Addressing vulnerability in cluster randomized trials involving people living with dementia in nursing homes

Charles Weijer

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Housekeeping

• All participants will be muted

• Enter all questions in the Zoom Q&A/chat box and send to Everyone

• Moderator will review questions and ask them at the end

• Want to continue the discussion? Associated podcast released about 2 weeks after Grand Rounds

• Visit impactcollaboratory.org

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Research team

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Dementia

569,600
124,000
1 in 5
$10.4 billion

That’s almost TRIPLE the number of people living with dementia by 2050!

Estimates based on the Landmark Study.

Canada

Total number of long-term care homes 2,076

Publicly owned 46%
Privately owned 54%
- Private for-profit 29%
- Private not-for-profit 23%
- Private (no breakdown) 2%

Notes
* Data for all jurisdictions is as of March 31, 2021, except Quebec (as of April 1, 2021) and Alberta (as of February 26, 2021).
† Private for-profit and not-for-profit ownership breakdown information for some long-term care homes in Quebec, Ontario and Alberta was not available at the time of publication.

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How to improve the quality of care and quality of life of PLWD in long-term care homes?

Research priorities identified by PLWD include:
✓ Care provider education
✓ Nonpharmacological management of symptoms

But how to conduct clinical trials in this setting ethically?
Ethical considerations within pragmatic randomized controlled trials in dementia: Results from a literature survey

Stuart G. Nicholls1 | Kelly Carroll1 | Hayden P. Nix2 | Fan Li3,4 | Spencer Phillips Hey5 | Susan L. Mitchell6,7 | Charles Weijer8,9,10 | Monica Taljaard1,11

Abstract
Introduction: This review aims to describe the landscape of pragmatic randomized controlled trials (RCTs) in the context of Alzheimer's disease (AD) and related dementias with respect to ethical considerations.

Methods: Searches of MEDLINE were performed from January 2014 until April 2019. Extracted information included: trial setting, interventions, data collection, study population, and ethical protections (including ethics approvals, capacity assessment, and informed consent).

Results: We identified 62 eligible reports. More than two-thirds (69%) included caregivers or health-care professionals as research participants. Fifty-eight (94%) explicitly identified at least one vulnerable group. Two studies did not report ethics approval. Of 57 studies in which patients were participants, 55 (96%) reported that consent was obtained but in 37 studies (67%) no mention was made regarding assessment of the patients’ capacity to consent to research participation.

Discussion: Few studies reported protections implemented when vulnerable participants were included. Shortcomings remain when reporting consent approaches and capacity assessment.

Keywords: capacity, consent, ethics, research participant
The Ottawa Statement on the Ethical Design and Conduct of Cluster Randomized Trials

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### Guidelines and Guidance

#### The Ottawa Statement on the Ethical Design and Conduct of Cluster Randomized Trials

<table>
<thead>
<tr>
<th>Ethical issue</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protecting vulnerable participants</td>
<td>Clusters may contain vulnerable participants. In these circumstances, researchers and RECs must consider whether participants additional protections are needed.</td>
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<tr>
<td></td>
<td>When individual informed consent is required and there are individuals who may be less able to choose participation freely because of their position in a cluster or organizational hierarchy, RECs should pay special attention to recruitment, privacy, and consent procedures for those participants.</td>
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</tbody>
</table>
Vulnerability
People who are at “an identifiably increased likelihood of incurring additional or greater wrongs” as a result of research participation
Respect for persons
Beneficence
Justice

Welfare wrongs
Justice wrongs
Autonomy wrongs

Protections
Protections
Protections
Bath trial
# Bath trial

| Aim | Evaluate the effectiveness of the Bathing Without a Battle intervention  
<table>
<thead>
<tr>
<th></th>
<th>Training to teach healthcare providers noncoercive, individualised, person-centered bathing techniques to make bathing safe and comfortable.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Healthcare providers were taught to (1) effectively communicate, (2) understand behavioural symptoms as an expression of unmet needs, (3) respect resident preferences, and (4) ensure the physical environment is safe.</td>
</tr>
</tbody>
</table>
| Data collection | Researchers directly observed each bath and documented physical and verbal aggressive behaviour.  
|     | Use of antipsychotic medication on bath days was collected from medical records. |
| Consent procedures | Care home administrators sought consent for participation from healthcare providers.  
|     | No reported capacity assessments.  
|     | Care home administrators sought consent for participation from residents or their family caregiver. |
Elastic trial
Elastic trial

| Aim                              | Evaluate the effectiveness of the Wheelchair-using Senior Elastic Band intervention  
|                                  | Group exercise sessions designed for wheelchair-using residents. |
| Intervention                     | Group aerobic and resistance exercise sessions led by volunteers, thrice weekly for 6 months.  
|                                  | Additional instructors present during sessions to monitor participants for physical discomfort. |
| Data collection                  | Researchers performed physical assessments, measuring activities of daily living, flexibility, joint range of motion, cardiopulmonary function, and muscle strength and endurance. |
| Consent procedures               | No reported capacity assessments.  
|                                  | Researchers obtained assent from residents and surrogate consent from their family caregivers. |
Managing agitation and raising quality of life (MARQUE) trial
# MARQUE trial

| **Aim** | Evaluate the effectiveness of the MARQUE intervention  
|         | Training to teach healthcare providers strategies to manage agitation. |
| **Intervention** | Developed with input from healthcare providers, patients, and community representatives.  
|         | Care home staff were trained in the causes and management of agitation and were given feedback on their performance. |
| **Data collection** | Cohen-Mansfield Agitation Inventory and the Neuropsychiatric Inventory at baseline and at 8 months post-training.  
|         | Proxy-rated quality of life of participant by interviewing a healthcare provider or a family caregiver. |
| **Consent procedures** | Gatekeeper permission obtained from care home managers.  
|         | Researchers obtained consent for participation from healthcare providers.  
|         | Capacity assessment using the Mental Capacity Act 2005 criteria.  
|         | Sought consent for participation from residents, or surrogate consent from a family caregiver or professional consultee. |
1. Inadequate comprehension
Inadequate comprehension

<table>
<thead>
<tr>
<th>Protections</th>
</tr>
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<tbody>
<tr>
<td>Bath trial</td>
</tr>
<tr>
<td>✓ No capacity assessment reported</td>
</tr>
<tr>
<td>Elastic trial</td>
</tr>
<tr>
<td>✓ No capacity assessment reported</td>
</tr>
<tr>
<td>MARQUE trial</td>
</tr>
<tr>
<td>✓ Capacity assessment (Mental Capacity Act 2005 criteria)</td>
</tr>
</tbody>
</table>
Inadequate comprehension

Protections

✓ MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR)
  • Trained personnel
  • 15-30 minutes
  • May bias the sample
  • May deter large trials

✓ Brief screening questionnaire
Inadequate comprehension

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Exceptions:</td>
</tr>
<tr>
<td>✓ Lack of decision-making capacity is an eligibility criterion</td>
</tr>
<tr>
<td>✓ Research procedures very similar to routine medical practice</td>
</tr>
<tr>
<td>✓ Surrogate decision maker</td>
</tr>
<tr>
<td>✓ Assent</td>
</tr>
</tbody>
</table>
2. Inadequate voluntariness

Inadequate voluntariness

**Protections**

**Bath trial**
- ✓ LTC home administrators sought consent

**Elastic trial**
- ✓ Researchers sought consent

**MARQUE trial**
- ✓ Researchers sought consent
Inadequate voluntariness

Protections

✓ Consent sought by researchers (and not LTC home staff)
  • “insulate[s] the patient from the hierarchical system”
  • Protects against recruitment bias, particularly important in cluster randomized trials

✓ Independent patient advocate
3. Invasion of privacy

https://www.moreability.co.uk/help-advice/2015/09/assisted-showering-solutions-for-long-term-care-settings
Invasions of privacy

Protections

✓ Stakeholder engagement
  • Resident, family, ombudsman...
  • Gain insight into privacy norms
  • Reduce risk of privacy wrongs
  • Ensure design is compatible with the intervention’s setting of intended use.
Invasions of privacy

Protections

Bath trial
Study intervention and data collection occur in resident’s bathroom

✓ Train LTC staff to observe resident behavior while providing care
✓ Train researchers to provide targeted aspect of care
✓ Behavior assessment by listening rather than observing visually
4. Risks of therapeutic procedure exceed potential benefits

https://sites.google.com/site/stotfoldgoodneighbourgroupinfo/chair-based-exercise-classes
Risks of therapeutic procedure exceed potential benefits

Protections

Elastic trial

Group aerobic and resistance exercise sessions

✓ Additional supervision by LTC staff or volunteers
  • Standardized protocols
  • Enhance generalizability to residents who would otherwise not be able to participate safely
Risks of therapeutic procedure exceed potential benefits

**Protections**

✓ Monitoring for severe agitation/aggression

✓ Exclude those unlikely to tolerate study procedures

✓ Presence of caregiver

✓ DSMB
5. Excessive risks of nontherapeutic procedures
Excessive risks of nontherapeutic procedures

**Protections**

✓ Identify PLWD prone to agitation

✓ Family members or familiar LTC home staff to fill out questionnaires

✓ Allows researchers to investigate patient-centered outcomes that might otherwise be inaccessible in PLWD who cannot self-report
6. Unjust exposure to burdens of research

Unjust exposure to burdens of research

Protections

✓ Gatekeepers, including LTC home administrators and medical directors

✓ Ensure that research activities do not compromise the care provided to all LTC home residents

✓ Gatekeeper permission
# Vulnerability framework

## Autonomy wrongs

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<thead>
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<td>Inadequate comprehension</td>
<td>✓ Formal capacity assessment</td>
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<tr>
<td></td>
<td>✓ Consent from surrogate decision maker</td>
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<tr>
<td></td>
<td>✓ Participant assent</td>
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<tr>
<td>Invasions of privacy</td>
<td>✓ Stakeholder engagement</td>
</tr>
<tr>
<td></td>
<td>✓ Train LTC staff to collect data</td>
</tr>
<tr>
<td></td>
<td>✓ Train researchers to administer care</td>
</tr>
<tr>
<td></td>
<td>✓ Limit observation</td>
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## Welfare wrongs

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## Justice wrongs

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<td>Unjust exposure to burdens of research</td>
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Questions?