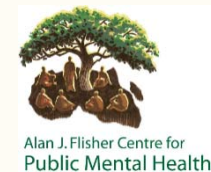


Research Ethics and Good Clinical Practice

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Institute of Psychiatry, King's College London



AFFIRM
Africa Focus
on Intervention Research
for Mental Health



History of Research Ethics

Nuremberg Code

- End of WWII- Nazi Doctors who had performed human experiments were tried for war crimes
- Drafted as set of standards for judging physicians and scientists who conducted experiments on concentration camp prisoners
- Prototype for later codes



UN & Helsinki Declarations

UN Declaration (1948)

- Declaration of Human Rights created in response to the Nazi atrocities of WWII

Declaration of Helsinki (1964)

- Ethical principles of Nuremberg Code were elaborated and clarified by World Medical Association
- Ethical foundation for ICH GCP
- 1996 updated declaration



Declaration of Helsinki (1996)

1. Research should be based on **sound scientific principles** and thorough knowledge of literature
2. Design should be considered by **independent reviewers**
3. Research should be conducted by **scientifically/clinically qualified people**
4. Importance of the objective should be **proportionate to inherent risk** to participant
5. **Concern for the subject** must prevail over interests of science and society
6. The right of the individual to their **integrity**
7. **Hazards should be predictable** and should not outweigh benefits
8. Published results should be **accurate** and in accordance with declaration
9. Potential participants must be **well-informed**
10. Awareness about dependent relationships and **potential for coercion**
11. Consent from legal guardian for **minors/mental incapacity**
12. Protocol must contain **statement of ethical considerations** and should indicate compliance with principles



ICH GCP

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (**ICH!**)

- Unified standard for EU, US and Japan
- International ethical and scientific quality standard for designing, conducting, recording and reporting trials that involve human subjects



How are standards applied in practice?

1. GCP requirements
2. Sponsor and investigator activities
3. Safety reporting
4. Study records
5. Informed consent



IRB/Independent Ethics Committee

- Safeguards the rights, safety and wellbeing of all trial participants
- Special attention if trials may include vulnerable participants
- Considers protocol and amendments
- Suitability of investigators
- Issues around recruitment/consent



Sponsor Responsibilities

- **Sponsor= individual/organisation** that takes **responsibility for ensuring proper arrangements** to initiate, manage, monitor and finance a trial
- Approvals & authorisations
- Substantial amendments
- Progress and end of trial reports
- Archive
- GCP satisfied and adhered to- monitoring & audit



Investigator Responsibilities

- **Investigator= responsible for the conduct of the trial at the site**
- Local approval in place
- Communication with Ethics Committee
- Qualifications
- Medical care of participants
- Protocol compliance
- Adequate resources
- Randomisation and unblinding



Serious Adverse Event/Reaction (SAE/SAR)

Any untoward medical occurrence that:

- Results in death
- Is life-threatening
- Causes hospitalisation/prolongation of hospitalisation
- Causes persistent/significant disability/incapacity
- Congenital anomaly/birth defect
- **Results in any other important medical event**



Safety Reporting

- Adverse event= any untoward medical occurrence
- Adverse reaction= reasonable causal relationship
- Unexpected Adverse Reaction= nature/severity not consistent with formal reference documents

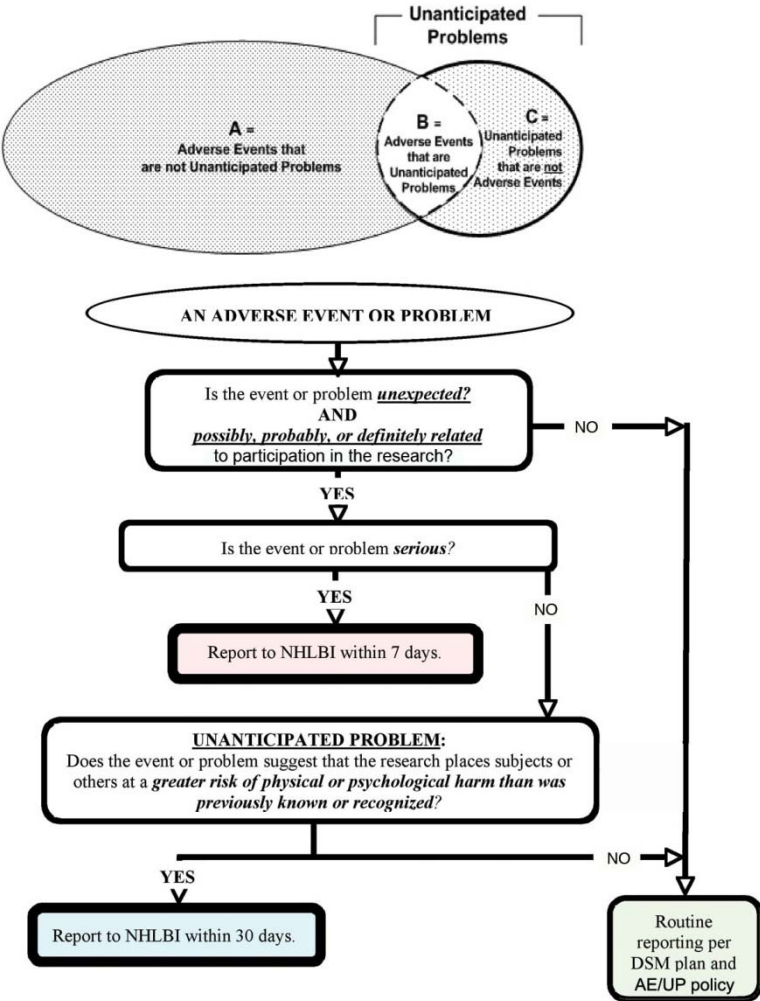


Safety Reporting- what to do

- Investigator: immediately report SAEs to sponsor
- Sponsor: Data Monitoring Committee should carry out trend analysis
- Serious unexpected adverse events should be reported to Ethics Committee



Dealing with adverse events



Study Records

- **Case Report Form**= printed/electronic document designed to record all the protocol required info to be reported to the sponsor on each trial participant
- Accurate
- Complete
- Legible
- Timely



Source Documents

- **Source data**= info in original records, observations/other activities necessary for the reconstruction and evaluation of the trial
- Should be available and suitable for audit



Essential Documents

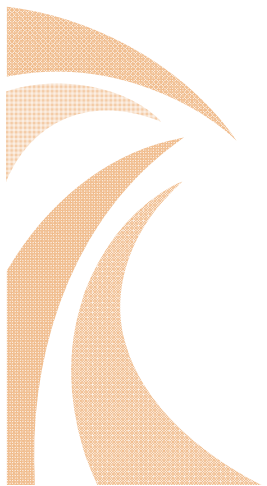
- **Essential documents**= enable both the conduct and the quality of the data to be evaluated
- I.e. training records, meeting minutes



Study Closure and Archiving

- Declaration of end point
- Premature termination/suspension → Ethics Committee
- Final study report by investigator/sponsor
- **Dissemination to participants**

- **Archive= sponsor's policies re. what to archive, where and for how long?**



Voluntary Informed Consent

“ A process by which a trial subject **voluntarily** confirms his or her **willingness** to participate in the trial after having been **informed** of all aspects relevant to the subject’s decision to participate”



Consent Documentation

- Participant Info Leaflet
- Consent form- multiple copies
- Local contact details
- New/updated consent form?



GCP Considerations

- “Ample time” to consider information and participation
- Encourage potential participants to discuss with family/friends etc.
- Consent should be signed/marked and dated
- Witness required? If participant unable to read
- **Acceptability of payment for participation?**



Does the participant have the capacity to consent?

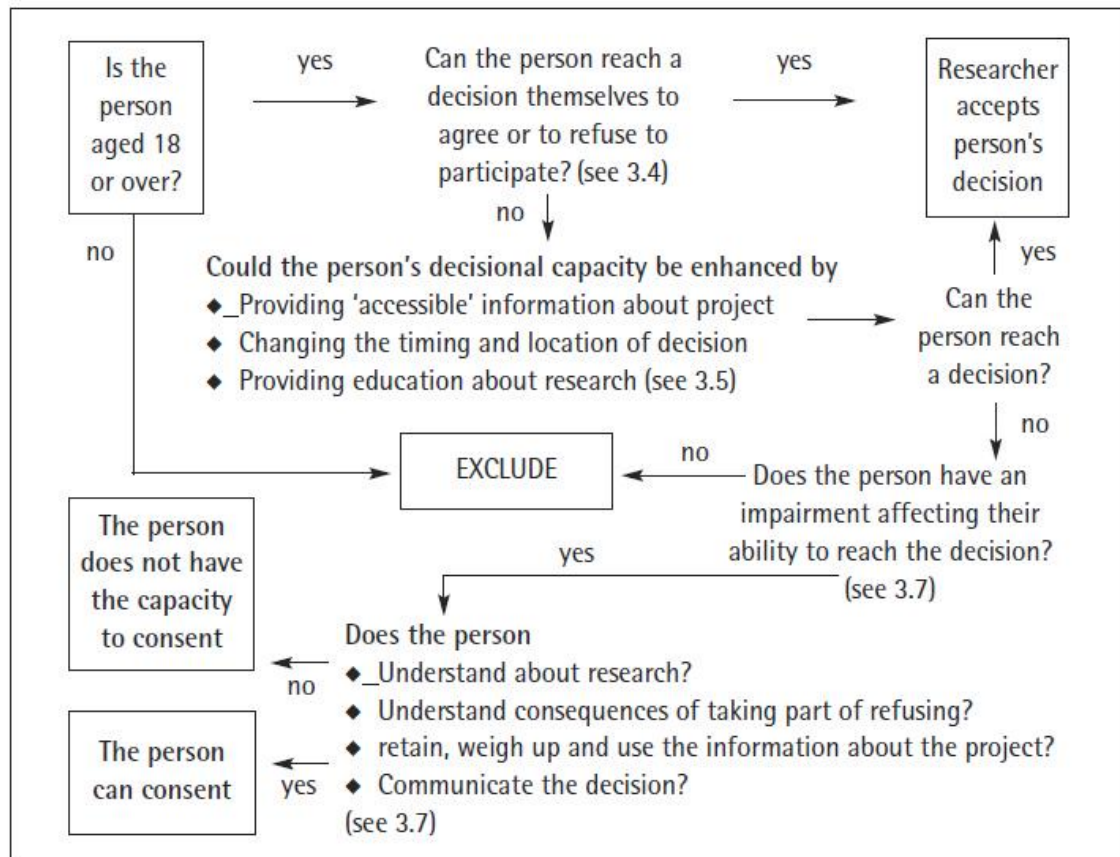
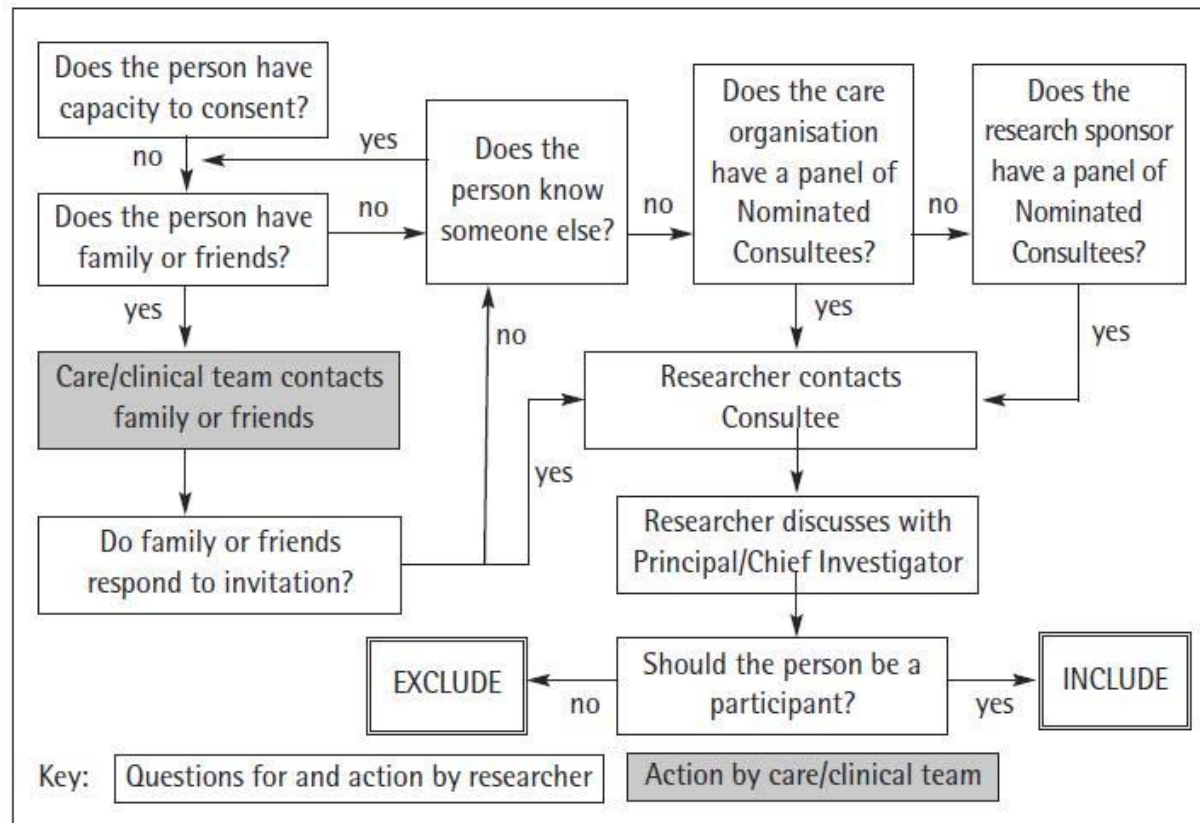


Figure 3: Decision-tree for researchers in assessing capacity to consent to participate in research.



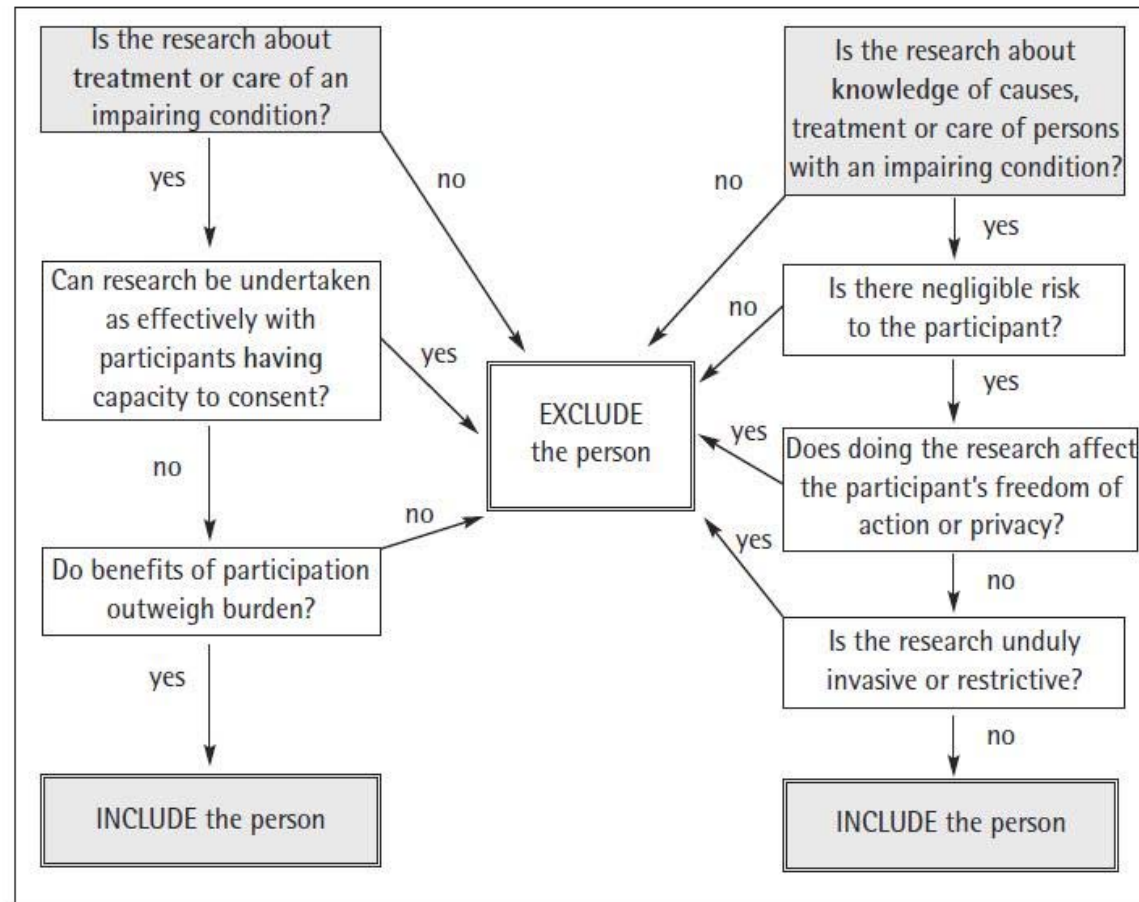
Seeking Advice from a Consultee

Figure 4: Seeking advice from a consultee.



Capacity: decisions about participation

Figure 5: Appraising an individual's involvement in a project.



Consent: Case Study

Susan, aged 25, married with two children, has been experiencing some mental health problems since the age of 16. She has been experiencing low mood, anxiety and low levels of paranoia but has been able to cope with her problems to date. She has been treated by her GP who has prescribed anxiolytics and anti-depressants and at times she has also been receiving input from the Community Mental Health Team (CMHT) in the area. Susan's marriage recently broke down and her ex-husband has been making threats to take the children away from her because of her mental health condition. Her mother died when she was still very young, her father is an alcoholic, and she has no brothers and sisters. Her friends have rejected her due to her mental health problems and Susan has no one to talk to and feels isolated.

As a result of these experiences her mental health problems have now become unmanageable and Susan has experienced a mental breakdown. She is now on a female ward and her ability to reason and make judgements is significantly impaired. After a detailed assessment of her symptoms by the psychiatrist Susan is diagnosed with a first episode of psychosis. Susan fulfils the necessary criteria to participate in your first episode study. The study involves participation in lengthy questionnaires that could take up to three hours to complete some of which need to be videotaped.

Would Susan participate in the research study?

