When Vulnerable Populations Are Subjects in Pragmatic Trials

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NIA IMPACT
COLLABORATORY
TRANSFORMING DEMENTIA CARE

The IMPACT Collaboratory's mission is to build the nation's capacity to conduct PCTs of interventions for people living with dementia and their care partners.

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Vulnerability

- Vulnerability is a prominent issue in research ethics
- Describes research participants who need additional protections
- Guidelines and regulations often refer to groups as vulnerable (e.g., pregnant persons, children, prisoners)
- But this might obscure:
  - Heterogeneity within groups
  - Intersecting sources of vulnerability
  - Other vulnerable participations

BUT WAIT…

Why enroll vulnerable populations, like people with dementia, in research at all?

Overview

- Provide a general framework for thinking about vulnerability
- Use case studies to see how identifying potential vulnerabilities can help us identify corresponding protections
- Dive a bit deeper into consent and waivers of consent

Vulnerability Framework

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ETHICS

Ethical analysis of vulnerabilities in cluster randomized trials involving people living with dementia in long-term care homes

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Vulnerability Framework

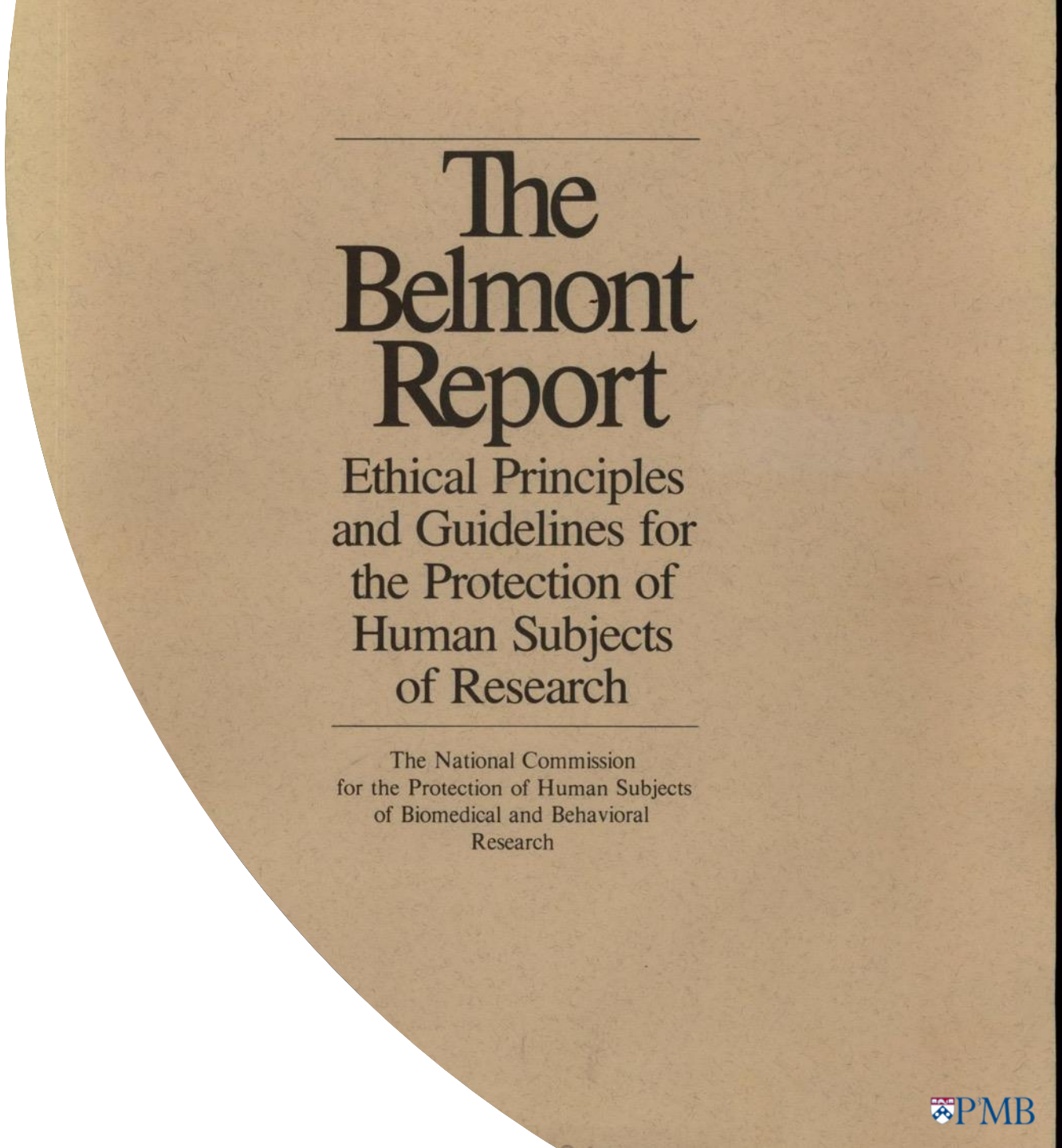
- One definition of vulnerability is “an identifiably increased likelihood of incurring additional or greater wrongs” as a result of research participation
- Q: How might researchers wrong participants?
- A: Researchers might fail to discharge duties to them

Nix, Hayden P., et al. "Ethical analysis of vulnerabilities in cluster randomized trials involving people living with dementia in long-term care homes." *Journal of the American Geriatrics Society* (2022).

Belmont Report

Researchers have duties of:

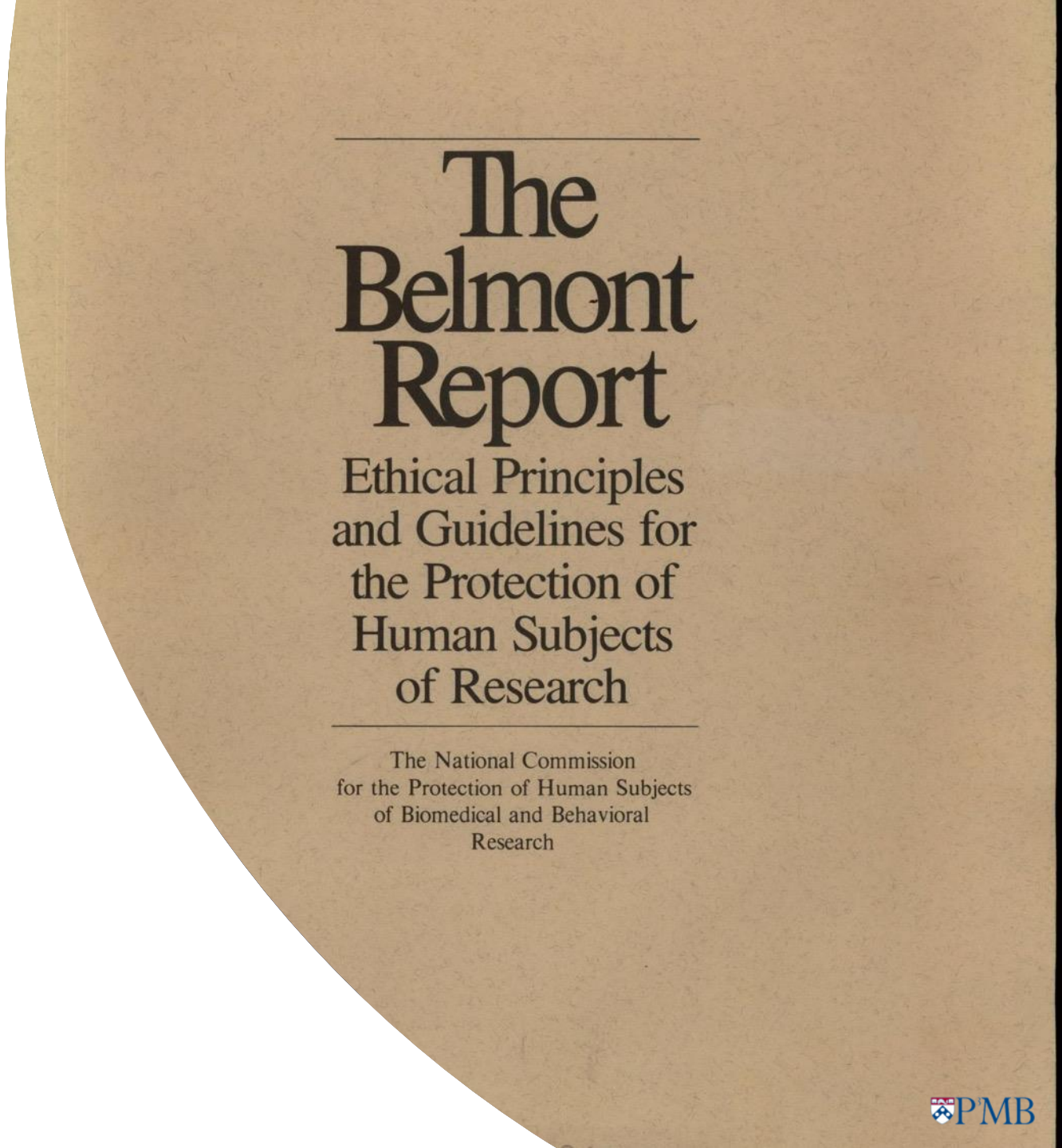
- Respect for Persons
- Beneficence
- Justice



Belmont Report

Researchers have duties of:

- Respect for Persons
  → Autonomy wrongs
- Beneficence
  → Welfare wrongs
- Justice
  → Justice Wrongs



More Granularly…

- Respect for Persons
  - Seek voluntary informed consent or, if participants lack capacity, seek permission from a surrogate
  - Respect privacy
- Beneficence
  - Minimize risks; ensure they stand in reasonable relation to potential benefits
- Justice
  - Ensure the burdens and benefits of research are fairly distributed

From these duties, we can derive wrongs…

- Respect for Persons → Autonomy Wrongs
  - Inadequate understanding in informed consent
  - Inadequate voluntariness in informed consent
  - Invasions of privacy
- Beneficence → Welfare Wrongs
  - Risks of therapeutic procedures are high
  - Risks of non-therapeutic procedures are not minimized
- Justice → Justice Wrongs
  - Unjust impact on care

Case Studies

Bath Trial

- **Aim:** Evaluate the effectiveness of the Bathing Without a Battle Intervention
- **Intervention:** Providers were taught individualized, person-centered bathing techniques
- **Data collection:** Researchers directly observed baths and collected use of antipsychotic medication from the bath
- **Consent:** LTC facility administrators sought consent from residents or family

J Am Geriatr Soc. 2014;62(5):797-804. doi:10.1111/jgs.12777

Elastic Trial

- **Aim:** Evaluate effectiveness of the Wheelchair-Using Senior Elastic Band Intervention
- **Intervention:** Group aerobic exercise sessions led by volunteers 3x per week for 6 months
- **Data Collection:** Researchers performed physical assessments
- **Consent:** Researchers obtained surrogate permission and assent from residents

Am J Phys Med Rehabil. 2016;95(11):789-799. doi:10.1097/PHM.0000000000000518

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MARQUE Trial

- **Aim:** Evaluate effectiveness of the MARQUE intervention
- **Intervention:** LTC staff were trained in the causes and management of agitation and given feedback on their performance
- **Data Collection:** Researchers gathered Cohen-Mansfield Agitation Inventory, proxy-rated QoL (from caregiver)
- **Consent Procedures:** Gatekeeper permission; after capacity assessment, researchers obtained surrogate permission and assent from residents

Lancet Psychiatry. 2019;6:293-304. doi:10.1016/ S2215-0366(19)30045-8

Wrongs	Examples
Inadequate understanding in informed consent	An investigator seeks informed consent from an individual who lacks decision-making capacity
Inadequate voluntariness in informed consent	Residents in a LTC facility feel as though they must participate in research because they are being approached by facility staff (on whom they depend)
Invasion of privacy	Researchers observe participants in their LTC facility bathrooms (where they depend on others for assistance with ADLS)
Risks of therapeutic procedures are high compared to potential benefits	People living with dementia have symptoms and comorbidities that unfavorably change the risk-profile of the proposed intervention
Risks of research procedures are not minimized	Cognitively impaired individuals experience distress completing questionnaires
Unjust impact on care	LTC facility residents are chosen to participate in research because it is convenient

Protections

- Once we understand the ways participants in a particular study might be wronged, we can identify corresponding protections

Wrongs	Examples	Corresponding Protections
Inadequate understanding in informed consent	An investigator seeks informed consent from an individual who lacks decision-making capacity	Conduct capacity assessment; if no capacity, identify a surrogate; seek surrogate permission and assent/dissent (if appropriate)
Inadequate voluntariness in informed consent	Residents in a LTC facility feel as though they must participate in research because they are being approached by facility staff (on whom they depend)	Consider having a researcher seek consent; enlist a patient advocate
Invasion of privacy	Researchers observe participants in their LTC bedrooms (where they depend on others for assistance with ADLS)	Engage stakeholders to help researchers gain insights into privacy norms in LTC setting; consider limiting direct observation (e.g., train staff, audio record)
Risks of therapeutic procedures are high compared to potential benefits	People living with dementia have symptoms and comorbidities that unfavorably change the risk-profile of the proposed intervention	Consider additional protections to minimize risks (e.g., increase frequency of monitoring, ensure adequate staff on hand)
Risks of research procedures are not minimized	Cognitively impaired individuals experience distress completing questionnaires	Consider whether proxy should complete questionnaires; allow caregiver to be present if participant must
Unjust impact on care	LTC facility residents are chosen to participate in research because it is convenient	Seek permission from gatekeepers (e.g., LTC administrators)

Consent

Assessing Capacity

- Alzheimer’s is a disease of autonomy; don’t take decision-making opportunities away prematurely
- Researchers seeking to enroll people living with dementia (or other cognitive disabilities) generally need a plan for assessing prospective participants’ capacity to consent to research participation

Involving the Person with Impaired Capacity

- When prospective participants lack capacity, researchers should identify an appropriate surrogate to give permission for enrollment
- Researchers should still find ways of involving the person with diminished capacity in research-related decision making–e.g., assent and dissent—if appropriate

Considering Caregivers

- Some studies enroll dyads comprised of a participant *and* the participant's "study partner" (i.e., an informant) – this individual might have to give their own consent

Waiving Consent

- Many PCTs are conducted with waivers of informed consent
- But when vulnerable populations are subjects in research, there may still be additional, important considerations

Challenges

- Depending on the nature of the intervention, outreach can be challenging even if you aren't getting consent:
  - Not always clear how to get uptake if contacting the individual with cognitive impairment
  - Hard to identify caregivers in medical records
  - Don't want to inadvertently disclose a dementia diagnosis

Conditions

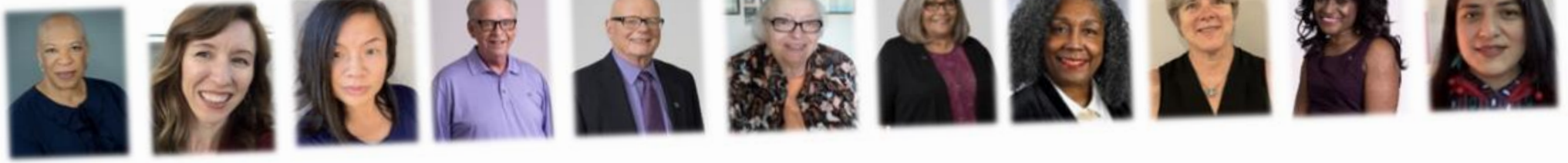
For an IRB to waiver or alter consent, it must find and document (among other things) that:

i. The research involves no more than minimal risk

ii. The research could not practicably be carried out without the waiver or alteration

iii. The waiver or alteration will not adversely affect the subjects' rights and welfare

iv. Subjects or LARs will be provided with additional information after participation, if appropriate



Ethical Challenges in Conducting Research Using a Waiver of Informed Consent with People Living with Dementia

Authors: Emily Largent, Jason Karlawish, Steve Joffe, Gary Epstein-Lubow

https://impactcollaboratory.org/lived-experience-panel/

Special Considerations

- Pay attention to risks for this population
- Rights and welfare may have particular significance when research is conducted in someone's home
- Notification should account for cognitive impairment

Consultation

- Researchers should design studies with input from vulnerable participants and, if appropriate, their caregivers

Conclusion