When Vulnerable Populations Are Subjects in Pragmatic Trials

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Disclosures

• I have grants from the National Institute on Aging and the Greenwall Foundation. The views I’m expressing today are my own.
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.
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
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

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

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

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

<table>
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<th>Examples</th>
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<td>Inadequate understanding in informed consent</td>
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<td>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)</td>
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<td>Researchers observe participants in their LTC facility bathrooms (where they depend on others for assistance with ADLS)</td>
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<td>People living with dementia have symptoms and comorbidities that unfavorably change the risk-profile of the proposed intervention</td>
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<td>LTC facility residents are chosen to participate in research because it is convenient</td>
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Protections

• Once we understand the ways participants in a particular study might be wronged, we can identify corresponding protections
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<td>Inadequate understanding in informed consent</td>
<td>An investigator seeks informed consent from an individual who lacks decision-making capacity</td>
<td>Conduct capacity assessment; if no capacity, identify a surrogate; seek surrogate permission and assent/dissent (if appropriate)</td>
</tr>
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<td>Inadequate voluntariness in informed consent</td>
<td>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)</td>
<td>Consider having a researcher seek consent; enlist a patient advocate</td>
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<td>Invasion of privacy</td>
<td>Researchers observe participants in their LTC bedrooms (where they depend on others for assistance with ADLS)</td>
<td>Engage stakeholders to help researchers gain insights into privacy norms in LTC setting; consider limiting direct observation (e.g., train staff, audio record)</td>
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<td>Risks of therapeutic procedures are high compared to potential benefits</td>
<td>People living with dementia have symptoms and comorbidities that unfavorably change the risk-profile of the proposed intervention</td>
<td>Consider additional protections to minimize risks (e.g., increase frequency of monitoring, ensure adequate staff on hand)</td>
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<td>Cognitively impaired individuals experience distress completing questionnaires</td>
<td>Consider whether proxy should complete questionnaires; allow caregiver to be present if participant must</td>
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<td>Unjust impact on care</td>
<td>LTC facility residents are chosen to participate in research because it is convenient</td>
<td>Seek permission from gatekeepers (e.g., LTC administrators)</td>
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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
• 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
For an IRB to waive 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
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