Natural History Study

Phase 1 Screening

Welcome to Type 1 Diabetes TrialNet and Phase 1 (Screening) of the Natural History Study of the Development of Type 1 Diabetes. We appreciate your interest in our study.

What Is TrialNet?

TrialNet is a network of 18 clinical centers working in cooperation with screening sites throughout the United States, Canada, Finland, United Kingdom, Italy, Germany, Australia, and New Zealand. This network is dedicated to the study, prevention, and early treatment of type 1 diabetes. TrialNet is supported by the National Institutes of Health, which is part of the United States federal government. It is also supported by other major diabetes organizations.

What Is the Natural History Study?

The Natural History Study is part of the TrialNet Type 1 Diabetes studies. The goal of this study is to learn more about how type 1 diabetes develops in "at-risk" individuals. Close relatives of people with type 1 diabetes are being studied in three steps (phases): Screening, Baseline Risk Assessment, and Follow-Up Risk Assessments. Participants in the Natural History Study may be offered the opportunity to enter into prevention or early treatment studies when these become available.

The purpose of screening is to identify people at risk for developing type 1 diabetes. Individuals at greater risk may be offered the opportunity to continue on to other phases of the Natural History Study to receive close monitoring for the development of diabetes. They may also participate in studies testing new treatments to delay or prevent the onset of diabetes. If participants develop diabetes during the Natural History Study, they may be eligible to participate in studies aimed at slowing the progression of type 1 diabetes.

What Is Type 1 Diabetes?

Type 1 diabetes is a life-long disease that occurs in both children and adults. It develops when the body attacks and destroys insulin-producing cells in the pancreas. Insulin is a hormone the body needs to use food for energy. Patients with type 1 diabetes lose the ability to produce insulin and need to take insulin injections.

Who Is at Risk for Type 1 Diabetes?

TrialNet will screen relatives of people with type 1 diabetes because they have a 10 to 15 times greater risk for developing the disease than people with no family history.

Who Can Participate in the Natural History Study?

To participate in Phase 1 of the Natural History Study, you must be:

- 1 to 45 years of age and have a brother, sister, child, or parent with type 1 diabetes, OR
- 1 to 20 years of age and have a cousin, aunt, uncle, niece, nephew, half-sibling, or grandparent with type 1 diabetes.

In general, your relative may have type 1 diabetes if they were diagnosed before age 40 and required insulin injections within a year of diagnosis.

What Is the Screening Test?

The screening test is a blood test to see if you have autoantibodies associated with a risk of developing diabetes. Autoantibodies are a sign that your immune system may be attacking the insulin-producing cells in your pancreas. Autoantibodies are proteins made by the immune system. About 3 to 4 percent of family members of people with type 1 diabetes have autoantibodies. The presence of some autoantibodies indicates you may be at risk for developing type 1 diabetes.

To do the test, a small sample of blood is drawn from your arm. It is sent to the TrialNet central laboratory for analysis. You can have the blood sample drawn in a TrialNet clinic or you can have a test kit sent to you. You can then take this test kit to a local laboratory or your own physician to have your blood drawn.

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Type 1 Diabetes TrialNet

You will be notified of your test results in one of two ways:

- By letter if the antibody test shows NO autoantibodies are present (**negative result**). Testing negative for autoantibodies does not mean you will never get diabetes. It does mean that the chances are much lower than if you tested positive. If you are under 18 years of age, you can be tested every year since antibody levels can change.

- By phone if autoantibodies are present (**positive result**). We will call you to discuss your results and future testing options. Testing positive does not mean that you will get type 1 diabetes. It means you have a greater chance than if you tested negative. You may return to the clinic for more tests to confirm these results. If the repeat tests indicate the presence of at least one of the same autoantibodies, you may have additional tests to determine your risk for developing diabetes.

Additional tests to further determine your risk of developing type 1 diabetes are done in **Phase 2 (Baseline Risk Assessment)** and will estimate your chances of developing type 1 diabetes over the next 5 years. Your estimated risk level may be indicated as being less than 25%, 25-50%, or greater than 50%.

If you wish to continue the testing, you may participate in **Phase 3 (Follow-Up Risk Assessments)**. In Phase 3 you will be closely monitored for the development of type 1 diabetes.

You may also be offered enrollment in diabetes prevention studies as they become available.

Individuals that develop type 1 diabetes while participating in the Natural History Study may be offered enrollment in a TrialNet study to save your ability to produce insulin.

All of these study options (Phase 2 and 3, and diabetes prevention studies) would require that you visit a TrialNet clinical center or Affiliate clinic. You would not be able to have a test kit sent to you for testing at a local physician's office or laboratory as can be done in Phase 1.

How Do You Give Consent for the Autoantibody Test?

Before you have the autoantibody screening test, you will be asked to sign an "Informed Consent" form. This form gives your permission to take the test. Parents must give permission for children under 18 years of age to be tested. Although a representative of the study will speak to you about the study, it is important that you read the consent form carefully. If you have questions or concerns, you should contact your TrialNet health professional. If you participate in Phase 1, you are not required to participate in any other phase of the Natural History Study.

If you choose to participate in Baseline Risk Assessment (Phase 2) or Follow-Up Risk Assessments (Phase 3) of the study, we will ask you to sign a separate consent form for each phase. Even if you do not wish to take part in Phase 2 or Phase 3, we might contact you in the future by phone or mail to see if you are interested in taking part in another diabetes-related research study. We would also like to learn if you have developed type 1 diabetes.

You may also learn about TrialNet at **www.DiabetesTrialNet.org**

Other TrialNet Fact Sheets Available Include:

- TrialNet Natural History Study, Phase 2: Baseline Risk Assessment
- TrialNet Natural History Study, Phase 3: Follow-Up Risk Assessments

TrialNet Is Sponsored By:

National Institute of Diabetes & Digestive & Kidney Diseases
National Institute of Allergy and Infectious Diseases
National Institute of Child Health and Human Development
National Center for Research Resources
National Institutes of Health
United States Department of Health & Human Services
Juvenile Diabetes Research Foundation International
American Diabetes Association

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Phase 2 Baseline Risk Assessment

Welcome to **Phase 2** of the TrialNet Natural History Study of the Development of Type 1 Diabetes. This phase is called **Baseline Risk Assessment**. You were screened in Phase 1 of the Natural History Study and learned that your blood sample tested positive for the presence of at least one autoantibody associated with type 1 diabetes. These results show that you are more likely to develop type 1 diabetes than most other people, but we do not know your actual risk.

What is the Purpose of Baseline Risk Assessment (Phase 2)?

The purpose of Phase 2 is to estimate your risk for the development of type 1 diabetes over the next 5 years.

How Do You Start Testing for Baseline Risk Assessment (Phase 2)?

Before you have any Phase 2 tests done, you will be asked to sign an "Informed Consent" form. This form gives your permission to take the tests. Parents must give permission for children under 18 years of age to be tested. The "Informed Consent" for the Baseline Risk Assessment study is different from the one that you signed for Phase 1 of the study. A TrialNet representative will speak to you about the study, but it is very important that you read the consent form carefully. You must have participated in Phase 1 to be eligible for Phase 2 but you are not required to participate in Phase 2.

What Happens in Baseline Risk Assessment (Phase 2)?

As part of Phase 2, you will have the following tests performed:

- Oral Glucose Tolerance Test (OGTT). After an overnight fast, a needle will be inserted into your arm and then removed, leaving a small plastic tube. You will be asked to drink a special sugar drink. We will look at your blood sugar (glucose) levels before and after you have the drink. Blood samples will be taken over a period of 2 hours.
- HLA test. HLA is an area on your chromosomes (part of your DNA) that contains a group of genes. Some people with certain kinds of HLA genes may have a higher risk of developing type 1 diabetes. Your HLA genes will only be tested to determine your risk of type 1 diabetes.
- HbA1c test. This test measures your average blood sugar (glucose) level over the past 2 to 3 months.
- Blood samples will be stored for possible later use, if you agree to this.

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In some cases we will ask to do an additional test called an Intravenous Glucose Tolerance Test (IVGTT). This test will be done on a different day to learn more about your risk of developing type 1 diabetes. For this test, several blood samples are drawn over 20 minutes to measure how your pancreas responds to receiving glucose into your vein.

At the end of Phase 2, we will provide you with an estimate about your risk for developing type 1 diabetes in the next five years. Your risk may be estimated as less than 25%, 25-50%, or greater than 50%. You will be notified of your estimated risk by telephone in 4 to 6 weeks. You will also be provided with feedback from your other testing unless you do not wish to know this information. Since there is still more to be learned about predicting who will develop type 1 diabetes, we cannot tell you for sure if and when you might develop type 1 diabetes. However, Phase 2 should provide more information about your risk for developing type 1 diabetes than can be determined in Phase 1.

What is the Next Step?

The next phase is **Follow-up Risk Assessments (Phase 3)**. If you participate in Phase 2, you are automatically eligible for Phase 3, but you are not required to participate in Phase 3. If you choose to participate in Phase 3, we will ask you to sign a separate consent form.

Depending on your risk for type 1 diabetes, you could be asked to take part in a prevention trial if one is available. If you qualify, we will ask you to sign a consent form for that specific trial. If a trial is not immediately available for you, and you do not wish to participate in Phase 3, you might be asked to return for repeat testing when a prevention study becomes available.

Even if you do not want to take part in Phase 3, we might contact you in the future to see if you are interested in taking part in another diabetes related research study. We would also like to learn if you have developed type 1 diabetes.

You may also learn about TrialNet at **www.DiabetesTrialNet.org**

Other TrialNet Fact Sheets Available Include:

- TrialNet Natural History Study, Phase 1: Screening
- TrialNet Natural History Study, Phase 3: Follow-Up Risk Assessments

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National Institutes of Health
United States Department of Health & Human Services
Juvenile Diabetes Research Foundation International
American Diabetes Association

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Phase 3 Follow-Up Risk Assessments

Welcome to **Phase 3** of the TrialNet Natural History Study of the Development of Type 1 Diabetes. This phase is called **Follow-Up Risk Assessments**. At this point, you have been through Phase 1 and Phase 2 of the study.** During Phase 1, your blood sample had autoantibodies present. You had additional tests in Phase 2 which provided an estimate of your risk for developing type 1 diabetes over the next 5 years.

What is the Purpose of Follow-up Risk Assessments (Phase 3)?

The purpose of Phase 3 is to see if your risk level for developing diabetes has changed. You will also be monitored closely for the possible development of type 1 diabetes. If you were to develop diabetes, it is possible it would be found earlier and that you might qualify for research studies of people with new-onset type 1 diabetes.

How Do You Start Testing for Follow-up Risk Assessments (Phase 3)?

Before you have any Phase 3 tests done, you will be asked to sign an "Informed Consent" form. This form gives your permission to take the tests. Parents must give permission for children under 18 years of age to be tested. This "Informed Consent" is different from the ones that you signed in Phase 1 and 2 of the study. A TrialNet representative will speak to you about the study, but it is very important that you read the consent form carefully. If you have questions or concerns you should contact your TrialNet health professional.

What Happens in Follow-up Risk Assessments (Phase 3)?

As part of Phase 3, you will be invited back to the clinic every 6 months for the next 5 years to have tests performed. The tests performed in Phase 3 are similar to the ones performed in Phase 2 (the Intravenous Glucose Tolerance Test is not repeated). You will again be asked to drink a special sugar drink after an overnight fast. A needle will be inserted into your arm and then removed, leaving a small plastic tube. Several blood samples will be taken from this tube over a period of 2 hours to perform the Oral Glucose Tolerance Test (OGTT). We will also take blood for a HbA1c test. The HbA1c blood test measures your average blood sugar (glucose) level over the past 2 to 3 months. You will be offered feedback on your test results. With your consent, we will also take blood to be stored for possible later use. The blood samples will be sent to a TrialNet central laboratory for analysis.

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What Happens after Follow-up Risk Assessments (Phase 3)?

The results of the follow-up tests performed in Phase 3 will help us learn more about risk factors associated with the development of type 1 diabetes. These results will also be used to see if you qualify for any of the following research studies:

- Prevention Studies, which will test different treatments to prevent or delay the onset of type 1 diabetes. If you qualify and choose to take part in a prevention trial, you will have no further visits for the TrialNet Natural History Study. You will also be asked to sign a separate "Informed Consent" form.
- New Onset Studies, which will test various treatments to preserve insulin production in people with newly diagnosed type 1 diabetes. These studies will test treatments that might help the pancreas to continue producing some insulin.

** If you participated in the Diabetes Prevention Trial (DPT-1), you will probably be entering the Natural History Study at Phase 3.

You may also learn about TrialNet at **www.DiabetesTrialNet.org**

Other TrialNet Fact Sheets Available Include:

- TrialNet Natural History Study, Phase 1: Screening
- TrialNet Natural History Study, Phase 2: Baseline Risk Assessment

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