An Ethical Framework for Clinical Research

Presented by Ben Wilfond, MD

3:25pm-4:25pm

UW Husky Union Building

Room 145

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An Ethical Framework for Clinical Research: Rethinking and Going Beyond Informed Consent

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Learning Objectives

By the end of the session, you will be able to:

- Describe the eight ethics benchmarks for ethical clinical research
- Discuss how empirical data illustrates challenges with informed consent
- Identify the role of researcher-participant interactions in the ethical conduct of research

Overview

- A framework for ethical clinical research (20 min)
- Case study: *A randomized study of financial incentives for hepatitis B vaccination in an immigrant community*
  - Small group discussion (15 min)
  - Large group discussion (15 min)
- Q&A (10 min)

What is the Value of Research Ethics?

- To prevent **exploitation** of human subjects
- To prevent unjustified or unnecessary **harm**
- To provide **guidance** to researchers who are unsure about their ethical obligations
- To ensure public **trust** in research and support for future research

“Born in Scandal”

- Guidelines for ethical research are largely responsive to research ethics scandals
  - Nuremberg Trials → Nuremberg Code (1947)
  - Tuskegee syphilis study and other research ethics scandals → Belmont Report (1979)

- “The voluntary consent of the human subject is absolutely essential.” – Nuremberg Code, 1st principle

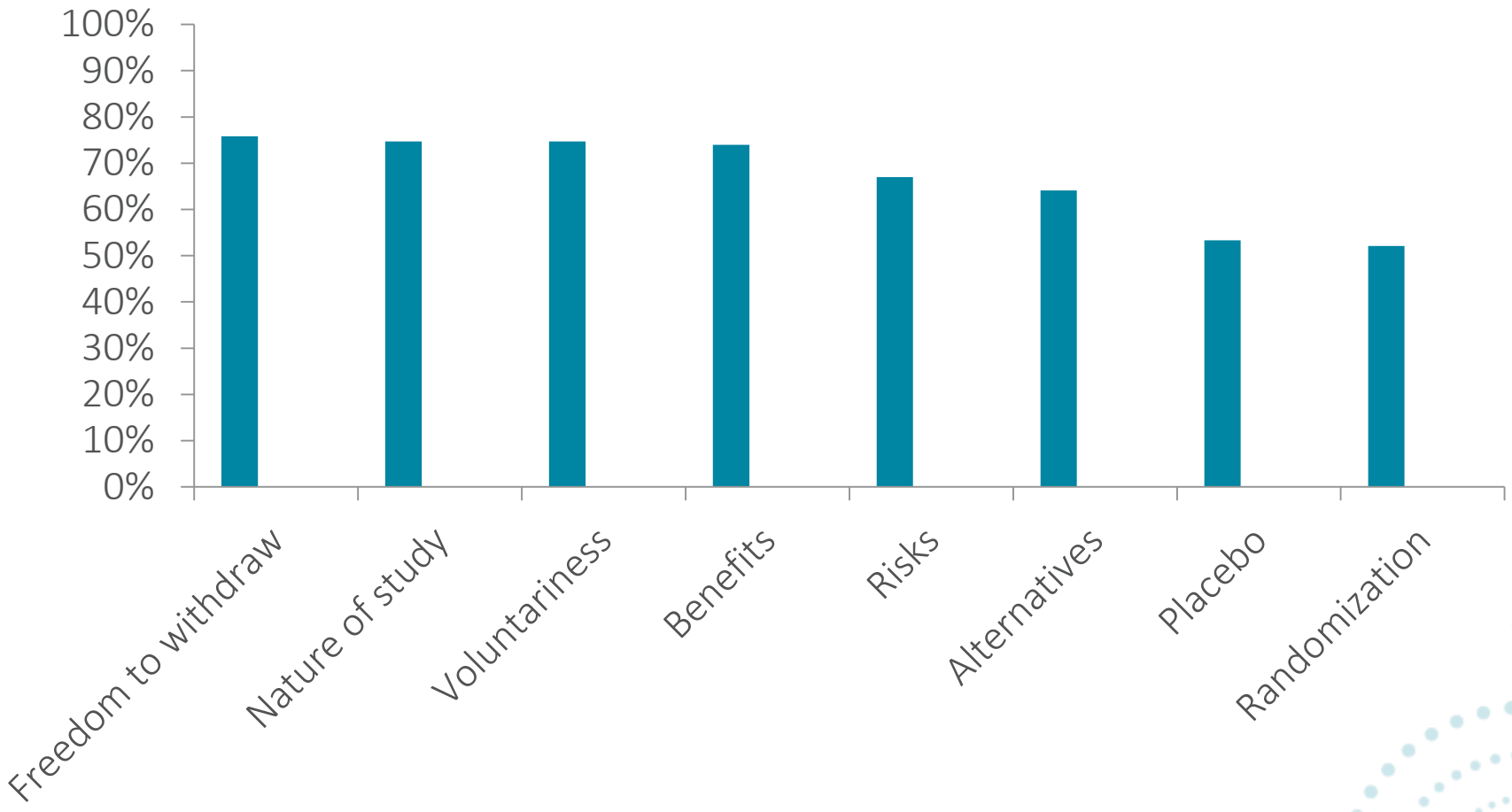
Elements of Informed Consent

- Capacity
- Disclosure
- Understanding
- Voluntariness
- Authorization

Elements of Informed Consent – Empirical Data

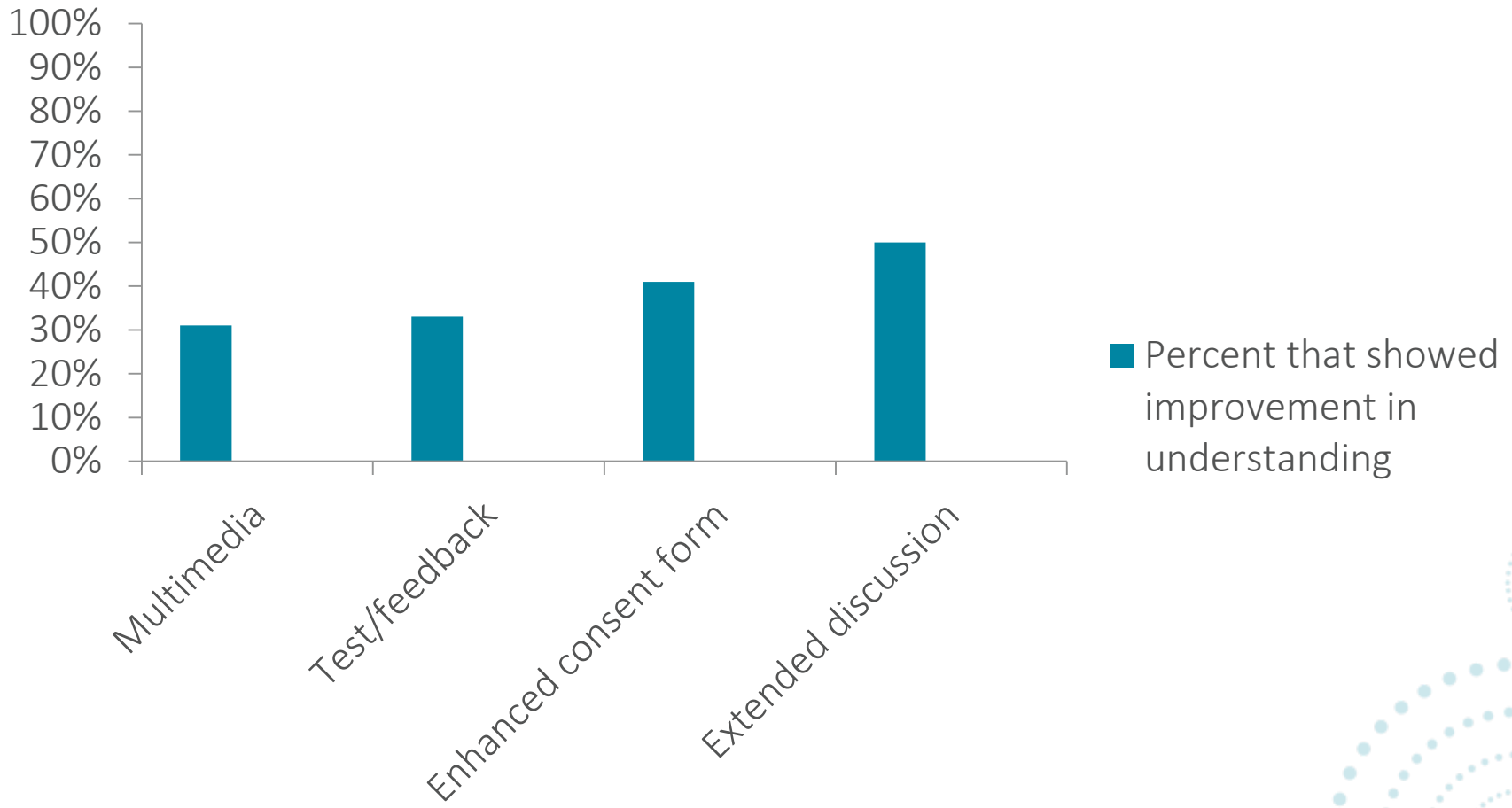
- Capacity
- Disclosure
- Understanding
- Voluntariness
- Authorization

Systematic Review of Participant Understanding of Consent Elements



Nguyen TT et al. Participants' understanding of informed consent in clinical trials over three decades: systematic review and meta-analysis. *Bull WHO* 2015.

Meta-analysis of Interventions to Improve Understanding



Nishimura et al. Improving understanding in the research informed consent process: a systematic review of 54 interventions tested in randomized control trials. *BMC Med Ethics* 2013.

The Enduring Challenges of Informed Consent

- Understanding is limited and hard to improve
- Empirical social science research is important but challenging
  - Better metrics for understanding, voluntariness, satisfaction, and other outcomes are needed
- Easy to study a form; harder to study the whole recruitment, enrollment, and study process
  - When do people actually make decisions about research?
  - What else informs their decisions?

→ Conceptual research to develop a systematic, comprehensive ethics framework can contextualize the role of informed consent

Eight Benchmarks to Balance

1. Collaborative partnership
2. Social value
3. Scientific validity
4. Fair subject selection
5. Favorable risk/benefit ratio
6. Independent review
7. Informed consent
8. Respect for participants and communities

Emanuel et al. What makes clinical research ethical? *JAMA* 2000;283:2701-11; *JID* 2004;189:930-37.

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1. Collaborative Partnership

Collaborative Partnership

- Clinical researchers should partner with the community in which or with which the research occurs
  - Community engagement in planning, conducting, and overseeing research (e.g., community advisory boards)
  - Sharing benefits with the community
- Many reasons for community consultation:
  - Transparency
  - Buy-in
  - Assessing risks and ensuring benefits are actually beneficial
- Challenges:
  - Different reasons may warrant different forms of engagement
  - Different definitions of community

Wendler & Shah. Involving communities in deciding what benefits they receive in multinational research. *J Med Phil* 2015.

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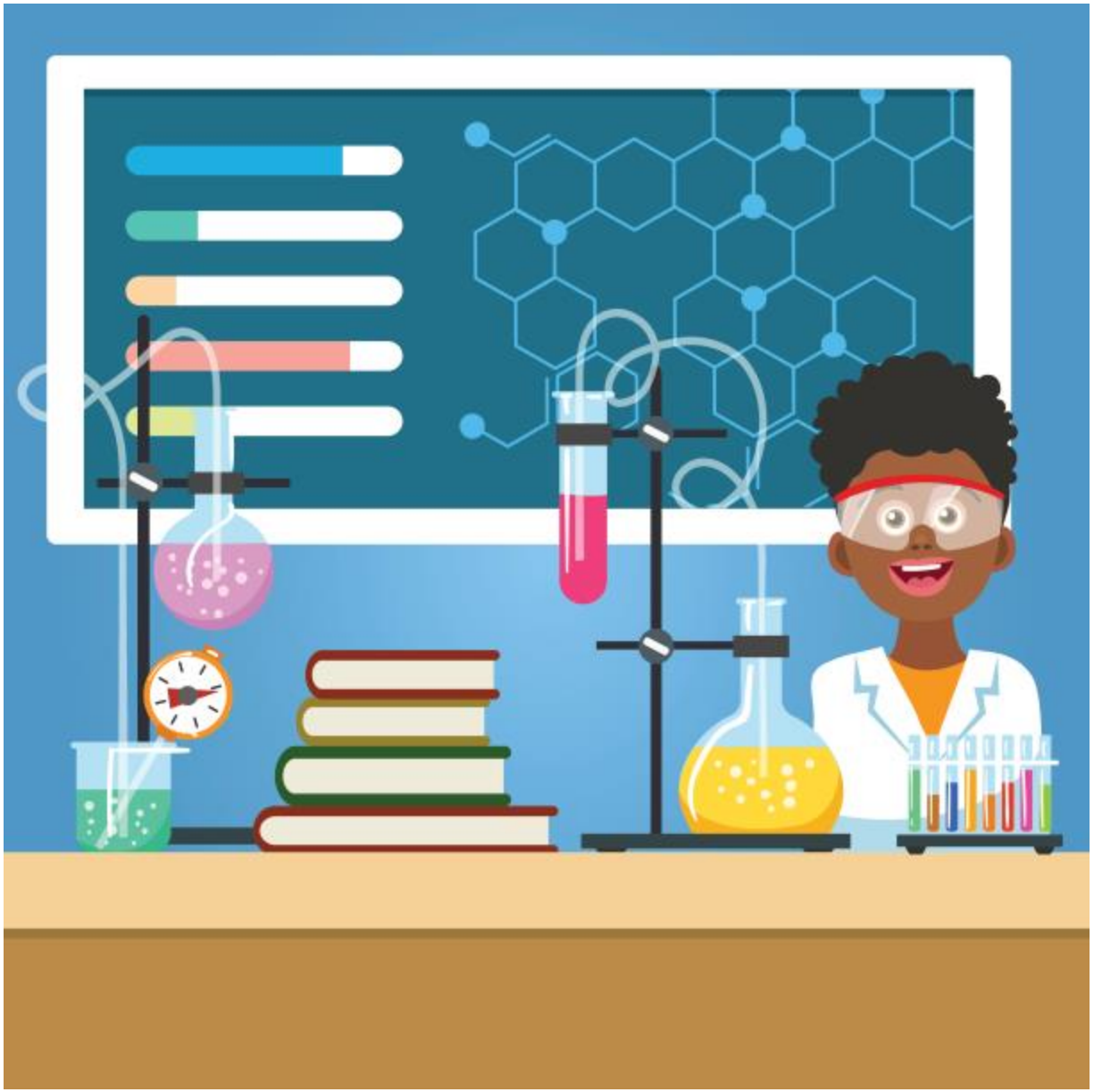
2. Social Value

Social Value

- Clinical research should lead to improvements in health or generalizable medical knowledge for:
  - Participants
  - Communities
  - Future patients

- Research with limited social value:
  - Unimportant questions
  - Limited advancement in knowledge
  - Non-generalizable studies
  - Non-disseminated research



3. Scientific Validity

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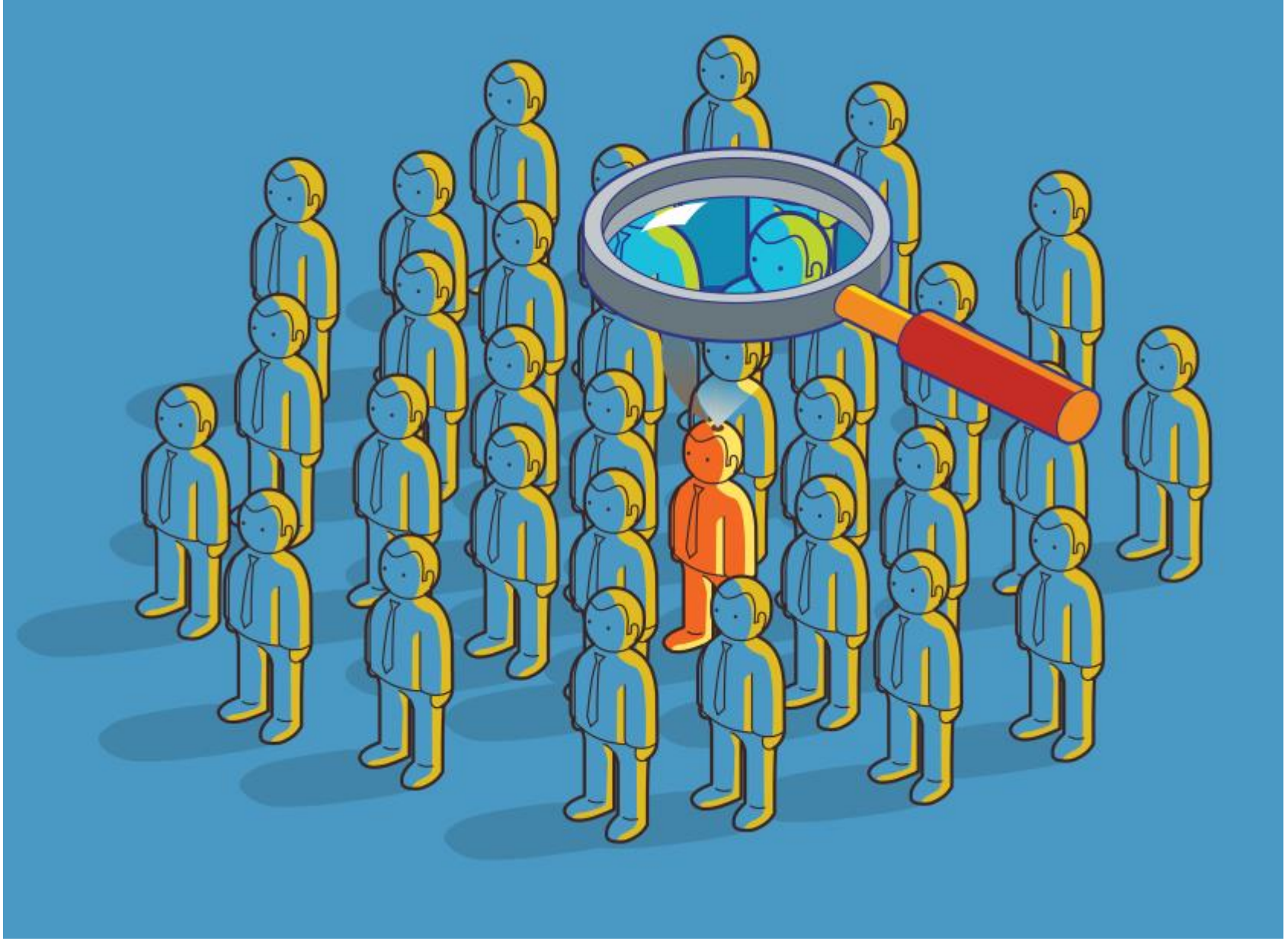
Scientific Validity

- Must be a reasonable possibility that research will produce valid scientific results
- If a study is not valid, there is no basis to justify:
  - Resources used to generate knowledge and promote health
  - Risks and burdens undertaken by participants
- Invalid research includes:
  - Underpowered studies
  - Studies with biased endpoints, instruments, or statistical tests
  - Studies that cannot enroll sufficient subjects

Wertheimer A. Non-completion and informed consent. *J Med Ethics* 2014.



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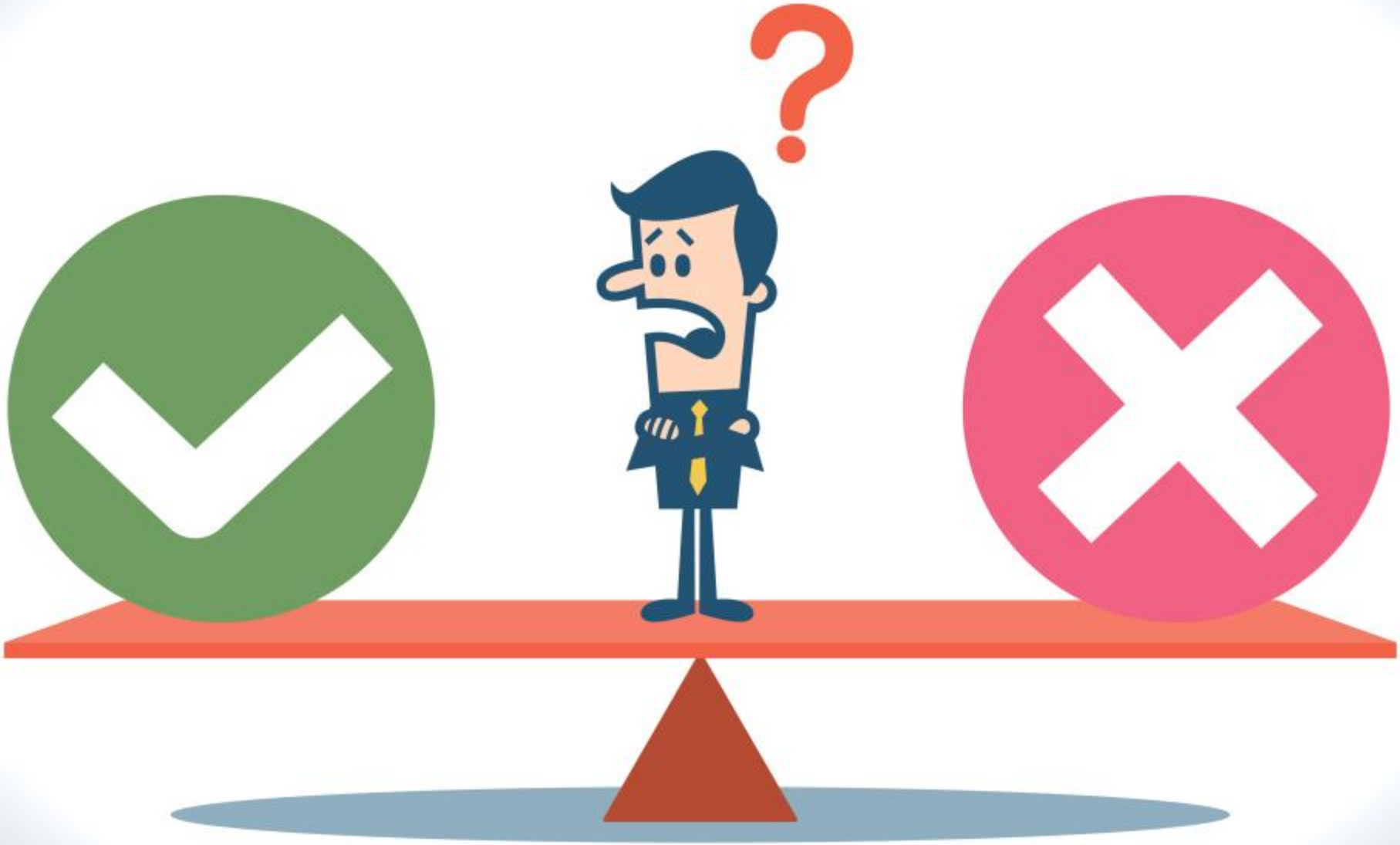
4. Fair Subject Selection

Fair Subject Selection

- Scientific objectives of the study, not vulnerability or privilege, should guide inclusion criteria and targeted populations
  - Vulnerability = decreased ability to protect one's own interests
- May be good reason to exclude certain groups (e.g., higher risk or unable to consent)
- Consider distribution of burdens and benefits of research
  - Research as burden: participants need protection
  - Research as benefit: participants need access



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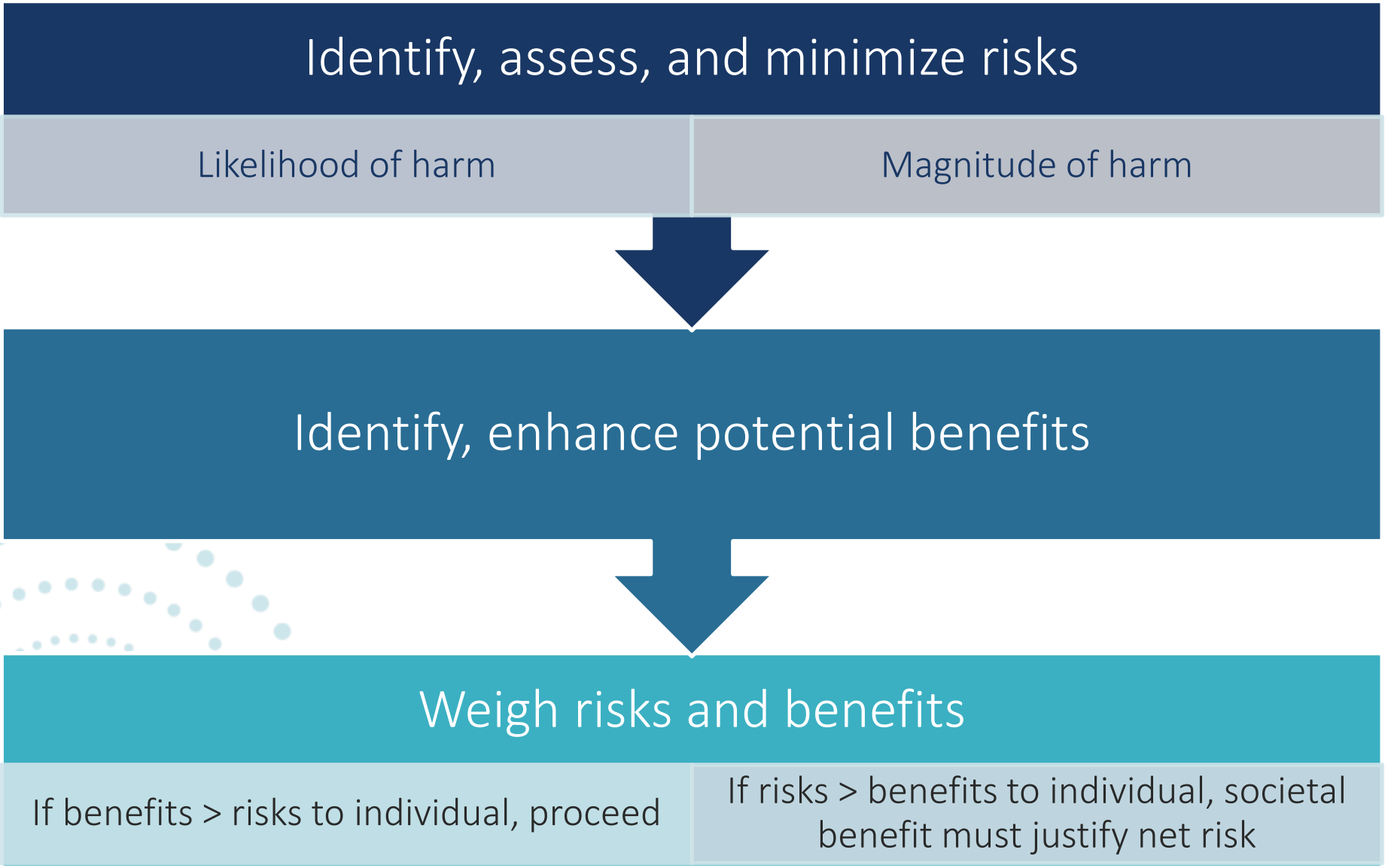
5. Favorable Risk/Benefit Ratio

Favorable Risk/Benefit Ratio



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6. Independent Review

Independent Review

- Investigators have multiple legitimate interests
- Can lead to conflicts of interest
- Independent review:
  - Minimizes the impact of conflicts of interest
  - Assures society that research is ethically appropriate and demonstrates trustworthiness

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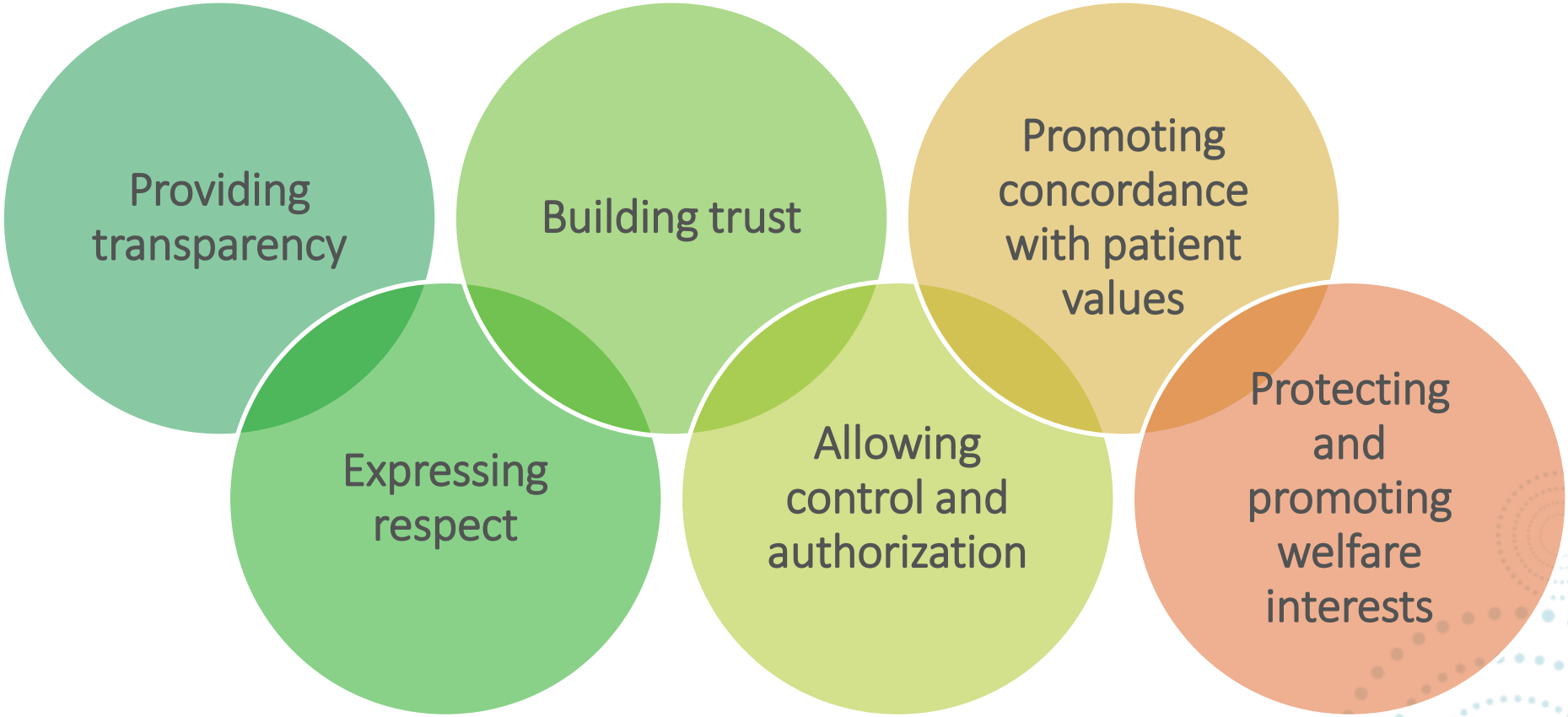
7. Informed Consent

Informed Consent

- A process (not a form or an episode) by which participants decide whether to take part in a study

- Some research can be ethical without consent, or without one or more elements of consent
  - E.g., research on de-identified biospecimens
  - E.g., waiver of documentation

Informed Consent Serves a Variety of Functions



8. Respect for Participants and Communities

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Respect for Participants and Communities

Ethical requirements of research do not start or end with signed consent document, and may include:

- Protecting confidentiality
- Respecting right to withdraw
- Developing monitoring plan, stopping rules
- Compensation for research injury
- Post-trial obligations

Conclusions

- There are historical and ethical reasons for caring about ethics of clinical research
- Eight benchmarks can help identify issues that need attention
  - Systematic approach
  - Balancing is often necessary
- Informed consent is ethically important, but imperfectly realized
  - And not the only benchmark we should care about

Learning Objectives

- Describe the eight ethics benchmarks for ethical clinical research
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Questions

Case Study

- Background:
  - Up to 75% of African-born individuals have evidence of past or current HBV infection; at least 25% are at risk for infection
  - In a large US city with a large African-born population, only 10% of at-risk adults completed vaccination when offered free of charge
  - Community focus groups revealed no particular objection to vaccination
- Proposed study: Compare effects of education vs. financial incentives ($10 or $20) on vaccination uptake
- Main question: Is it ethically appropriate to offer financial incentives for hepatitis B vaccination in a randomized trial?

Discussion Questions

1. How should the research team **partner with the community**? About what? When in the research process?
2. How would you describe the **value** of this research? Are the results likely to be generalizable?
3. What other study designs might be feasible and **scientifically valid**?
4. Does the selection of this **study population** seem fair?
5. What is the **risk/benefit ratio** in this study? Is it appropriate?
6. Should all participants be **informed** that some people in the study are getting a larger financial incentive? How and when might this disclosure be done?

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Research Bioethics Consultations

The ITHS Research Bioethics program provides a forum for discussion and analysis of ethical issues in clinical and translational research.

The Consultation Process

ITHS offers research bioethics consultations to researchers, trainees, research staff, and personnel involved in the protection of human subjects. Discussions with consultants can take place by telephone or in person. There is generally no charge.

Bioethics consults are advisory and provide a forum for in-depth conversation and analysis of ethical issues in clinical and translational research. Recommendations are supplemental to the authority and oversight of review groups such as an Institutional Review Board or Data Monitoring Committee.

To ensure a balanced understanding of the facts or to facilitate resolution of a conflict, the consultant is available to talk with others involved in the issue if the requestor so desires.

Acknowledgments

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Questions?

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