Minors and research decision-making capacity: consent considerations

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Overview

- History of minors and research participation
- Research consent
- Health care decision-making and minors
- TCPS2 2014, decision-making capacity assessment
- Case discussion
- US regulations
- Questions/discussion

What is missing?
But we will need your help!

- Practical issues in implementation
  — Strategies?
- Investigators
  — How do we help?
- Anyone asked teens what they think?
- Anyone asked parents?
- Matching Canadian and US standards

Case 1 – Literacy development in children

- **Purpose:** to test the effect of narrative language intervention in children with language impairment
- **Sample:** 8-14 years
- **Method:** 3 groups, parent-assisted, standard and wait list control. Intervention involves using children’s literature to introduce and practice story content, vocabulary and grammatical structure.
- **Outcomes:** oral and written narrative samples using standardized pictures

Case 2 - Exercise Capacity in Juvenile Idiopathic Arthritis

- **Purpose:** to determine how inflammatory disease impacts joint function and health compared to health and injured control populations
- **Sample:** age 13-19yrs
- **Measures**
  — joint function (biomechanics, muscle strength and balance)
  — joint health (MRI)
  — psychosocial (depression, QOL, reduced physical activity participation)
  — physiological (pain, fatigue, blood, adiposity, aerobic fitness)
  — dietary intake
  — health care utilization
- **Recruitment:** Children’s hospital, sports teams, community
Case 3 – Ph. 1B Drug Trial in Cystic Fibrosis

- **Purpose:** safety evaluation, dose ranging study, drug intended to promote production of functional protein
- **Sample:** 2-3 local participants of 64 total (multisite), ages 16-25
- **Methods:** inpatient stay (5 days), multiple visits, drug given by nebulizer, outcome assessments – vitals, blood, urine, sputum, oximetry, spirometry, sweat chloride test, ECG, questionnaires
- **Risks:** related to tests and study drug, latter largely unknown - possibility of fatal allergic reactions, reproductive risks
- **Reimbursement:** for expenses (~$150/day)

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Minors in research

- Historical examples:
  - Edward Jenner and James Phipps 1796
  - First Nation Nutrition studies 1942-52
  - Willowbrook, 1950s-70s
These studies abused the principle of respect for persons

- Participation
  - Not consented
    - Not informed
    - Not voluntary
- No consideration of capacity

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Research ethics standards

Evolution:

- Nuremburg 1947 – only competent adult with consent
- Helsinki 1964 – children if consent from legal guardian
- Helsinki 1983 – minors may give consent where possible
- TCPS 1998, 2010:
  - TCPS 1998, 2010 – “legal competence,” “legal capacity,” provision for assent, surrogate consent, dissent to be respected
- 45 CFR 46.116, 21 CFR 50.20, ICH GCP – “legally effective informed consent” or LAR
Past Standard under TCPS 1998 and 2010

- Requirements with respect to legal capacity/competence applied in terms of age of majority
  - 18 in AB, MB, ON, PEI, QC, SK
  - 19 in BC, NB, NL, NT, NS, NU, YT

- Parental consent and the minor’s assent required for research participation
  - Exceptions granted in specific cases e.g., (studies involving sexual behaviour, illegal behaviours)

TCPS 2 Consent requirements

Consent

- Voluntary
  - Free choice may be undermined by
    - undue influence, coercion or offers of incentives may

- Informed
  - Full disclosure of all information necessary, procedures, risks, benefits etc.

- Necessary condition is that the person have capacity
  - where lacking, assent appropriate

Consent and capacity

TCPS2 (2014)

- Capacity –
  - Understanding
  - Appreciate consequences
  - Varies
    - Complexity
    - Circumstances
    - Time (Ch. 3, Section C)
Chapter 3 – Consent

3.3 Consent to be based on decision-making capacity, not chronological age

Consistent with provisions of some privacy Acts (e.g., Alberta’s Health Information Act (Section 104))

s 104: Exercise of rights by others (consent from children, parents, surrogates)

- minors can consent to use of their health information if they are deemed competent to make that decision; not competent – parental consent required

How do we perceive minors?
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Consent of Minors to Medical Treatment

- TCPS2 position consistent with some provincial positions
- Common law applies in provinces where there is no consent and capacity legislation (AB, MB, NS, NL, NT, NU, SK)
- Supreme Court has endorsed "mature minor" doctrine
- In these provinces minors capable of providing consent if they have maturity, intelligence and capacity to understand nature and purpose of proposed care as well as ability to appreciate reasonably foreseeable consequences of decision
- Requirements not met, parental consent needed

Consent of Minors to Medical Treatment

- Other provinces address this more directly through various provincial statutes (BC, MB, NB, ON, PEI, QC, YK)
  - ON Health Care Consent Act - capacity/mature minor
  - PEI Consent to Treatment and Health Care Directives Act - capacity/mm
  - YK Care Consent Act - capacity/mature minor
  - MB The Health Care Directives Act - 16 yrs.
  - QB Civil Code of QC – conditional, 14 yrs.
  - BC Infants Act – conditional, “best interests”
  - NB Medical Consent of Minors Act – capacity/mature minor or 16
Consent of minors to medical treatment

- Where the minor lacks capacity, the consent of the parents or guardians is required.
- All provinces and territories have child protection legislation, which overrules the common law in certain circumstances (e.g., the court may override mature minor’s wishes when the child’s life is threatened).
- The court may exercise its parens patriae (parent of the nation) jurisdiction to determine treatment course regardless of child/parent wishes.
- Based on an assessment of what would be most conducive to the child’s welfare, with the child’s views carrying increasing weight in the analysis as his or her maturity increases.

Research decision-making capacity assessment

- Generally, when the proposed participants are 14 years of age and older, capacity considerations should be made.
- To have research decision-making capacity requires that the minor can understand and appreciate the risks and benefits of participating and of not participating.

Capacity considerations – PI responsibilities

Onus on PI to determine and describe how this capacity will be assessed.

Considerations:
- the minor’s ability to appreciate the reasonably foreseeable consequences of his or her actions;
- the stage of the minor’s physical, emotional and mental development;
- the degree of responsibility the minor has assumed in his/her life; and
- the intelligence of the minor.
Assessment of research decision-making capacity

- Context important to capacity judgment
  - Risk of study
  - Risk of health condition
  - Risk/availability of effective standard of care

- Ideal is to have parents and children in agreement
  - Beyond larger considerations, practicalities of getting child to study-related appointments, following regimens etc.

Assessment of research decision-making capacity

- Principle of proportionality important

- Likelihood and magnitude of risks associated with the research integral

- Lower risk - general knowledge of child development may be sufficient

- Higher risk – more formalized/objective procedure may be required

Decisional capacity assessment tools

- A small number of decisional capacity assessment instruments specific to research available

- Informal "in house" checklists - example
  - University of Rochester guideline “Determination of capacity to give informed consent for minors”

- Published instruments - examples
  - MacArthur Competence Assessment Tool (M-CAT) for Clinical Research*
  - Brief Informed Consent Test
  - Evaluation to Sign Consent

* most widely adopted, most empirical support
Sample templates for documenting capacity assessment:

Example 1:

- Why is this study being done?
- What will happen to you if you participate?
- What are the potential risks of participating in this study?
- What are the benefits of participating in this study?
- Do you have to be in this study?
- What will happen if you decide not to participate?
- What will happen if you decide to be in the study and then change your mind?
- Who should you call with questions or concerns?
- Do you have any questions?

Capacity assessment checklist, continued (paraphrased)

Potential participant was able to:

- convey purpose of study
- convey study procedures
- convey potential risks
- convey potential benefits
- convey alternatives to participation
- recognized voluntary nature of the study
- questions were answered to the subjects satisfaction

Sample templates for documenting capacity assessment:

Example 2 – Likert scale, level of understanding

1=none  2=poor  3=unclear  4=good  5=excellent

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**Score of less than 4 on any item means capacity lacking**
MacArthur Capacity Assessment Tool

MacArthur Competence Assessment Tool for Clinical Research (MacCAT-CR)

In Stock (!)
Your Price: $24.95

Structured, formal capacity assessment adaptable to particulars of any given research project
Reliable and valid
Administration time 15-20 minutes
Project-specific disclosures, then understanding, appreciation, reasoning and ability to make a choice assessed
Has been adapted by some for use in children


Capacity assessment

Outcomes

- 1. Minor lacks capacity – parental/guardian consent
- 2. Minor has capacity – minor can consent

Implications
- entitled to confidentiality, information can be shared with permission
- might require "operational" support (parental permission) to participate in study

Complicated outcomes

<table>
<thead>
<tr>
<th>Parental &quot;Assent&quot;</th>
<th>Child Consent YES</th>
<th>Child Consent NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
<td>YES/YES</td>
<td>NO/YES</td>
</tr>
<tr>
<td>NO</td>
<td>YES/NO</td>
<td>NO/NO</td>
</tr>
</tbody>
</table>
What to do when there is discord?

Minor – with capacity (Downie – 1999):
  - Minor NO, parent YES:
    * no enrollment
  - Minor YES, parent NO:
    * 1. parent support required for study:
      * no enrollment
    * 2. parent support not required:
      * researcher should make case for enrollment and REB to make case by case assessment, considering benefits and harms of research, harms of parental exclusion

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What kinds of questions would you ask to assess capacity?

Are there any special considerations/concerns?

Do you inform parents if minor is capable and consents to research?

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Questions/discussion

(Aerial view of Toronto, 1812)
What about the common rule?

Glad you asked!

Things are a bit different south of the border

- 21 CFR 50.20 and 45 CFR 46.408

Children – “persons who have not attained the legal age for consent to treatment or procedures involved in the research, under the applicable law of the jurisdiction in which research will be conducted” 45 CFR 46.402(a)

US regulations – parental permission

- Parental/legally authorized rep (LAR) permission required
- Under 45 CFR 408(b) and 21 CFR 50.55 (e)(2)
  - one parent required if research is minimal risk (45 CFR 46.404 and 21 CFR 50.51) or greater that minimal risk but offers the prospect of direct benefit to child (45 CFR 46.405 and 21 CFR 50.53)
Under 45 CFR 408(b) and 21 CFR 50.55 (e)(2)
- The permission of both parents is required when the research involves greater than minimal risk and no prospect of direct benefit to the child, but the research is likely to yield generalizable knowledge about the child’s condition (45 CFR 46.406 and 21 CFR 50.53)

Requiring parental permission based on presumption that parents are acting in the best interests of their child

Parental permission seen to provide protection to children who are considered a vulnerable population

Developing decision-making capacity respected by obtaining informed assent

REB to take into account age, maturity, physical and psychological state

REB to make the determination for all children to be enrolled, or for each child, case by case (45 CFR 46.408a and 21 CFR 50.55b)
US regulations – children’s assent

- REB may determine that assent is not required if the capability of the child is so limited they cannot reasonably be consulted OR the research holds out the prospect of direct benefit that is important to health/well being of the child and is only available through the research

(45 CFR 46.408a and 21 CFR 50.55c 1 and 2)

Canadian vs US Research Ethics Standards

Principle-based difference

- Canada – based on decision-making capacity, autonomy
- US - based on assumption those under age of majority lack autonomy, are a vulnerable population in need of protection, assumes parents act in best interest
- Impacts just/fair treatment of minor research participants

Two key questions

1. What are the pros and cons of the US and Canadian positions?

2. Can the US and Canadian standards be reconciled?
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Summary

Researchers, REBS are responsible

- to ensure the research discussion is understandable, research decisions are made by those with capacity to do so
- to ensure that a process for assessing capacity is in place
- to ensure those who are vulnerable (lacking capacity) are respected/protected
Thank you – Questions?