INSPIRE: Research Made Easy

Clinical Trials: an overview

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What is a clinical trial?

A study where a potential treatment for a health problem is tested.

Usually on the sick.

May be human or animal, but the sick animal is naturally sick, e.g. veterinary trials.

Different from laboratory experiments.

The welfare of the research participant is our primary concern.

We shall be concerned today with human medicine.

How trials work:

- ❖ phases,
- ❖ research team,
- ❖ acronyms,
- ❖ funders,
- ❖ trial teams,
- ❖ getting permission,
- ❖ recruitment,
- ❖ analysis,
- ❖ reporting.

Phases:

Trial research is usually grouped into three phases.

Phase I: First steps

- First in human, healthy volunteers, e.g. MABGEL
- Dose finding
- Pharmacokinetics

Phases:

Trial research is usually grouped into three phases.

Phase 2: Efficacy

- Small comparative trials
- Proof of concept trials, e.g. aspirin for venous leg ulcers.
- Cross-over trials, e.g. automated monitoring of glucose for insulin-using people with diabetes who have impaired glycaemic awareness

Phases:

Trial research is usually grouped into three phases.

Phase 3: Effectiveness

- Large comparative trials
- Multicentre and multinational trials, e.g. ICSS, 50 academic centres in Europe, Australia, New Zealand, and Canada
- Economic analyses
- Cluster randomised trials, e.g. CADET

Research team:

Very difficult to do clinical trial research alone; need a team.

Multiple skills: clinical, may need more than one specialty, e.g. UKTAVI.

Multiple disciplines: clinical (medical, nursing, etc.), statistics, economics, psychology, sociology, etc.

Clinical trials units, e.g. York Trials Unit.

Patient representatives.

Acronyms

Every trial needs a name.

UKTAVI: **U**nited **K**ingdom **T**ranscatheter **A**ortic **V**alve **I**nsertion Trial.

MABGEL: A randomised double blind phase 1 study to assess the pharmacokinetics of C2F5, C2G12 & C4E10 when administered together in a gel vehicle as a vaginal microbicide. (**M**onoclonal **a**nti**b**odies in a **gel** vehicle.)

CADET: Multi-centre Randomised Controlled Trial of Collaborative Care for Depression (Collaborative **Ca**re for **De**pression **T**rial)

VenUS: **Ven**ous Leg **U**lcer **S**tudy (+ II, III, IV)

Funders:

Public: NIHR, MRC, Scottish Office, EU, etc.

Charity: British Heart Foundation, Cancer Research UK, Wellcome Foundation, etc.

Commercial: pharmaceutical industry, medical device manufacturers, etc.

Trial teams:

Trial Management Team runs the trial from day to day. This has the principal investigator, who was the lead applicant, trial coordinator, trial statistician, economist, some of the main collaborators, trials unit staff.

Trial Steering Committee represents the funders. Independent chairman, independent clinicians, statistician, and economist, patient representatives, plus the PI, some members of management team.

Data Monitoring and Ethics Committee represents the participants. Usually two independent clinicians and an independent statistician. Totally independent, reports to steering committee. The only people to see unblinded data during the trial.

Trial teams:

Other trial workers include research nurses, computing staff, etc. Employed on the grant or by NHS or by pharma.

Trial sponsors: NHS trust, pharma company, university. The people to sue.

Getting permission:

Research Ethics Committee: protects trial participants.

Research Governance Committee: protects the health service.

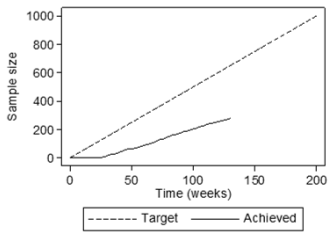
MHRA: Medicines and Healthcare Products Regulatory Agency, for pharmaceutical and similar trials.

Recruitment:

Trial participants. Should give informed consent. Problems: may be unconscious, may be incompetent, e.g. babies, dementia.

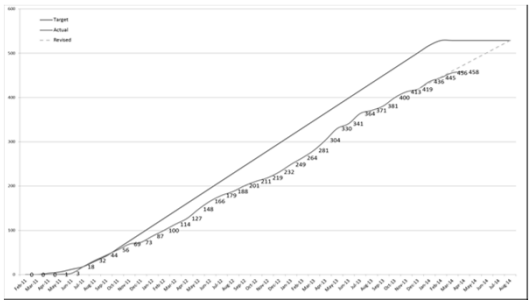
Often recruited by busy clinicians: doctors, nurses, etc.

Often lags behind our target.



Recruitment:

The HEELS trial (Evaluation of fibreglass heel casts in the management of ulcers of the heel in diabetes).



Recruitment:

Sometimes need to extend recruitment in time.

Sometimes need to apply for more money.

Sometimes have to abandon the trial.

E.g. trial of sublingual nitrates in myocardial infarction. Death rate much lower than anticipated. Only least ill were being recruited.

CANPOP (cannabis for peri-operative pain): could not recruit enough participants for the dose ranging study.

In research you are doing something nobody has ever done before. Things can go wrong.

Analysis:

Analysis plan agreed before recruitment finished.

Dangers of multiple testing.

Need for primary outcome variable and primary analysis.

Reporting:

And finally, a paper in the *Lancet*:

Clinical and cost-effectiveness of compression hosiery versus compression bandages in treatment of venous leg ulcers (Venous leg Ulcer Study IV, VenUS IV): a randomised controlled trial

Rebecca L Ashby, Rhian Gabe, Shehzad Ali, Una Adderley, J Martin Bland, Nicky A Cullum, Jo C Dumville, Cynthia P Iglesias, Arthur R Kang'ombe, Marta O Soares, Nikki C Stubbs, David J Torgerson

Summary

Background Drawbacks exist with the standard treatment (four-layer compression bandages) for venous leg ulcers. We have therefore compared the clinical effectiveness and cost-effectiveness of two-layer compression hosiery with the four-layer bandage for the treatment of such ulcers.

Methods We undertook this pragmatic, open, randomised controlled trial with two parallel groups in 34 centres in England and Northern Ireland. The centres were community nurse teams or services, family doctor practices, leg ulcer clinics, tissue viability clinics or services, and wound clinics. Participants were aged 18 years or older with a

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See Comment page 850

Department of Health Sciences
(R L Ashby PhD, R Gabe PhD

Reporting:

or a paper in the *BMJ*:

BMJ 2013;347:f4913 doi: 10.1136/bmj.f4913 (Published 19 August 2013)

RESEARCH

Clinical effectiveness of collaborative care for depression in UK primary care (CADET): cluster randomised controlled trial

OPEN ACCESS

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Reporting:

Now we need to publicise it to people who might put the research into practice.

Speaking at meetings. A job for the clinical members of the team.

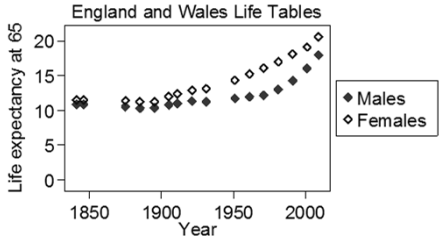
Very important.

It can take a long time for research to get into practice.

Is it worth the effort?

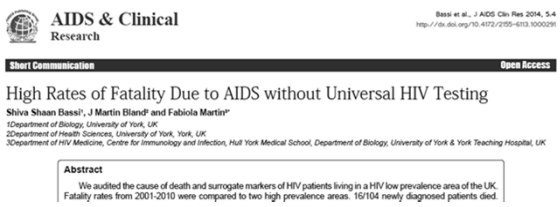
YES!!!

Since the first randomised clinical trial was published in 1948, life expectancy has improved dramatically.



Clinical trials are not the only useful research

Randomised clinical trials are very important, but other kinds of medical research are important, too!


AIDS & Clinical Research

Bassi et al., J AIDS Clin Res 2014, 5:4
http://dx.doi.org/10.4172/2155-6113.1000291

Short Communication Open Access

High Rates of Fatality Due to AIDS without Universal HIV Testing

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Abstract

We audited the cause of death and surrogate markers of HIV patients living in a HIV low prevalence area of the UK. Fatality rates from 2001-2010 were compared to two high prevalence areas. 16/104 newly diagnosed patients died.