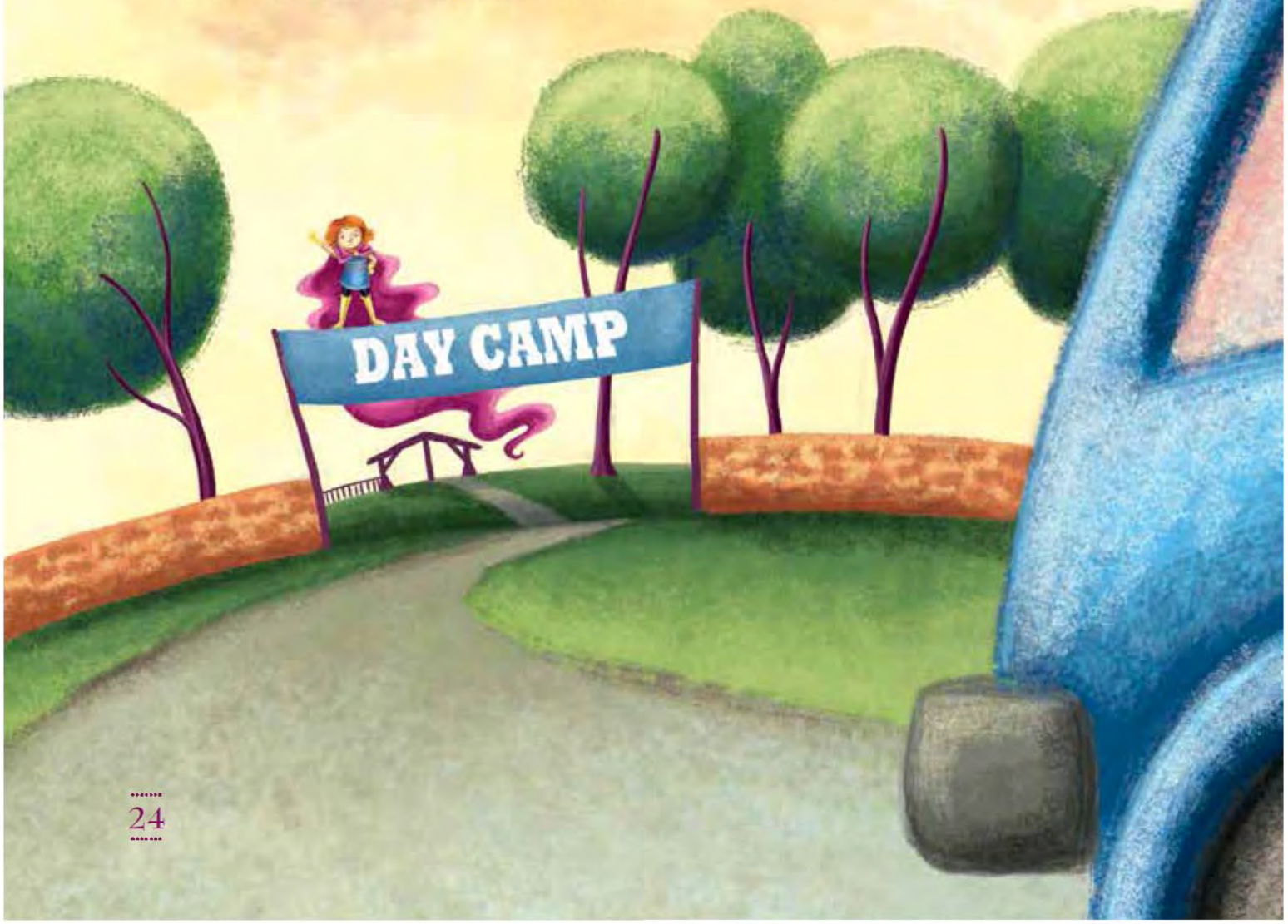
"It's true! I'm here to help!" said Katie Kate.

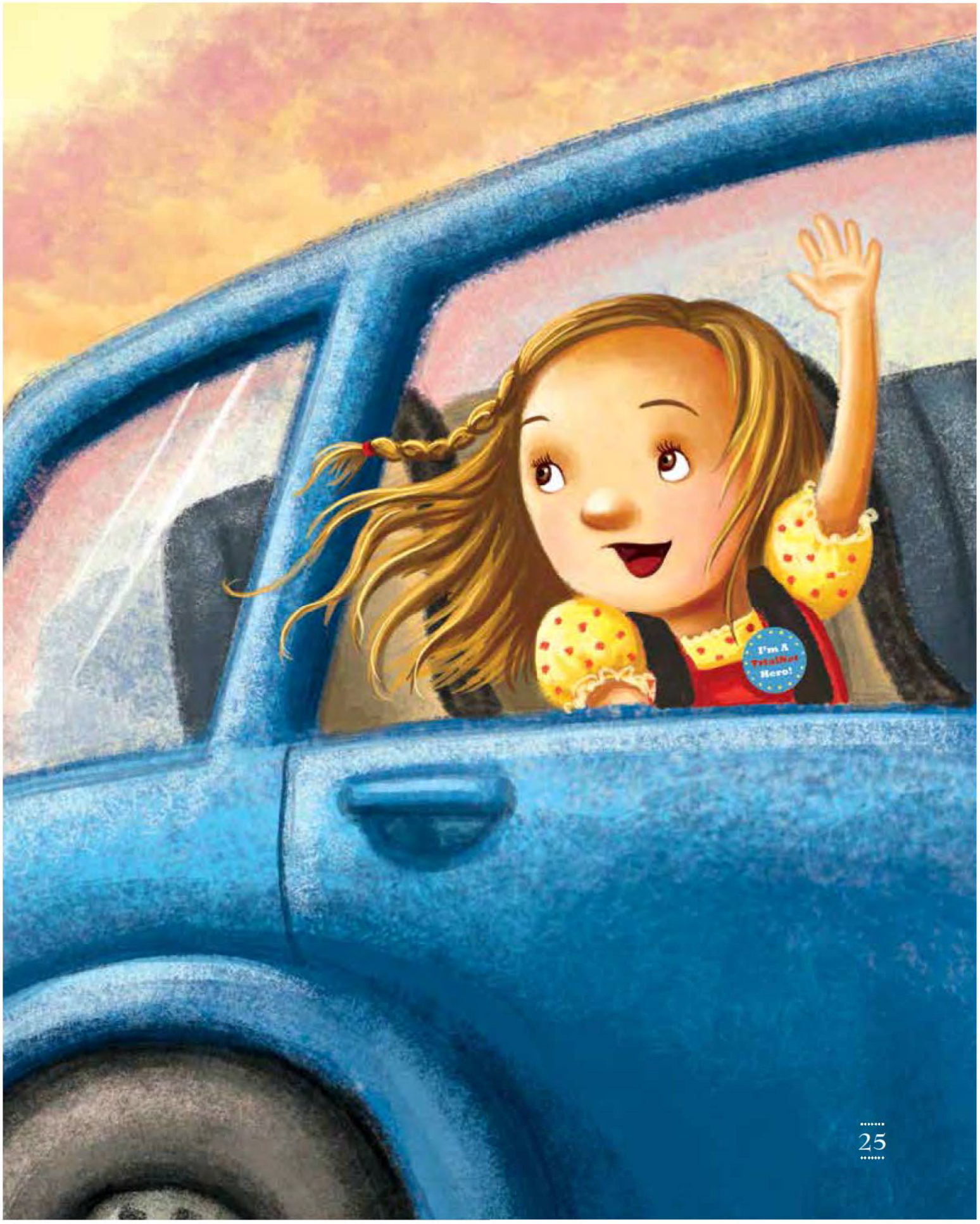
Andrew held Claire's hand and they began to sing while Katie Kate hopped to the tune. Claire did a great job by holding very still.

"You're all finished, Claire!" said Katie Kate as she pressed a big colorful sticker that said "I'M A TRIALNET HERO" on Claire's shirt. "You were so brave and did such a great job. Thank you so much for helping today!"

"That was it?" said Claire. "That hardly hurt at all. It felt just like a tiny pinch."

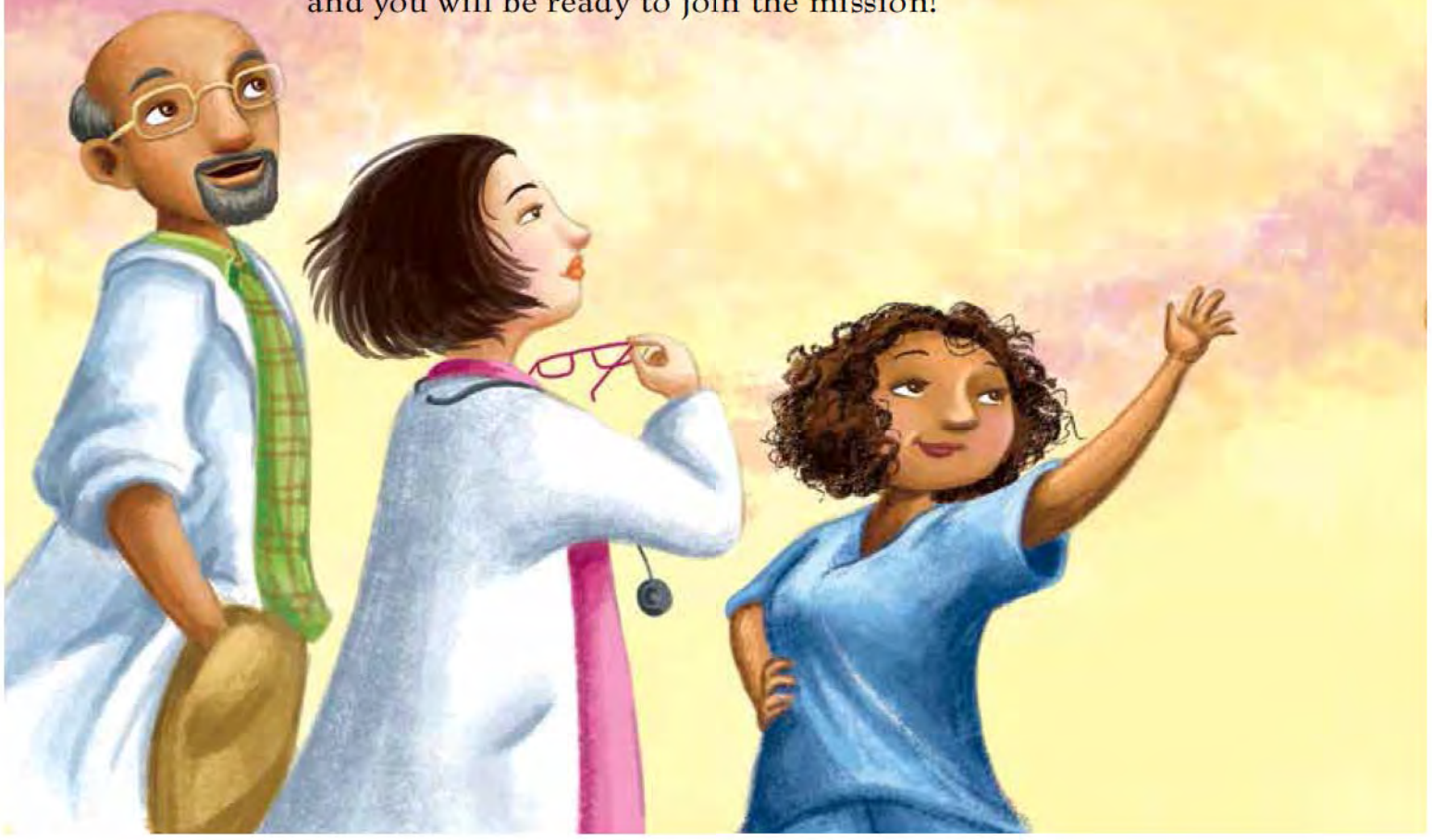
Claire left camp that day with a very special feeling inside. She had been worried about the blood test, but she thought about Andrew and all the other kids she had met who were living with diabetes. She made a big decision. She decided it was important to help find a way to keep other kids from getting diabetes. Claire really was a hero!

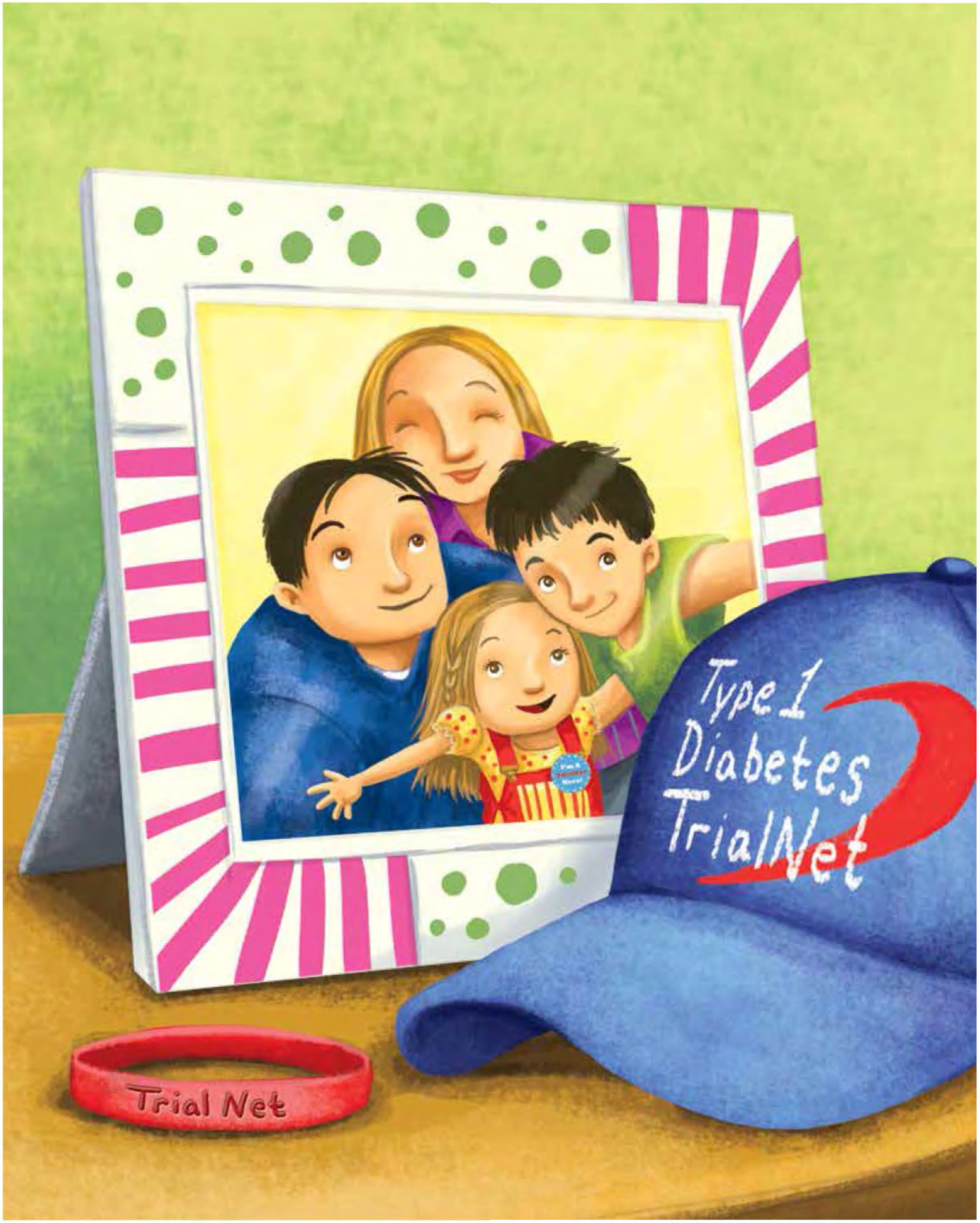



I'm A
Hero!

All kids like Claire, who have a brother or sister with diabetes, are special and can help scientists find a way to keep other kids from getting diabetes. Even if they do not want to have a blood test, they can be a hero by supporting their sister or brother with diabetes. And they can participate in diabetes organizations and community events to help people learn about diabetes and to tell others about the importance of research.

There will be times in the future when you will receive the call to be a hero. When that time comes, think about all the things Katie Kate said to make Claire feel brave and you will be ready to join the mission!




Type 1
Diabetes
TrialNet
Trial Net

Type 1 diabetes is an autoimmune disease in which the immune system attacks and destroys the cells in the pancreas that produce insulin. Proteins called autoantibodies are markers for the destruction of these cells.

TrialNet is an international network of researchers who are exploring ways to prevent, delay, and provide early treatment for type 1 diabetes. TrialNet offers a screening test that can detect these autoantibodies in the blood up to ten years before someone is diagnosed with type 1 diabetes. A major goal of the TrialNet studies is to delay or prevent diabetes in people with these autoantibodies.

Only 4 to 5 percent of relatives tested will have autoantibodies. If positive, participants can be monitored in the Pathway to Prevention study and will be offered enrollment in a prevention study, if eligible. Benefits to monitoring include early detection of type 1 diabetes, which may help maintain insulin secretion and avoid dangerous complications.

You can find out whether you or your children are at risk for type 1 diabetes if:

- you or your children are one to forty-five years old and you have a parent, child, brother, or sister with type 1 diabetes,

or

- you or your children are one to twenty years old and have a niece, nephew, aunt, uncle, grandparent, half sibling, or cousin with type 1 diabetes.

If either of these applies, you or your children can have a blood test as part of the Pathway to Prevention study. TrialNet has over two hundred study centers. Screenings are provided at no cost. To find the study center that is closest to you, visit www.diabetestrialnet.org or call 1-800-425-8361.

You can also provide your consent by going online at www.pathway2prevention.org.

At no cost, TrialNet will mail you a test kit that can be taken to a local lab to be administered by a healthcare professional. The sample will be mailed directly to TrialNet, and results will be reported within six weeks.

More About Summer Day Camp for Children with Diabetes

The screening test described in this story is performed with the consent of the child's parent. The story takes place at a diabetes day camp, where children with diabetes and their sisters and brothers without diabetes can attend together. We recognize that not every diabetes camp offers this arrangement. To find out more about diabetes camps and specific programs offered in your area, contact the Diabetes Education & Camping Association (DECA) at www.diabetescamps.org.

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Fishing for Flowers

ABOUT THE AUTHOR

M. Maitland DeLand, M.D., is a radiation oncologist specializing in the treatment of women's and children's cancer. She is the founder and former owner of Oncologics, a group of cancer treatment centers in the southern United States. One of the leaders in her field, she is the chairman of the Health Education Authority of Louisiana Board that serves to promote medical education, research, and healthcare throughout the state. Dr. DeLand also serves as a member of the Breastcancer.org Professional Advisory Board. She has dedicated her career to helping her patients and their families lead balanced and rewarding lives.

ABOUT THE ILLUSTRATOR

Jennifer Zivoin is a children's book illustrator living in Carmel, Indiana. Although she has been trained in media ranging from figure drawing to virtual reality, her passion is bringing stories to life through her watercolor paintings. Her most recent work has been creating illustrations for Brian James's popular Pirate School series.