Introduction To Clinical Research

Contents

Course Objectives and Contents

Objectives

Upon completion of this course, you will have an understanding of:

- the basic concepts of clinical research e.g. what it is, how it differs from standard care and why it is undertaken
- the purpose of ethics in research, what informed consent is and why it is necessary
- five of the most commonly used study designs
- how high ethical standards, data quality and uniformity are maintained in a study

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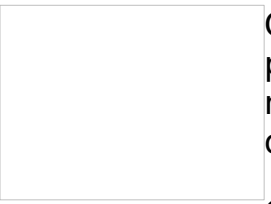
What Is Clinical Research?



Clinical research is scientific study that involves people. Individuals volunteer to participate in carefully conducted studies which ultimately uncover improved methods and knowledge on screening, diagnoses, treatment and prevention of disease and on the promotion of health and health care.

Clinical research can be interventional or observational. Observational studies are projects where there is no investigational product assigned to participants, e.g. research on how therapies work, health economic research and qualitative clinical research such as understanding patients' experiences, etc.

Interventional studies are controlled experiments, like clinical trials, where every participant is allocated to the treatment or control group at the start of the study. The WHO's International Clinical Trials Registry Platform states that *'interventions can include drugs, cells and other biological products, surgical procedures, radiologic procedures, devices, behavioural treatments, process-of-care changes, preventive care, etc*'.

Studies can be run in just one location and are referred to as 'single centre studies', or they can be run across many sites, and these are called 'multi-centre studies'. Whether a study is single or multi-centred will depend upon the type and scale of the research being undertaken.

How Does Clinical Research Differ From Standard Care?

The difference between clinical research and standard care is that clinical research:

- involves human volunteers, these may be patients or can all be healthy individuals who are not suffering from an illness or condition.

- is carried out with the ultimate aim of improving standard care. The research may be testing an intervention (e.g. a product or procedure) or collecting data through interviews or observations about a topic such as patient experience, disease management etc.
- measures effects over a period of time using robust and reliable methods to identify a lack of knowledge on issues such as costs, improved care, better drugs, treatments or therapies, additional support etc.
- may involve a comparison 'control' group, depending on the type of research.
- focuses on unknowns such as the effect of intervention, the likelihood of a community to change their practices, etc.
- must stick to a protocol without deviation (within the investigator's clinical judgement). By comparison standard care is all about clinical judgment, decisions and flexibility.

Why Do We Perform Clinical Research?

Clinical research is undertaken to collect data on usual and unusual events, conditions, and population groups to allow us to:

- observe treatment and health management practices so that we learn how they can be improved upon
- test interventions to develop new drugs and vaccines and to find new uses for existing therapies
- learn more about specific diseases so we can better understand how to manage, treat and prevent them

Ultimately the aim is to better understand how, with clinical research, we can improve health outcomes.

During the 20th century the huge improvements seen in global health were mainly a result of the knowledge gained through clinical research, examples include:

- 1920s: research found that improving childrens' nutrition helped combat rickets and other childhood diseases.
- 1950s: epidemiological research proved that cigarette smoking caused lung cancer.
- 1980s: trials proved that giving folic acid to high-risk women resulted in a reduction of babies born with spina bifida.
- 1990s: clinical trials showed that the progress of AIDS could be delayed by combining antiretroviral drugs.

Why Do We Perform Clinical Research?

Areas of highest disease burden, such as low-income countries, stand to gain the most from clinical research as there is the greatest potential for improving health in numerical terms, and there is enormous possible gain from relatively simple interventions. However, these populations are currently under-represented in research activities worldwide.

Current and future research efforts will hopefully bring more effective treatments and vaccines for diseases like malaria, HIV, tuberculosis, and neglected diseases such as dengue, visceral leishmaniasis, etc. These efforts should also allow us to improve both our understanding of the health care needs of different individuals, groups and populations, and the health care provisions required to meet these needs.

The most reliable way of improving health outcomes is through continuous, rigorous, credible and varied clinical research that involves different people and communities.

Introduction: Key Points To Remember

- Clinical research investigates questions about human disease, diagnosis, prevention, outcomes and treatments and about promoting health and health care.

- Clinical research can be observational (e.g. health economic research) or interventional (e.g. clinical trials).
- Improving standard care is one of the aims of clinical research.
- Clinical research has resulted in huge improvements in global health in the 20th century.
- Though currently under represented in world-wide research activities, areas of highest disease burden, such as low-income countries stand to gain the most from clinical research.

What Are The Main Principles Of Research Ethics?

The Belmont report lists three basic principles which are particularly relevant to the ethics of research that involves human participants.

These three principles are as follows:

- Justice: no group should carry more than their fair share of the burdens of research, those who participated should have access to the benefits of the results and no group should be unfairly excluded from research. In their paper, Minnies et al. (2008) emphasise that *'poverty, disease, lack of education, hardship, submissiveness, the effects of war, famine, pandemics, and social insecurity prevalent in developing countries all make participants more vulnerable to research exploitation'.*
- Beneficence: possible harms should be minimised and possible benefits should be maximised.
- Respect for autonomy: individuals' freedom to choose and act must be respected and vulnerable individuals must be protected.

The Council for International Organisations of Medical Sciences (CIOMS) 2002 'International Ethical Guidelines for Biomedical Research Involving Human Subjects' list an additional principle:

- Non-maleficence: participation in the study should result in no intentional injury or harm for the individual.

What Are The Main Principles Of Research Ethics?

Research governance is the broad range of regulations, principles and standards of good practice that are in place to ensure participants are protected and quality is assured across all aspects of clinical research. It is a mechanism for ensuring that all human research complies with the relevant ethical and legal standards.

However as the CIOMS guidelines state:

'The challenge to international research ethics is to apply universal ethical principles to biomedical research in a multicultural world with a multiplicity of health-care systems and considerable variation in standards of health care. Research involving human subjects must not violate any universally applicable ethical standards, but the guidelines acknowledge that, in superficial aspects, the application of the ethical principles, e.g. in relation to individual autonomy and informed consent, needs to take account of cultural values, while respecting absolutely the ethical standards.'

What Is Informed Consent And Why Is It Needed?

The main mechanism for ensuring an individual's rights are protected is 'Informed Consent'.

The process of informed consent involves explaining to the potential participant about all of the study-related activities that are beyond standard care and to ask for that person's consent to be included in the study.

Following famous cases such as the Nazi's experiments on concentration camp prisoners in WWII and the Tuskegee syphilis study (1932 –1972) on black American men, agreements for the conduct of clinical research were created. These agreements included the 1947 Nuremberg code, the 1964 Declaration of Helsinki and the 1979 Belmont Report, and led to the development of the International Conference on Harmonization Principles of Good Clinical Practice (ICH GCP) 1996 guidelines . Though the ICH-GCP guidelines are for trials, most of the principles can be applied to any type of study. These guidelines define informed consent as:

'the process by which a person freely confirms their willingness to participate in clinical research after having been informed of all parts of the study that are relevant to the individual's decision to participate'.

What Is Informed Consent And Why Is It Needed?

The challenges and issues around gaining fully informed consent are one of the most highly discussed and important elements, particularly from an ethics perspective, in the conduct of clinical research. In their paper, Mystakidou et al. (2009) emphasise that the process of obtaining consent should be an on-going process, and that it is not a single event (i.e. reading and signing a form) and is not just based on the information and the form. There should be a wider consideration of what information should be conveyed, when and by whom. This will lead to the development of a study-specific consent process, including a training plan and operating procedures, which can be just as important as the consent form itself.

When thinking through an appropriate consent process you might wish to consider factors such as the benefits or risks for the individuals or groups (e.g do benefits outweigh risks), the length and level of participation required, the vulnerability of the proposed study population (e.g. impoverished, low education level, children) and the perception of the community (e.g will approval of the research activity from community leaders be required before the individual members of the community consider being involved).

What Is Informed Consent And Why Is It Needed?

When taking consent from a participant, the investigator should:

1. fully inform the potential participant of all applicable parts of the study such as its purpose, duration, required procedures, and key contacts
2. be sensitive to the needs of individuals who are part of vulnerable groups e.g. children, someone from a poor background who won't normally have access to medical care, someone with very little or no schooling, someone who has limited mental capacity to understand, etc.
3. explain the benefits and risks involved in taking part
4. encourage questions and give reassurance that, if the person agrees to participate, they can always ask the research team for additional information throughout the study
5. ensure that the participant understands that if they change their mind about participation they can leave the study and are under no obligation to explain why they are leaving
6. be able to communicate using simple, non-technical wording in a language the person can understand (or have an independent person who can)
7. treat the potential recruit with upmost respect even if they decline to participate

What Is Informed Consent And Why Is It Needed?

Informed consent should be documented by means of a written, signed and dated informed consent form. In some cases the volunteer may be unable to sign for themselves, e.g. young children, the very old or even someone with an injury to their hand. In these cases someone who is independent from the study should sign as a witness that the individual agreed to participate. No study procedures are allowed to take place before the informed consent process is complete and the informed consent document is signed.

It is essential that the participant understands that the informed consent form is not a contract.

Different kinds of clinical research require different types of information sheets and consent forms, specific to each study, to be designed. Care should be taken in designing consent forms as a common error in consent forms is mixing research-only processes and standard care procedures. This can risk those who decline to participate being opted out of a procedure they should receive regardless of the research.

Examples of some consent forms can be found through the link provided in the 'References and Resources' section of this module.

What Is Informed Consent and Why Is It Needed?

However it should be noted that there are certain populations where signing a form is not considered appropriate e.g. communities and populations that are illiterate. Creed-Kanashiro et al. (2005) cite examples of nutritional studies run in the highlands of Peru where “the rural community were suspicious of signing a document they were unable to read because they had lost land by signing a document”. In these cases the ethics committee felt signed forms were unsuitable and consent was based first on approval of the project by the community leaders and then on the verbal consent of the individuals.

The 2002 CIOMS guidelines state that

“Informed consent should be obtained according to the legal requirements and cultural standards of the community in which the intervention is carried out.”

It is very common for communities in low-income countries to have high levels of illiteracy. In such situations the participant cannot read the information sheet themselves and a signature is not possible. In these cases an impartial witness is involved. This witness signs the consent form to confirm that they have observed the participant (or where appropriate the parent or guardian of the participant) has had the information sheet read out to them in full and that they have understood the information and have had all of their questions answered. The witness signs and the participant (or their parent/legal guardian) then provides their thumbprint, with the person taking consent writing their name and the date. Other methods used for non-paper based societies includetaking an audio or video recording of the consent process.

Why Do People Participate In Clinical Research And What Are The Benefits And Risks Involved?

The majority of clinical research studies offer no potential benefit for the participant. The person is simply involved in activities such as supplying samples, agreeing to undergo tests, providing information through questionnaires and interviews, or agreeing to be observed. Therefore most people participate in scientific research hoping that it will benefit future patients rather than for personal gain.

However, even when providing samples, information or undergoing tests there can be ‘risks’ involved. These risks can include things like: being asked highly sensitive questions, sharing genetic data, undergoing diagnostic tests, having to take time off from work to participate, etc. Sometimes inconvenient amounts of travel, or travel over long distances, may be required as

clinical research can be run in varied locations such as hospitals, doctors' offices, community clinics, universities and schools.

Why Do People Participate In Clinical Research And What Are The Benefits And Risks Involved?

In the case of interventional clinical trials some participants may volunteer in the hope that the drug/treatment/therapy being tested is better than their existing regime. However it is important to explicitly explain to potential recruits that new does not necessarily mean better and that they may actually receive a placebo (where one is being used) . Participation may even require that the individual stops using their current drug, treatment or therapy.

Other risks of participation can include: side effects which could vary from mild to life-threatening and may or may not resolve, additional tests, more trips to the study site than the person would normally make to their doctor, extra doses/sessions of the experimental drug/therapy/treatment, etc.

The members of the research team responsible for recruitment must be careful to emphasise that the purpose of the study is to find an answer to a specific scientific question and not to offer individualised or specialist medical care.

The processes for consenting individuals to the study and the procedures for continued communication and follow up e.g. letters, newsletters, etc., should be outlined in the protocol.

Research Ethics: Key Points To Remember

- Non-maleficence, beneficence, respect for autonomy and justice are the main principles of research ethics.
- The application of ethical principles should take account of cultural values, while respecting the ethical standards.
- The purpose of informed consent is to explain about all of the study related activities and to ask for that person’s consent to be included in the study. Informed consent is an on-going process throughout the study.
- The signed informed consent document (where one exists) is not a contract and is not in any way binding.
- The main reason people agree to participate in clinical research is for the potential benefit of future patients.
- There are risks involved in both observational and interventional research and these can include: being asked sensitive questions, sharing genetic data, long or inconvenient amounts of travel and potentially dangerous side-effects from experimental drugs.

Study Designs

There are different types of clinical research. The design used in any study is dependent on the question being investigated. This section will look at some of the most commonly used study designs:

- Cohort studies
- Case control studies
- Cross sectional surveys
- Case reports
- Clinical trials

Cohort Studies

This type of study design follows specific groups of people (e.g. those with a disease, with exposure to a treatment or who are alike but for one lifestyle factor

such as occupation or high alcohol consumption etc.) over a period of time to see how outcomes differ when they receive different treatments and interventions.

This study design allows you to collect specific data over a given time, and allows for interaction with participants. However cohort studies can be expensive and can take years to complete.

Examples of research carried out using this type of design can be seen in the papers:

- Observational cohort study of HIV-infected African children by Laufer et al (2006).
- Do we adequately respect the potential of routine primary health care services in reducing neonatal mortality in developing countries? The example of the Denizli cohort by Uner et al (2010).

Case Control Studies

In these studies cases are matched to measure the impact of an intervention or disease. People with a specific disease or experiencing a specific intervention (the cases) are compared with individuals who do not have the disease or have not experienced the intervention (the controls). Once matched data is collected from both groups, it is then compared to investigate whether other characteristics (e.g. nutrition) are different.

The aim is to try to uncover what caused the outcome in one group but not the other. To reduce the number of factors that could be related to the difference in cases and controls, all participants should be recruited from the same population.

This study design can be subject to recall bias (events can be reported differently between the two groups e.g. those with the disease may remember interventions or exposures more easily than those in the control group). However this design is relatively inexpensive, can be completed in a short period of time and can be carried out by individuals or small groups of researchers.

Examples of research carried out using this type of design can be seen in the following papers:

- Results from an international case-control study of childhood brain tumours: the role of prenatal vitamin supplementation by Preston-Martin et al (1998).
- Changing patterns in demography of cleft lip-cleft palate deformities in a developing country: the Smile Train effect - what lies ahead? by Patil et al (2011).

Cross Sectional Surveys

These surveys are used to gather information from a specified number of cases (e.g. individuals, systems, etc) in a population at a single point in time. The design is used to examine factors expected to remain unchanged during the period of data collection. These surveys are a basic variety of descriptive or observational epidemiology.

Mosby’s Dictionary states that:

"this study design aims to describe the relationship between diseases (or other health-related states) and other factors of interest as they exist in a specified population at a particular time, without regard for what may have preceded or precipitated the health status found at the time of the study."

This study design is relatively quick and easy but it does not allow for a distinction to be made between cause and effect.

Examples of research carried out using this type of design can be seen in the papers:

- Quality of pharmacies in Pakistan: a cross-sectional survey by Butt et al (2005).

- Prevalence of stroke and related burden among older people living in Latin America, India and China by Ferri et al (2011).

Case Reports

Case reports are the detailed histories of single cases. They provide the symptoms, signs, diagnosis, treatment, and follow-up of an individual patient. Vandenbroucke (2010) listed six topics that most case reports focus on and these are:

- unexpected associations between diseases or symptoms
- unexpected events in the course of observing or treating a patient
- findings that shed new light on the possible pathogenesis of a disease or an adverse effect
- unique or rare features of a disease
- unique therapeutic approaches
- a positional or quantitative variation of the anatomical structures

The advantage of this type of design is that case reports allow us to uncover unexpected effects, new diseases, etc., which can lead to increased knowledge. However, as case reports are essentially ‘anecdotal’ they are the lowest level of scientific evidence, because they have not been gained through rigorous scientific study.

Examples of research carried out using this type of design can be seen in the papers:

- Occupational asthma in Korea by Oh & Kim (2010).

- Obstructive jaundice at the initial presentation in small-cell lung cancer by Ochi et al (2010).

Clinical Trials

Randomised controlled trials (RCTs) allow data on the safety and efficacy of health interventions (e.g., drugs, diagnostics, devices, therapy protocols) to be collected. Trials can be conducted using healthy volunteers or patients, depending on what the trial is investigating and its stage of development. Trials are usually one of four phases (Phase I to Phase IV):

- Phase I tests an experimental drug or treatment in a small group of healthy people for the first time to evaluate its safety, determine a safe dosage range, and identify side effects. This phase usually involves less than 100 participants.
- Phase II tests the drug or treatment in a small group of people with the condition or disease to see if it is effective and to further evaluate its safety. This phase usually involves no more than a few hundred participants.
- Phase III is carried out on large groups of people to confirm effectiveness, monitor side effects, make comparisons with commonly used treatments, and collect information that will allow the experimental drug or treatment to be used safely. This phase usually involves several hundred to several thousand participants.
- Phase IV is considered the surveillance stage and collects additional information including the drug's risks, benefits, and optimal use. This phase will involve the general population.

Clinical Trials

If well designed, RCTs are thought by some to be the ‘gold standard’ of clinical research as they eliminate bias and spurious causality (a false connection between two factors because of a third factor, e.g. it could be said that children with larger feet are better at maths - however, the older the child, the larger their feet and also the more practised at maths they are; or you could

conclude that the more fire trucks it takes to put out a fire, the more damage there is - until you consider that there are more trucks needed when there are larger fires and so the size of the fire is the cause of the greater damage, not the number of fire trucks). However RCTs can be very expensive, can take a long time to recruit adequate numbers of participants and may take a long time to complete particularly if there is participant follow-up.

Examples of research carried out using this type of design can be seen in the papers:

- Effect of a participatory intervention with women's groups on birth outcomes and maternal depression in Jharkhand Orissa, India: a cluster-randomised controlled trial by Tripathy et al (2010).

- Complementary foods fortified with micronutrients prevent iron deficiency and anemia in Vietnamese infants by Phu et al (2010).

Study Designs: Key Points To Remember

- There are different types of clinical research designs and the question being investigated will determine the study design used e.g. a clinical trial is used to test a new drug, an observational study is used to collect epidemiological data, etc.
- The various forms of clinical research allow different types of data to be extracted and analysed so that different types of questions can be answered.
- Cohort studies follow specific groups of people over a period of time to see how outcomes differ when they receive different treatments and interventions.
- Case control studies compare people with a specific outcome to individuals without that outcome to investigate the exposures that may have caused the outcome.
- Cross sectional surveys aim to describe the relationship between a health-related state and other factors of interest in a specified population at a given time, regardless of what may have preceded or precipitated the health status found at the time of the study.
- Case reports are detailed histories of single cases and allow us to uncover unexpected effects, new diseases, etc., which can lead to increased knowledge.
- Clinical trials allow for collection of data on the safety and efficacy of health interventions. They are thought by some to be the 'gold standard' of clinical research.

Maintaining High Ethical Standards, Data Quality And Uniformity In A Study

How are high ethical standards, data quality and uniformity in the study ensured?

To ensure high ethical standards, data quality and uniformity, studies use both a protocol and 'Standard Operating Procedures' (SOPs, or a Manual of Operations).

The protocol provides the background and justification for the study and covers issues such as the design, methodology, statistical considerations and organisation, study timetable, type of recruits, governance, etc. It must capture every step to ensure that the study's result is, firstly, the answer to the research question, and secondly, that the answer is reliable.

The ICH GCP 1996 guidelines define SOPs as: *"detailed written instructions created to achieve uniformity of performance of a specific function within a study."*

SOPs ensure that a task will be performed the same way each time it is undertaken. They translate the protocol into practice and allow the protocol to operate accurately and to reliably answer the research question. SOPs are very beneficial for all types of studies.

SOPs are useful as they:

- Identify the person responsible for each task e.g. the investigator recruits the participants.
- Describe the study procedures and how they are to be completed e.g. the steps to be followed if collecting samples.
- Help train staff into their role: following the SOPs means that everyone in a given role is trained in the same way every time.
- Help monitor site performance: this allows any deviation from the protocol to be identified and corrected.

Maintaining High Ethical Standards, Data Quality And Uniformity In A Study

All research study staff should be trained in and have access to a copy of the SOPs. It is essential that each staff member follows the study's SOPs to ensure the protocol is being followed and therefore the participants' safety and welfare are protected and that the study data is credible and robust. SOPs should be reviewed regularly (at least annually) to ensure any listed regulations are up to date and that, if applicable, outlined procedures are updated e.g. if a change is made to the data collection system due to a more efficient system being identified through the course of the study.

SOPs are needed when a variation in how a task is carried out could lead to inconsistent, inaccurate or misleading data. For example, sample transportation in a multi-centred genetic study in Africa. Here all the samples need to be stored and transported carefully to avoid analytical problems with the samples. In each site logistics will differ and so each site needs to write their SOPs to ensure the integrity of their samples.

Quality assurance procedures and procedures for assuring quality of data handling and processing should all be guided by SOPs. ICH GCP (1996) defines quality assurance as *'all those planned and systematic actions that are established to ensure that the study is performed and the data are generated, documented (recorded), and reported in compliance with GCP and the applicable regulatory requirement(s)'.* SOPS for these procedures should include plans for data checking (how much will be checked, by whom, and how); audit trails (detailed log showing which data have been changed, why it was changed, who changed it and when); and source verification procedures (how much data will be checked against the source documents e.g. medical records).

Key Points To Remember

- Uniformity of study and of quality assurance procedures are ensured by the implementation and use of standard operating procedures (SOPs).
- SOPs identify who is responsible for which task, provide the steps to be followed for study procedures, help all staff to carry out a particular task in the same way, and help to monitor site performance.
- All research study staff should be trained in and have access to a copy of the SOPs.
- SOPs also see to it that the quality of the data handling and processing is maintained.

References And Resources

References

1. Butt Z A, Gilani AH, Nanan D, Sheikh AL, White F. Quality of pharmacies in Pakistan: a cross-sectional survey: Int J Qual Health Care 2005; 17(4): 307-313.
2. Creed-Kanashiro H, Ore B, Scurrah M, Gil A, Penny M. Conducting Research in Developing Countries: Experiences of the Informed Consent Process from Community Studies in Peru: J Nutr 2005; 135: 925–928.
3. Ferri CP, Schoenborn C, Kalra L, Acosta D, Guerra M, Huang Y, Jacob KS, Llibre Rodriguez JJ, Salas A, Sosa AL, Williams JD, Liu Z, Moriyama T, Valhuerdi A, Prince MJ. Prevalence of stroke and related burden among

older people living in Latin America, India and China: J Neurol Neurosurg Psychiatry 2011; Epub ahead of print.
4. Hackshaw A. A Concise Guide to Clinical Trials 2009; Wiley-Blackwell, Chicester.
5. Laufer MK, van Oosterhout JJ, Perez MA, Kanyanganlika J, Taylor TE, Plowe CV, Graham SM. Observational cohort study of HIV-infected African children: Pediatr Infect Dis J 2006; 25(7): 623-7.
6. Minnies D, Hawkridge T, Hanekom W, Ehrlich R, London L, Hussey G. Evaluation of the quality of informed consent in a vaccine field trial in a developing country setting: BMC Med Ethic. 2008; 30(9): 15.
7. Mosby's Medical Dictionary 8th ed. 2008. Mosby Publications.
8. Mystakidou K, Panagiotou I, Katsaragakis S, Tsilika E, Parpa E. Ethical and practical challenges in implementing informed consent in HIV/AIDS clinical trials in developing or resource-limited countries: SAHARA J 2009; 6(2): 46-57.
9. Ochi N, Takigawa N, Yasugi M, Ishida E, Kawamoto H, Taniguchi A, Harada D, Hayashi E, Toda H, Yanai H, Tanimoto M, Kiura K. Obstructive jaundice at the initial presentation in small-cell lung cancer: International Medical Case Reports Journal 2010; 2010(3): 9-12.
10. Oh SS, Kim KS. Occupational asthma in Korea: J Korean Med Sci 2010; 25(Sup): S20-5.
11. Patil SB, Kale SM, Khare N, Math M, Jaiswal S, Jain A. Changing patterns in demography of cleft lip-cleft palate deformities in a developing country: the Smile Train effect-what lies ahead?: Plast Reconstr Surg 2011; 127(1): 327-32.
12. Phu PV, Hoan NV, Salvignol B, Treche S, Wieringa FT, Khan NC, Tuong PD, Berger J. Complementary foods fortified with micronutrients prevent iron deficiency and anemia in Vietnamese infants: J Nutr. 2010; 140(12): 2241-7.
13. Preston-Martin S, Pogoda JM, Mueller B A, Lubin F, Modan B, Holly EA, Filippini G, Cordier S, Peris-Bonet R, Choi W, Little J, Arslan A. Results from an international case-control study of childhood brain tumors: the role of prenatal vitamin supplementation: Environ Health Perspect 1998; 106(Sup3): 887–892.
14. Tripathy P, Nair N, Barnett S, Mahapatra R, Borghi J, Rath S, Rath S, Gope R, Mahto D, Sinha R, Lakshminarayana R, Patel V, Pagel C, Prost A, Costello A. Effect of a participatory intervention with women's groups on birth outcomes and maternal depression in Jharkhand and Orissa, India: a cluster-randomised controlled trial: Lancet 2010; 375: 1182–92.
15. Uner S, Cakir B, Yildirak K. Do we adequately respect the potential of routine primary health care services in reducing neonatal mortality in developing countries? The example of the Denizli cohort: Cah Sociol Demogr Med 2010; 50(4): 477-99.
16. Vandenbroucke JP. In Defense of Case Reports and Case Series: Ann Intern Med 2001; 134(4): 330-334.

Websites:

1. The WHO's International Clinical Trials Registry Platform
2. The Tuskegee Study
3. Nazi experiments on WWII concentration camp prisoners

Resources

1. Examples of consent form templates
2. The Nuremberg Code
3. The Belmont Report
4. The Declaration of Helsinki 2013
5. ICH Good Clinical Practice Guidelines
6. WHO Handbook for Good Clinical Practice
7. The CIOMS Guidelines
8. Global Health Trials' Glossary of Terms

Quiz

Summary

1. The purposes of clinical research is to improve knowledge in, and methods of, which of the following:
    - Screening
    - Diagnoses
    - Treatment
    - Prevention
    - Health and health care promotion
    - All of the above
2. Qualitative research designed to understand patient's experiences is classed as which of the following:
    - Observational research
    - Interventional research
3. Which of the following statements is true: Clinical research....
    - Pays people to join studies.
    - Is not just about finding new and better drugs, it is also about improving healthcare systems and services.
    - Participation means that you will receive specialised medical care.
4. Huge global health improvements have been seen in the 20th century. Though low income countries have historically been under-represented they stand to gain the most from clinical research because....
    - It is cheaper to run studies in developing countries
    - Relatively simple interventions could result in enormous gains
    - People are more willing to participate because of lack of health care systems
5. When undertaking clinical research which ethical principles do the CIOMS guidelines recommend following:
    - Respect for autonomy
    - Beneficence
    - Non-maleficence
    - Justice
    - All of the above
6. Just one system should be used to apply ethical principles in all countries regardless of cultural values.
    - True
    - False
7. Which of the following end statements is true: Informed consent is when you....
    - Convince a person to sign a consent form so that they are obliged to participate in the study.
    - Offer someone money or other benefits to encourage them to agree to take part in the study.
    - Explain to an individual about all of the study related activities and ask for their consent to be included in the study.
8. Special considerations should be in place when consenting individuals who fall into which one of the following groups:
    - People who are hoping for individualised medical care
    - People who are hoping to get a better treatment for their condition
    - People from very poor communities who do not have access to medical care outside of research
    - People who want to participate so that others may benefit in the future
9. Which of the following statements is true:
    - Once a participant has signed the consent form they are obliged to participate in the research.
    - Most people participate in clinical research hoping that it will benefit future patients rather than for personal gain.
    - Participating in a clinical trial testing a new drug means that you will get better treatment for your condition.

- People categorised as vulnerable e.g. the very poor, children, the illiterate, etc. should not be recruited to research studies.

10. The study design is dependent on which of the following:
    - The number of individuals you want to recruit
    - The research question being investigated
    - The country you are conducting the study in
    - The size of the research team
11. The Cohort study design is used to:
    - Study histories of single cases
    - Test the safety and efficacy of health interventions
    - Follow groups over a period of time to see how outcomes differ with different treatments and interventions
12. Of the following types of study design which one is considered to be expense and time consuming:
    - Clinical trials
    - Case reports
    - Cross sectional surveys
    - Case control studies
13. Which of the following study designs is useful for identifying unexpected events and associations:
    - Case control studies
    - Cross sectional surveys
    - Case reports
    - Clinical trials
14. Standard operating procedures (SOPs) ensure that a task is carried out in the same way each and every time.
    - True
    - False
15. SOPs replace the need for a protocol.
    - True
    - False
16. SOPs identify who is responsible for which task.
    - True
    - False
17. SOPs allow for autonomy so that investigators can try out different methods of taking consent and collecting data.
    - True
    - False
18. The SOPs should be written before the study starts and should never be changed.
    - True
    - False

Submit