Randomization Alters Risk

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Does Randomization Alter Risk?

• Yes, unquestionably
• Does randomization increase risk?
  • Sometimes
  • It depends

• Two helpful discussions:
  • Feudtner et al., NEJM 2013; 369:892-894
  • Kim & Miller, NEJM 2014; 370:769-772
What Risks May Participants Face?

• Risks of harm and discomfort arising from receipt of an intervention that they would not have been assigned off-study at this institution

• Risk of inconvenience and failure of preference satisfaction arising from receipt of an intervention that they would not have been assigned off-study at this institution

• Risk of protocol rigidity

• Risk of therapeutic misconception
  • failure to appreciate the certainty of having a different experience, with different goals, from receiving the same intervention off-study

• Dignitary considerations matter too: not all risks are of harm
Elaboration #1

- Risks of harm and discomfort arising from receipt of an intervention that they would not have been assigned off-study at this institution
  - (1) “We do A here, not B”
  - (2) “Some of us do A here, and some of us do B”
  - (3) “Nationwide, some do A and some do B” is NOT sufficient to inform patient-participants

- Risk of inconvenience and failure of preference satisfaction arising from receipt of an intervention that they would not have been assigned off-study at this institution
  - This is a design-dependent problem: e.g., comparison of surgical vs. non-surgical treatment for low back pain, or interventions vs. watchful waiting in prostate CA
  - Arises from differences in availability & discussion of alternatives
Elaboration #2

• Risk of protocol rigidity
  • Design-dependent problem
  • Matter of degree

• Risk of therapeutic misconception
  • Risk of “pure” TM: not appreciating differences in experience arising from incorporating research goals, even when receiving standard interventions
    • e.g., “a computer will choose your treatment”
    • e.g., need for LTFU
  • This risk is greatly increased when consent form and process are truncated (or informed consent is waived)

• Key question: What respect are research participants owed?
What Other Risks May Arise?

• **The real risk in “SOC” research is to clinical practice**
  - Potential patient-participants in “SOC” research should be told what treatments are in common use (whether validated or not) for their condition AT THIS INSTITUTION
  - This should result in clearer, more comprehensive discussion of treatments offered by this provider and at this institution, whether on-study or off-study
  - This prospect affects clinicians because it is more demanding than usually practiced for informed consent to treatment
    - It is easy to misunderstand and misconstrue the real requirements of informed consent to treatment
    - It is tempting to avoid self-scrutiny in clinical practice

• **Good informed consent in “SOC” research could improve informed consent off-study in much-needed ways that are quite complementary to the anticipated role of “SOC” research in clinical practice improvement**