Understanding T1D
Clinical Trials

JDRF

How does research get to an approved treatment?

Cells

Understand what a cell does by looking at its behaviour and features such as DNA

Systems

Understand how different cell types and organs work together as a system to carry out a process

Treatment

Develop a treatment to target a system and change its behaviour

Preclinical studies

Test the treatment in the lab to work out an effective dose and check for safety

Clinical trials

Test the treatment in clincial trials with people to check for effectiveness and safety

Application

Submit the treatment with evidence for approval with regulatory bodies

Approval

Treatment approved for clinical use

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What happens in a clinical trial?

Approval
Regulatory bodies give approval for the trial to take place

Recruitment


Participants are recruited and give consent to take part in the trial

Start treatment
Participants are split into groups and receive the new treatment, or the best treatment currently available or a placebo

End treatment


The researchers assess how effective and safe the treatment was

Publish
The results of the trial are published so that others can learn from the results

Progress


The treatment may progress to the next stage of trials or be approved for use, depending on the evidence from the results

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Section 1: How does research get to a clinical trial?

You may have heard that getting a new treatment from discovery to market can take 15 years or even longer. This is because there are many steps that must take place before a treatment can be approved for use. JDRF funds research at all stages of this pathway. Each stage of research is highly regulated to ensure that researchers work ethically, and risk of harm is minimised.

Cells research

The first step on the research pathway is to investigate individual cell types relevant in a disease. At the cells research level, researchers are trying to understand what a particular cell type does.

For example, in T1D, we are interested in the insulin-producing beta cells, and the immune system cells which attack them.

Systems research

Once researchers understand how individual cell types work, they can look at systems. Systems in the body are collections of cells and organs that work together to carry out a process. If we can understand how a system behaves normally, and we can see where or why that system is not behaving as it should in a disease, it could indicate possible points in the system that could be targeted with treatments.

For example, in T1D, we are interested in understanding how the immune system behaves, and how / why islet cells stop working in the pancreas.

Development of treatment

Treatments can take many forms, including drugs, medical technology, or education programs. Because treatments take many forms, research at this level can be very varied and the path to advance a treatment to trials is unique for each new treatment.

For example, in T1D, researchers are developing drugs to change the behaviour of the immune system to stop the immune cells from attacking the beta cells.

Preclinical studies

Once a new treatment is developed, it will be tested extensively in the lab before it can be tested in people. Preclinical studies involve testing the treatment in human tissue samples or in animals in the lab. The aim of preclinical studies is to check as far as possible that the treatment is likely to be safe to use in humans and to work out what would be the most effective dose.

For example, a drug developed to stop the immune cells from attacking beta cells would be tested in a special strain of mice with T1D.

Clinical trials

Clinical trials are the last step in developing a treatment, and they can only occur when there is enough evidence to suggest that the treatment will be safe to use in humans. In Canada, Research Ethics Boards and Health Canada are responsible for approving clinical trials.

There are three main phases of clinical trials, and a treatment must show safety and efficacy in all of them to be approved for clinical use. These phases are explained in Section 2.

Application & Approval

When a new treatment has successfully completed all three phases of testing in clinical trials, all of the evidence on the treatment's safety and effectiveness collected through the clinical trials is submitted to regulators (i.e., Health Canada) for review.

The regulator will then decide whether there is sufficient evidence of benefits versus risks to approve a new treatment for use in clinical practice.

Key points
Research goes through a series of stages before culminating in clinical trials
It is necessary for research to follow these stages so we can check for safety and effectiveness as far as possible before we start clinical trials
Clinical trials are essential to test the safety and effectiveness of a new treatment in people
A new treatment will only be approved for clinical if there is convincing safety and efficacy evidence from clinical trials

Section 2: How does a clinical trial work?

Clinical trials can be separated into two types. **Interventional** clinical trials are where something is *given* to the participant such as a drug, a new device, or an exercise program. **Observational** clinical trials are where nothing is *given* to the participant, but information is *recorded from* the participant at one or more time points. An example of this is a disease registry.

Trial phases

Interventional clinical trials are run in a series of stages, known as phases. Treatments must demonstrate efficacy, or a greater benefit than risk, to progress onto the next phase.

Phase 1: a new treatment is usually given to a small number (~20-80) of volunteers. This is to check that the treatment is safe to use in people and assess possible side effects. In cases where the treatment is already being used for other conditions or diseases, this phase may be skipped.

Phase 2: a treatment is tested in a slightly larger number (~100-300) of volunteers with the condition the treatment is designed to benefit. This is to check whether the treatment is effective, and to fine-tune doses.

Phase 3: tests the new treatment in a large number (~500-3000) of volunteers with the condition. This is to check further that the treatment is safe and effective to use in a range of people with different bodies and metabolisms, and at different stages of the condition.

Approval

All clinical trials must be reviewed by a Research Ethics Board (REB), and in some cases, Health Canada. REBs are independent boards that approve and monitor research to ensure the ethical conduct of research involving humans. REBs ensure participant respect, protection of welfare, and that the benefits of the research outweigh the risks.

In addition, any clinical trial involving a drug, natural health product, biologic or genetic therapy, and medical devices (such as CGMs or insulin pumps) must be approved by Health Canada.

Recruitment and Informed Consent

During recruitment, the researchers will explain the benefits and risks of the trial to potential participants. The participants (or a parent/legal guardian) will need to sign a consent form to show they have understood the risks and are willing to participate. Participants are free to leave the trial at any time, for any reason.

Eligibility criteria is set to test the treatment in the group of people that will have the most benefit and the fewest risks. These criteria typically widen as the phases progress.

Clinical Trial Interventions

To determine efficacy, clinical trials compare the new treatment to a similar treatment currently being used or a placebo. A placebo is a pretend treatment: it is usually designed to look and feel just like the real treatment, even to the medical staff and researchers. If the condition is serious and there is no treatment currently available, the new treatment may be given to all participants (for example, T1D cell therapy trials).

When treatments are being compared, researchers will try to use ‘blinding’ to minimize bias. This is where the researchers, and/or the participants don’t know what treatment is being received to minimize the impact of the “placebo-effect”.

Clinical Trial Results

Once the clinical trial finishes, the participants do not have to do anything else. The researchers will analyse the data they have collected and often report their findings in a paper published in a scientific journal. It is best practice for the researchers to let the participants know the outcomes of the study.

Ultimately, the results of the trial may mean the treatment can progress to the next stage of testing, or it may be that more evidence is needed before this can happen. Following a phase 3 clinical trial, the results may be submitted to Health Canada for regulatory approval, as was described in Section 1.

Taking part

Participating in a clinical trial can bring great benefits, such as access to an innovative treatment, or increased medical care, but it is also important to remember that there are always risks when trialling any treatment. This is why it is crucial that anyone participating in a trial understands both the benefits and the risks. It is important to always talk to your healthcare team about any clinical trial you are considering getting involved in. They will be able to offer advice on the risks and benefits of taking part in a clinical trial.

Key points
Participating in a clinical trial helps to accelerate research
Clinical trials are essential to test a new treatment for safety and effectiveness
Clinical trials are conducted for new drugs, treatments or medical devices; but they are also performed for the application of an existing drug to a new population or disease, behavioural interventions, and observational research
There are 3 phases of clinical trials to thoroughly test for safety and effectiveness of a new treatment in an increasing number of people
Taking part in a clinical trial is entirely voluntary, and participants can leave whenever they choose
If you take part in a trial, you may not receive the new treatment – you may receive the best currently available treatment, or a placebo instead