UNDERSTANDING SCIENCE TOOLKIT
Are you interested in type 1 diabetes research? Would you like to learn more about how research and clinical trials work?

Or maybe check the quality of the research behind a dodgy headline?

JDRF UK has developed the Understanding Science Toolkit to address all of these questions and more. We hope that you will find this toolkit helpful in finding, reading and assessing the quality of research.

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Glossary of terms
Clinical trials are the last step in a long pathway of research. You may have heard that getting a new drug to market can take 15 years. This is because there are a number of steps that have to take place before a drug or treatment can be approved for use. JDRF funds research at all stages of the pathway, so that one day the pathway will lead to approved new treatments or a cure for type 1 diabetes. Each stage of research is highly regulated to ensure that researchers work ethically and risk of harm is minimised.

**How does research get to a clinical trial?**

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**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. This could include looking at the cell’s DNA sequence, looking at which genes are switched on or off, and looking at what proteins are made by the cell. *For example, in type 1 diabetes, 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. At the systems research level, researchers are trying to understand how the different cells and organs behave and interact together. 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. Research at this level therefore informs the development of new treatments. *For example, in type 1 diabetes, we are interested in understanding how the immune system behaves, and how it differs from someone without type 1 diabetes.*

**DEVELOPMENT OF TREATMENT**

When researchers understand how a system works, they can develop new treatments to target it appropriately. Treatments can take many forms, including drugs, medical technology and education programmes, and can have very different actions, and so research at this level can be very varied. Treatments may act to:

- Stimulate or block a process in the body
- Increase or decrease the presence of a molecule
- Change a person’s behaviour or lifestyle
- Deliver an existing drug in a new way

*For example, in type 1 diabetes, some researchers are developing drugs to change the behaviour of the immune system, and stop the immune cells from attacking the beta cells.*
PRECLINICAL TRIALS

Once a new treatment is developed, it will be tested in the lab before it can be tested in people. Preclinical trials involve testing the treatment in human tissue samples or in animals in the lab. The aim of preclinical trials 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 type 1 diabetes.

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 clinical trials, a new treatment is tested in human volunteers. There are three main phases of clinical trials, and a treatment has to pass all of them in turn to be approved for clinical use. These are explained in Section 2.

APPLICATION & APPROVAL

When a new treatment has successfully completed all three phases of testing in clinical trials, it can be considered for general approval for use in patients by the relevant governing body. In the UK, this is the Medicines and Healthcare products Regulatory Agency (MHRA) or the European Medicines Agency (EMA). All of the evidence on the treatment’s safety and effectiveness collected through the clinical trials is submitted for review. The governing body will then decide whether there is sufficient evidence to approve a new treatment, or if more evidence is needed before it can make a decision. In the UK, only once approved by the governing body will the treatment be considered by the NHS for funding.

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 considered for approval for clinical use by the relevant governing body if there is convincing safety and effectiveness evidence from the clinical trials
HOW DOES RESEARCH GET TO AN APPROVED TREATMENT?

- **CELLS**
  - Understand what a cell type does by looking at its behaviour and features such as DNA

- **SYSTEMS**
  - Develop a treatment to target a system and its behaviour

- **TREATMENT**
  - Test the treatment in clinical trials with people to check for effectiveness and safety

- **PRECLINICAL TRIALS**
  - Test the treatment in the lab to work out an effective dose and check for safety

- **CLINICAL TRIALS**
  - Submit the treatment, with evidence, for approval with regulatory bodies

- **APPLICATION**
  - Treatment approved for clinical use

- **APPROVAL**
  - Understand how different cell types and organs work together as a system to carry out a process
How does a clinical trial work?

When researchers develop a new treatment, the last stage of testing will be clinical trials. In clinical trials, the new treatment is tested in human volunteers to check for safety and to see if it works. Clinical trials are essential, as a new treatment has to complete all clinical trials successfully before it can be approved for general use.

TRIAL PHASES

Clinical trials are run in a series of stages, known as phases. This is to check the safety and effectiveness of the new treatment. A new treatment must pass all phases to be considered for approval for general use. If a treatment fails at any phase of testing, it will not progress onto the next phase in its current form.

- In Phase 1 trials, the new treatment is usually given to a small number of healthy volunteers, although sometimes people with the condition may participate. This is to check that the treatment is safe to use in people.

- Phase 2 trials then test the new treatment in a slightly larger number of volunteers with the condition the treatment is for. This is to check whether the treatment is effective, and to fine-tune doses. A lot of treatments fail at this stage because the phase 2 trial shows that the new treatment is no more effective than the currently available treatment.

- Phase 3 trials test the new treatment in a large number 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.

BEFORE THE TRIAL

Before a trial can be given the green light, the plans have to be reviewed by the HRA (Health Research Authority) and sometimes the MHRA (Medicines and Healthcare products Regulatory Agency) who decide if the trial is ethical. They will want to be sure that the trial is as safe as possible, and that the researchers have thought about how they can reduce the risk of harm for the volunteers.

Once ethical approval is granted, the next step will be to recruit participants. This often takes a long time, as trials usually have strict criteria for taking part, which limits the numbers of possible participants.

During recruitment, the researchers running the trial will explain the benefits and risks of the trial to all potential participants. The participants will need to sign a consent form (or have a parent/legal guardian sign it for them if they are underage) to show they have understood the risks and are willing to participate in the trial. Clinical trial participants are free to leave the trial at any time, for any reason.
DURING THE CLINICAL TRIAL

Clinical trials may take a number of different forms, depending on the treatment being tested. Often, a new treatment is compared against the best treatment currently used. This way, all participants are receiving a treatment, and the new treatment can be compared to the most effective treatment already being used.

In some cases, the new treatment may be tested against 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. This is to avoid bias, which we talk about below.

If the condition is serious and there is no treatment currently available, it may be that the new treatment is given to all of the participants.

Where possible, researchers will try to run a ‘double-blind’ trial. This means that neither the researchers nor the participants know which treatment they are receiving, until the end. This is so that no-one can inadvertently bias the results - if a researcher or participant thinks the treatment will work, they might be more inclined to notice improvements in people receiving the treatment.

Depending on the treatment being tested, researchers may run a ‘single-blind’ trial, where either the researchers or the participants know which treatment they are getting, but the other group does not. In some cases, it is not possible to run blinded trials, for example when testing new medical technology, when the people taking part will know that they have been given an intervention, like an insulin pump. In these cases, researchers will run ‘unmasked’ or ‘open’ trials, where both the researchers and the participants know which treatment they are getting.

Once the clinical trial finishes, the participants don’t have to do anything else. The researchers will analyse the data they have collected and report their findings in a paper published in a journal (Section 4). 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. Publishing the results is therefore a crucial step in the process. We talk about reading published research papers later on.
Key points

• Clinical trials are essential to test a new treatment for safety and effectiveness

• There are different 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

• Researchers try to avoid bias in the results by running double-blind or single-blind trials where possible

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 new 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.

There are several places to find out about how to participate in a clinical trial:

NIH database of clinical trials around the world: clinicaltrials.gov

NHS gateway: www.ukctg.nihr.ac.uk

Type 1 Trial Finder: jdrf.org.uk/find-clinical-trials/
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
How to find a research paper

Many people with type 1 and their families want to find out more about the latest research into type 1. This type of research doesn’t always make it into the national or regional media, and if it does, media outlets vary in their success at communicating the truth behind new scientific findings accurately. One way to find out for yourself whether the ‘next big breakthrough’ is all that the news claims is to check out the source. The source will likely be a science research paper, published in a journal.

WHAT IS A SCIENTIFIC JOURNAL?

Scientific journals are like magazines, filled with write ups of scientific studies. Journals are a way for researchers to share the findings from their research, and keep up to date on the latest studies in their field. This information sharing allows the scientific community to build collective knowledge, and to avoid ‘duplication of effort’, which means repeating a study which has already been tried many times with repeated results. It is also important for scientists to publish their work for professional reasons: senior researchers are expected to have over a hundred published papers to their name as evidence of their success in their chosen field.

Journals can cover a broad range of scientific disciplines (e.g. Nature or Science, which cover topics across biology, chemistry and physics), or they can be very niche (e.g. Cellular and Molecular Gastroenterology and Hepatology). Journals used to be printed, like magazines, but today almost all scientific journals are either exclusively online, or have an online edition.

FINDING A PAPER

If you are looking for a paper in a particular area, in this case type 1 diabetes, there are some key places to search. Individual journals can be useful, but to find the widest range of papers, the best option is to use a search engine.

Google Scholar
Google Scholar is very intuitive, and easy to use if you are already familiar with Google search. Simply type in keywords related to your search and hit enter. Alongside the results screen will be a filter for date of publication. You can narrow down the articles further by running an advanced search, using filters such as journal name and author.

PubMed
PubMed is a search engine used by many people who work in research. PubMed is run by the U.S. National Institute of Health’s National Library of Medicine, and covers almost every journal on life sciences and biomedical research published across the globe. It allows users to search papers by keywords and filters. Users can set up regular alerts that deliver new articles in a particular area of research via email.

PubMed Central
This is an open access version of PubMed (see below for open access). This search engine only looks for articles that are open access, and therefore free to read, download and print. This is particularly useful to anyone not affiliated with a major scientific institution or university.
FILTERS

Searching for research can be overwhelming - for example, typing “type 1 diabetes” into PubMed can lead to over 78,000 results. Using filters on the search engines can help narrow your search into areas you are most interested in, such as only looking at research which has been in humans.

PAYWALLS

Unfortunately, many journals ask for a fee to read their articles. Major scientific institutions and universities often shoulder the cost of subscriptions to a large range of journals for their staff and students, but for those not working in academia it can be very expensive to access a paper – often £20-30 for a single article. There are, however, increasing numbers of ‘open access’ journals. Open access journals cost nothing to read and download. The cost of publication is instead covered by the authors’ institute or company.

Some important journals in the area of type 1 diabetes are listed below. Good quality research on type 1 diabetes can also be found in journals not listed here:

- ADA Diabetes Care
- Diabetes and Endocrinology
- ADA Diabetes
- Diabetologia
- Endocrine Reviews
- Cardiovascular Diabetology
- Diabetic Medicine
- Nature Reviews Endocrinology

Key points

• The results of scientific experiments and trials are written up and published in journals

• Journals are found online or in print

• You can search for scientific papers on a topic either by looking in a particular journal, or via certain search engines

• Filters can be used to narrow down your search

• Papers may be behind a paywall
GOOGLE SCHOLAR:
search bar

filters

search results
How does a clinical trial work?

There are thousands of scientific journals available online. Many of these are dedicated to diabetes research and related fields. With so much research available, how can we tell what is valuable, well conducted, sound science, and what is less reliable?

Just because an article looks well written, and is published in a scientific journal, we cannot be sure that it is scientifically sound. The internet has made it very easy and cheap to set up scientific journals that are not very selective about the papers they publish. These are some signs to look out for to tell if a journal is reliable.

**PEER REVIEW**

A reliable journal will clearly state that it is peer reviewed, and give details of that peer review process. Peer review is a long-established method for the scientific community to police the integrity of its published research. Peer review is a process whereby a scientific paper submitted to a journal for publication is read and reviewed by one or more independent scientists working in the same field. With their expertise, these peer reviewers can check if the research, as written in the paper, was well-considered; whether the scientific method they used made sense; and if the conclusions they come to are supported by the results.

**EDITORIAL BOARD**

The journal should have an editorial board made up of experts in the relevant field of research. The editorial board of a journal should have a range of researchers from a number of different institutions. A board made up of scientists from only one institution is a warning sign, as is a board made of up researchers only from one country (unless it is a country-specific journal, e.g. the Chinese Journal of Physics).

**PUBLISHER**

The publisher of the journal can sometimes be an indicator of quality. If the journal is published by a major publisher, it likely has good quality control. Googling the publisher name can usually bring up information on the publisher’s background. Some journals are published by societies, e.g. the Royal Society’s Royal Society Open Science. These are also normally reliable sources. New, or smaller publishers are not necessarily publishing bad research, but should be approached with more caution.
A journal can apply for an impact factor. This is a rating that can indicate the quality of the science the journal publishes. A journal must fulfil certain criteria to qualify for an impact factor, which takes into account the number of articles published in the journal and the number of citations of those articles (a citation is where an author will make a note of another paper he or she used to write their own article). A journal will usually state their impact factor on their website.

A high impact factor indicates that the journal’s contents have been used a lot by other scientists, which suggests they are of high quality. A low impact factor indicates that a journal is producing sound science, but the quality of the published papers is possibly not as high or the content not as interesting as in other journals.

However, a journal without an impact factor, or with a low impact factor, is not necessarily a bad journal. Other factors can prevent a journal getting an impact factor. For example, a journal must have been in publication for at least three years to get an impact factor, and if a journal publishes good but not very interesting research, it might not be very widely read and so not achieve a high impact factor.

For example, the world renowned journal of the British Medical Association, the BMJ, has an impact factor of 20.7, which is very high. The journal Diabetologia, which is also a very good but more niche journal focused on diabetes research, has a lower impact factor of 6.08.

Impact factors should be used a bit like sell-by dates – they are a good indication of quality, but a journal shouldn’t necessarily be thrown out if it doesn’t have one, just read with a little more caution.

**Key points**

**Checklist of indicators of reliability:**

- Peer reviewed
- Diverse editorial board
- Good quality publisher
- Impact factor
There are three main types of research paper:

1. Primary research paper – original research
2. Review paper – summary of key research findings in a particular area
3. Meta-analysis paper – research that involves analysing lots of primary research papers altogether to see if there are wider patterns across all of them

All of these types of research papers can produce useful new information, but as primary research papers are the most common type, we are going to focus this section on this type.

**PRIMARY RESEARCH PAPERS USUALLY COMPRISRE THE FOLLOWING:**

<table>
<thead>
<tr>
<th>Section</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title</td>
<td>Summarises the aim and results of the research</td>
</tr>
<tr>
<td>Abstract</td>
<td>A short summary of the article, which can allow the reader to assess the usefulness of the article before reading the whole paper</td>
</tr>
<tr>
<td>Introduction</td>
<td>Summarises existing knowledge on the topic, and the reasons why the authors decided to carry out their research</td>
</tr>
<tr>
<td>Methods</td>
<td>How the authors carried out their research</td>
</tr>
<tr>
<td>Results</td>
<td>The findings from the research, often displayed as graphs, diagrams and images</td>
</tr>
<tr>
<td>Discussion</td>
<td>The authors describe what they learned from the result, and place their findings within the context of existing research</td>
</tr>
<tr>
<td>Conclusion</td>
<td>A summary of the project and its limitations, and recommendations for the next steps needed</td>
</tr>
</tbody>
</table>

**TITLE**

The title is a summary of the research project aims. This can often be long and full of technical terms, but it will summarise the aim and results of the research.

**ABSTRACT**

After the title, the first block of text is the abstract. An abstract is a summary of the paper. Normally less than 500 words, it will state why the authors carried out the study, how they did it, and what they found. The abstract is a great place to start to find out if this paper is really about the topic about which you want to read. This is particularly important, as many articles are behind paywalls. Abstracts will always be visible, and if you are considering purchasing an article, reading the abstract will give you a bit more information about the article content before paying for access. Some journals now include lay summaries, which are versions of the abstract written for non-scientists.
INTRODUCTION

The introduction is the first section of the full paper. The introduction sets out the background behind the research and summarises existing knowledge. The introduction will set out the authors’ reasons for the carrying out this research.

METHODS

The methods section describes how the authors carried out the research. The methods section is necessary so that other scientists can see if the methods used by the researchers are suitable for what they were investigating, and lead to reliable results. Other scientists may try to replicate the findings to check them for accuracy, and so they will use the information in the methods section to carry out the work in the same way.

RESULTS

The results section is where the authors of the paper display their findings, and state whether they are significant or not (See Section 6: When is a result significant?). This section is for presenting findings only – the implications of the findings will be covered in the Discussion.

DISCUSSION

The discussion is the key part of the paper, as this is where the authors discuss the implications of their results, and set them in context of previous findings.

CONCLUSION

The conclusion is used to summarise the project, and highlight its limitations. The authors may also make recommendations for the next steps needed to take the results further.

A NOTE ON STRUCTURE

Note that the structure above is a typical layout for a paper, but some journals prefer different layouts. For example, some journals may put the Methods section at the end of the paper, and others may combine the Results and Discussion into one section. The Conclusion is sometimes incorporated into the end of the Discussion rather than existing as a separate section. The important thing, however, is that all of the aspects covered in each section are present in the paper.
OTHER PARTS OF A SCIENTIFIC PAPER

Papers may have a section called **Supplementary Information**. This section will include extra data and information relating to the project, but that wasn’t key data to include as part of the Results.

Papers should also have a declaration of any potential conflict of interests, and details of who funded the project. This is because the group funding the project might benefit from a certain result, so if that result is achieved, readers might be a bit more thorough with checking how sound the science is.

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**Key points**

- There are different kinds of research paper
- Primary research papers are the most common type of paper
- Papers are made up of different sections
- Each section serves a different purpose and informs the reader of a different aspect of the research
When is a result significant?

Interpreting statistics can be one of the hardest aspects of reading about scientific studies.

WHY DO WE NEED STATISTICS?

Researchers need to judge whether the result they have found is down to the treatment they are testing, or if it has happened by chance.

Imagine if researchers gave 100 people with a cold a drug called BetterFeel. After checking up with the participants once a fortnight over two months, 80 participants got better. The researchers might think that their drug has worked, but they can't be sure. What if many of those 80 people would have felt better anyway, and it was simply a coincidence that they took the drug?

Similarly, it may be that during the trial, 20 people had upset stomachs and 15 had a fever. Is it a coincidence, or are these side effects from the drug that we need to consider when evaluating safety?

HOW DO SCIENTISTS KNOW IF THEIR INTERVENTION HAS MADE A DIFFERENCE AND IS SAFE?

Before they get started, the researchers will use mathematics to work out the probability that the results will suggest that their treatment has worked, just by chance.

Using our imaginary BetterFeel trial, the researchers might calculate that, if their study goes exactly as planned (everyone takes the drugs when they should and everyone comes for their check-ups) then 12 in every 100 people will get better regardless of whether they receive BetterFeel or not. The researchers now know that if close to 12 or fewer people get better after taking BetterFeel, it may not be because of the drug.

The more likely a result is down to a treatment, and not chance, the more significant it is. When research papers talk about significance in this way, it has a similar, but different meaning to everyday language. If a result is significant, it means that it is likely to have happened because of the treatment, not by chance. But, it does not always mean that the results are very impressive, or could make a big difference beyond the study. If a result is not significant, it means that we cannot be sure whether it happened because of the treatment or by chance.

There are universally accepted thresholds for significance, and researchers have to show that their results meet or exceed this threshold level to be able to conclude that their results are significant.
As discussed earlier, in clinical trials we usually test a new treatment against the best existing treatment. We can use statistics to check how effective the new treatment is in comparison with the best existing treatment.

Say researchers wanted to test if BetterFeel was more effective than the best existing drug for a cold, ColdAway. They give 100 participants BetterFeel, and 100 ColdAway. After checking up on the participants fortnightly over two months, they find that 80 got better on BetterFeel, and 75 got better on ColdAway.

The small difference between 80 and 75 people might just be a coincidence, so how can we check whether BetterFeel is a more effective cold drug, or if there is no real difference between the drugs?

Using the results they have obtained, the researchers can use special statistical tests to check whether the difference between 80 and 75 people is likely to be significant, or if it is likely to be down to chance, based on universally accepted thresholds for significance.

Key points

• Statistics help scientists assess whether the result of their study is down to chance, or the treatment they are testing

• Researchers will work out beforehand how likely it is that their experiment will show the results they expect, just by chance

• By analysing their final results, researchers can check if their results are significant – more likely to have happened because of the experiment than by chance – based on a universally accepted threshold

• A significant result probably didn’t happen by chance, but it doesn’t mean the results are going to be important in broader terms
GLOSSARY OF TERMS

Abstract
A short summary of a research project’s aims, methods, results and conclusions, found at the beginning of a research paper.

Clinical trial
A test of the safety and/or effectiveness of a new treatment in humans.

Double-blind trial
When neither the researchers nor the participants know which treatment they are receiving in a clinical trial.

Impact factor
A number score allocated to journals based on the quality and wider importance of the work they publish.

Journal
An online or printed collection of scientific papers.

Peer review
When independent experts review someone else’s work to check it for accuracy and reliability.

Phase
Refers to the stage of testing of a clinical trial.

Preclinical trial
Research that is carried out in animals or in human tissue samples to check the safety and effectiveness of a new treatment.

Scientific paper
The formal, written up results of an experiment or clinical trial.

Significance
How likely a result has occurred due to the treatment being tested rather than chance.

Single-blind trial
When either the researchers or the participants know which treatment they are receiving in a clinical trial, but the other group does not.
Thank you to everyone who helped to develop and improve this toolkit. Every comment has helped to shape it into what we hope will be a useful and straightforward guide to understanding science.

A particular thanks goes to Dr Kerry McLaughlin (University of Oxford), Dr Helen Walkey (Imperial College London) and Dr Yuk-Fun Liu (King’s College London), who kindly reviewed this toolkit to make sure it is accurate.