Component analysis: a systematic approach to benefit-harm analysis

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Component analysis

• A systematic and comprehensive approach to the ethical analysis of research benefits and harms

• A refinement of the risk framework developed by the National Commission in its report on IRBs and the Belmont Report

• As these documents served as the basis for the Common Rule, component analysis serves as a basis for the interpretation of the Common Rule
Two steps

1. If the protocol relies upon the presence of standard therapy, separate standard therapy from research interventions
   - The purview of the IRB is limited to research interventions

2. For research interventions, separate therapeutic procedures from nontherapeutic procedures
   - Distinct ethical analysis for each type of research procedure
   - Often only the second step is referred to.
Step 1

- Separate standard therapy from research interventions
- Ordinary therapeutic practice is managed within the physician-patient relationship
- Ruled by professional norms
- Treatment is the product of joint deliberation and agreement between patient and physician
- What counts as standard therapy may be diverse
- Defined as: treatment accepted by at least a respectable minority of expert practitioners.
Step 2

- For research interventions, separate therapeutic procedures from nontherapeutic procedures.

- **Therapeutic procedures** are administered on the basis of evidence sufficient to justify the belief that they may benefit research subjects.
  - Clinical equipoise

- **Nontherapeutic procedures** are administered solely for the purpose of answering the scientific question.
  - Risks must be minimized consistent with sound scientific design and
  - Stand in reasonable relation to knowledge to be gained.
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Protocol

Therapeutic procedures

Distinguish therapeutic and nontherapeutic procedures

Nontherapeutic procedures

Risks minimized consistent with sound scientific design

Vulnerable population?

Risks reasonable in relation to knowledge to be gained

No more than minor increase over minimal risk

Yes

Consistent with competent care

No

Clinical equipoise exists

Risks reasonable in relation to potential benefits to subjects

Yes

Both therapeutic and nontherapeutic procedures pass

Acceptable

No

Unacceptable

No
Study A

Physician prescribed treatment A

Physician prescribed treatment B

Study B

Treatment A

Treatment B

Patients

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Study A

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Physician prescribed treatment A

Step 1
- Separate standard therapy from research interventions
- Physician prescribed treatments are standard therapy

Step 2
- Separate TP from NTP
- There are no TP
- IRBs task is to ensure NTPs fulfill requirements
Step 1

- Separate standard therapy from research interventions

Two views. The first:
- Treatments A and B fall within the standard of care and thus are standard therapies
- Treatments A and B are demarcated in Step 1
- As they are not research interventions, they do not fall within the purview of the IRB.
Step 1

- Two views. The second:
  - Treatment A and B do not fall under the norms of the physician-patient relationship
  - They are assigned randomly
  - Neither a physician recommendation, nor a product of patient values
  - Not the product of joint deliberation and agreement between patient and physician
  - Should be considered a research intervention.

Study B

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Step 2

- Separate therapeutic and nontherapeutic procedures

- **Therapeutic procedures**: treatments A and B

- Straightforwardly satisfy clinical equipoise.

- **Nontherapeutic procedures**: randomization and outcome assessment

- IRB must ensure that risks are minimal and reasonable in relation to knowledge to be gained.

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Informed consent

- Component analysis has some useful implications for moral informed consent
- In all cases, research subjects must be clearly informed of the study purpose
- Emphasis on the implications of participating in the study and declining study participation. What difference will study participation make to me?
- TPs and NTPs should be described separately to avoid therapeutic misconception
- Even if standard of care RCTs pose minimal risk, a waiver of consent is generally not appropriate.

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