Assessment of Risks and Benefits in Ethics Review

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Definitions

- Risk
  - The term risk refers both to the **probability** of a **harm** resulting from an activity and to its **magnitude**.
  - `Risk' often stands for the **combined** probabilities and magnitude of several potential harms.

Identification of Risks

- Types of Risks
  - Physical risks
    - Bodily harm
    - simple inconvenience
    - Clinical risks related to clinical interventions
  - Psychological risks
    - Emotional suffering
    - Breach of confidentiality
  - Social risks
    - Employment or social discrimination
  - Economic risks
    - Financial costs related to participation

Definitions

- Benefit
  - A benefit refers to any sort of favorable outcome of the research to **society** or to the **individual**.
  - In practice, 'benefit' often stands for the combined probabilities and magnitudes of several possible **favorable outcomes**.

Assessment of Anticipated Benefits

- Direct benefits
  - Improvement of disease
  - Comfort from suffering
- Indirect Benefits
  - Generalizable knowledge
  - New drug/effective interventions in the future
  - Change in practice standards decreasing morbidity and mortality

Levels of Risks

- Low/ Minimal Risk
  - A risk is minimal where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Examples of low/ minimal physical risk in research

Physical Risks

- Physiological experiments involving exercise, collecting urine, measurements of weight/height, collection of nail clippings or small samples of hair, developmental assessment, routine physical examination, observation of behavior or changes of diet, etc.
- A questionnaire designed to measure the behavioral results of physical interventions performed for therapeutic reasons (*e.g.*, effects on memory of brain surgery performed for the relief of epilepsy).

Increase in levels of low/ minimal risk interventions

Other sources of risks

- The research **topic** may cause stigma or involve privacy issues
- The research involves vulnerable **subjects**
- The **intervention** may involve additional risks to the participants.
- Intervention in research refers to **any procedure** done in the course of research
- It may be behavioral, diagnostic, therapeutic, etc.

Levels of Risks

Medium to high risks /More than minimal risk intervention: Examples

- Procedures such as behavioral interventions likely to cause psychological stress.
- Diagnostic tests involving clinical procedures
- Clinical trials involving new drugs and medical devices
- Research about new techniques, e.g. surgery, etc.

Proper Review Channels/ Types of Review

Risk	Negligible	Low	Medium - High
Effect	Incon-venience	Discomfort	Harm
Type of IRB Review	Exempt	Expedited	Full board

EC Function

- Minimize risks
- Maximize benefits

Risk – Benefit Assessment

- Degree of uncertainity
  - lack of precision inherent in risk/benefit analysis
- Risk Evaluation
  - Probability or relative magnitude of harm.
  - Process of combining the results of risk identification and estimation with the *perceptions of those involved*.
  - It is the perception of a risk formed by patient that is of overriding importance compared with investigator's perception

Risk Assessment in Protocol Review

- Investigator qualifications/ facilities
- COI management
- Site characteristics
- Source of funding
- Sound protocol design
- Adequate sample size
- Distribution and method of randomization
- Placebo
- Inclusion exclusion criteria
- Clinical and other risks
- Privacy & confidentiality
- Vulnerability
- Withdrawal criteria
- Consent form procedures

Determine that risks are reasonable in relation to anticipated benefits

- Interventions or procedures that hold out the prospect of **direct** diagnostic, whether therapeutic or preventive
- Justified to be advantageous to the individual subject, in the light of foreseeable risks and benefits, as any available alternative.
- Risks of such 'beneficial' interventions or procedures must be justified in relation to expected benefits to the individual subject.

Determine that risks are reasonable in relation to anticipated benefits

- Risks of interventions that **do not** hold out the prospect of direct diagnostic or preventive benefit must be **justified** in relation to the expected benefits to society (generalizable knowledge).
- The risks presented by such interventions must be **reasonable** in relation to the importance of the **knowledge** to be gained.

Minimize risks

Risks related to research design

- Use **sound research design** procedures that do not expose subjects to unnecessary risk
- Use procedures already being performed on the subjects for diagnostic or treatment purposes
- **Justify placebo** and ensure that all study groups are not deprived of standard treatment
- Include **subjects** who will be able to provide answers to the research questions.
- Exclude **subjects** who may confound the research results

Minimize risks

Risks related to research design

- Check risks related to research procedures
  - Washout period
  - Diagnostic procedures
  - Use of placebo
- Address risks
  - Frequency of monitoring
  - Require SAE reporting
  - Evaluate risks when changes are introduced

Minimize risks

Investigator related risks

- Ensure PI is qualified to do the study (education, training, experience)
- Declare and manage COI of the PI and the research team
- Require GCP training for clinical trials
- Monitor compliance by the PI to GCP, regulations and approved version of the protocol

Minimize risks

Risks related to IRB review

- Submit the protocol to a **GCP compliant IRB**
- **Site** selected should be able to address potential risks
- IRB should use competent and **knowledgeable reviewers** with related clinical practice
- IRB should make **recommendations** how risks can be minimized and benefits maximized
- IRB should **monitor** the conduct of the study in accordance with documents that it has approved

Minimize risks

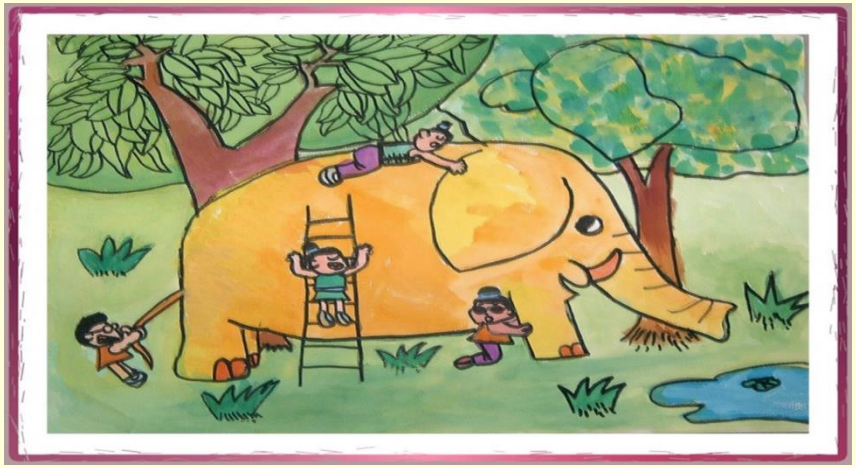
Monitor risks during continuing review

- Assess risk/ benefit ratio when reviewing
  - Amendments
  - SAE reports
  - Protocol deviation/ violation reports
  - Progress reports
  - Early termination
- EC may recommend modification of documents, reconsent, etc.

Maximize benefits

- Require referral to care of patients who are excluded during screening
- Share study results
- Provide emergency care
- Treat patients
- Post trial access to medical care and successful interventions

Minimizing Risks



- Addressing ethical issues to protect humans in research
- Requires ongoing commitment of research stakeholders
- REC plays a strategic role in resource poor settings