New Angles in Surrogate Consent - Adults

Karen E. A. Burns MD, FRCPC, MSc
St Michael’s Hospital, Toronto
burnsk@smh.ca
“Consent to Research” Process in the ICU

Need to balance

**Interests of vulnerable patients**
- Participant safety and well-being
- Ethical conduct

**vs. Need for rigorous clinical research**
- Generalizable results
- Timely identification of beneficial/harmful Rx
- Not deny vulnerable patients the opportunity to benefit from research participation

- Investigators, REBs, hospitals and funding agencies have a *mandate to conduct high quality, scientifically and ethically sound* research that ensures timely and effective care is provided to critically ill patients

- Maintain the public’s confidence in our competence, our work, & ethics

- Investigator ensure that participants understand risks & benefits
How Does Consent Differ in the ICU?  
Research vs. Care

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ATS Guidance Document, 2004 170:1375-84
“Research on Process of Conducting Research”

“Consent to Research Process”
1. Surrogate decision-making (SDMs) process for critically ill patients to participate in research
2. How to approach SDMs in the ICU

Decisions Regarding Participation
3. SDM’s rationale for providing/declining consent
4. Physician refusals of patient/SDM being approached
5. Patients/SDMs opinions on use of deferred consent
6. Patients/SDMs perspectives on use of waived consent
7. Research participation involving bereaved family members
SDM Decision-making Process

The Consent Study

Objective
• To describe SDMs experiences in being approached for consent for critically ill patients to participate in research.

Methods
• A multicenter qualitative study, nested in a 23 center observational study of research recruitment practices/processes
• Interviews with 26 SDMs (provided or declined consent) in 5 ICUs.
• Data were analyzed in duplicate using grounded theory + narrative critical analysis.

Burns et al, Submitted CMAJ
SDM Decision-making Process

Results

• SDMs were guided by an overarching desire for the patient to live.

• Surrogate research decision-making involved 3 *sequential stages*:
  
  Stage 1: being approached
  Stage 2: reflecting on participation
  Stage 3: making a decision.
SDM Decision-making Process

Results

In stage 1, SDMs identified factors that characterized their consent encounter

- How they were approached
- Attributes of the person approaching them
- Study risks/benefits
- Their expectations/patients wishes

SDMs expressed a clear preference to be approached in-person.

If SDMs perceived the risk of participation to be too high or felt patients may not benefit from participation - they did not contemplate participation further.
In stage 2, SDMs who knew the patient’s wishes or had an understanding of research - prioritized the patient’s wishes and the perceived benefits of participation.

Without this knowledge, SDMs prioritized obtaining more/better care for the patient, considered their (SDM/Pt) best interests, and valued healthcare professional’s knowledge (health care providers/about the patient).

Trust in healthcare professionals was essential to proceed to stage 3.
SDM Decision-making Process

*In stage 3,* SDMs considered 6 factors in rendering decisions.

- Trust in the healthcare professionals
- Patients interest/wishes
- Characteristics of the study/perceived risks
- Information (impacted/not imparted) about the study
- SDM hopes/needs/expectations
- SDM past experiences/relationship with the patient

All 3 stages - surrogate’s assessed the ‘risks and benefits of participation’
Research Decision-Making Process

1st Stage: The Approach
- Risk too high or unlikely to benefit: DECLINE CONSENT
- Risk not too high: Enter Stage 2

2nd Stage: The Reflection
- Prior directives: Enter Stage 2
- Prior lack of SDM knowledge: Prioritize the patient's interests

3rd Stage: The Decision
- No trust in healthcare professionals: Trust in healthcare professionals Enter Stage 3
- Characteristics of the study and the perceived risk of participation
- SDM hopes, needs, and expectations
- SDM past experiences & relationship with patient
- Information imparted/not imparted about the study

Risks & Benefits
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How To Approach SDMs

Mixed Methods Study (RCT + nested qualitative study)

Pilot RCT: compared MD introduction vs. Non-MD introduction of research to SDMs

Nested qualitative study: What is the experience of SDMs in being approached for consent for research participation?
How to Approach SDMs

The Approach Trial

138 SDMs randomized

1 incorrect randomization

137 SDMs randomized with intent to approach

67 SDMs with a physician introduction
(84 eligibility events)

Randomized, No Approach

Randomized, Approached
Consent Provided

Randomized, Approached
Consent Declined

Randomized, Approached
Consent Provided & Declined

Randomized, Approached
No reply returned

70 SDMs with a non-physician introduction
(78 eligibility events)

Randomized, No Approach

Randomized, Approached
Consent Provided

Randomized, Approached
Consent Declined

Randomized, Approached
No reply returned
Approach Trial: RCT Results

- Achieved all pre-specified feasibility metrics (missed few MD introductions, identified low protocol violation rates, approached most SDMs) evaluating potential threats to study validity.

- High average comfort, satisfaction and acceptance scores among participants between MD and non-MD groups.

- No difference in consent rates between approaches or based on study risk (investigator or SDM-assigned).

- SDMs introduced by an MD were significantly more likely to provide consent when a patient status update was provided.

Approach Trial: Qualitative Results

In the nested qualitative study (n=14; 7 MD approach and 7 non-MD approach), we found:

- Poor SDM recall of MD involvement

- Several participants ‘perceived’ benefits to MD involvement
  - Enhanced the credibility of research
  - Provided reassurance, comfort and confidence during decision-making
  - Ensured broad awareness of patient participation by the clinical team

- SDMs perceived that physician time would be better spent providing patient care

Approach Trial: Qualitative Results

7 themes important to SDMs in how they were approached

1. The personality & professionalism of the person approaching them
2. The importance of timing (when not in crisis) & having space to make decisions
3. Personal sense of responsibility in their role as SDM
4. A need to appraise the risks and benefits of participation and evaluate the potential benefit to the patient/others
5. Personal & patient values toward research
6. Trust in the healthcare team
7. Knowledge of the voluntary nature of participation

# The Approach Trial: Risks vs. Benefits

<table>
<thead>
<tr>
<th>SDM Rationale for Providing Consent</th>
<th>MD Introduction</th>
<th>Non-MD Introduction</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Will benefit from participation (benefits &gt; risks)</td>
<td>14</td>
<td>17</td>
<td>31</td>
</tr>
<tr>
<td>Have a strong desire to help others (future patients, medical community)</td>
<td>13</td>
<td>11</td>
<td>24</td>
</tr>
<tr>
<td>Want to advance medical knowledge and science</td>
<td>5</td>
<td>13</td>
<td>18</td>
</tr>
<tr>
<td>Desperate to try anything</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Loved one would want to participate</td>
<td>5</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>I trust the medical team</td>
<td>2</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>I wanted to please the medical/research teams</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
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Why Do SDMs Provide Consent?

**Objective**
Explore SDMs reasons for providing/declining consent for critically ill patients to participate in research

**Methods**
2 questionnaires (AGREE, n=68) and (DECLINE n=27)
- Explore attitudes toward research in general, timing of approach, the informed consent process
- Elucidate reasons for participation/non-participation
Why Do SDMs Provide Consent?

Table 3: Major reason provided by SDM for agreeing to participate in the research study (N = 44)

<table>
<thead>
<tr>
<th>Responses</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>To help my loved one recover faster</td>
<td>17</td>
</tr>
<tr>
<td>To improve patient care in the future</td>
<td>14</td>
</tr>
<tr>
<td>Research is important to improve medical care</td>
<td>9</td>
</tr>
<tr>
<td>The research study was recommended by the physician</td>
<td>1</td>
</tr>
<tr>
<td>Study treatment is better than standard care</td>
<td>1</td>
</tr>
<tr>
<td>The research study was not invasive</td>
<td>1</td>
</tr>
<tr>
<td>The research study did not interfere with patient’s primary care</td>
<td>1</td>
</tr>
</tbody>
</table>
Why Do SDMs Provide Consent?

AGREE group

Fig. 1 SDMs’ reasons for consenting for an ICU research study ($N = 68$)

- Research studies are important for medical progress
- SDM wanted to contribute to medical research
- The research study may positively affect clinical care
- SDM agreed to not disappoint the medical team
- SDM wanted to give something in return for the patient care
- SDM liked the presentation of the research study
- The research study may help others
- SDM trusted the medical team
- Patient may receive new treatment rather than standard care
- Any study treatment is better for this medical condition
- Research study could benefit the patient
- Patient had been enrolled in a research study before
- The patient would have agreed to the research study

Percent of SDMs

[Bar chart showing the distribution of reasons for consent]
Why Do SDMs Provide Consent?

<table>
<thead>
<tr>
<th>Responses</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fear of harm or discomfort to the patient</td>
<td>8</td>
</tr>
<tr>
<td>SDM too worried/anxious to consider research at that time</td>
<td>6</td>
</tr>
<tr>
<td>SDM was satisfied with the standard care provided</td>
<td>2</td>
</tr>
<tr>
<td>Personal reasons</td>
<td>1</td>
</tr>
<tr>
<td>Lack of discussion with attending physician regarding research study</td>
<td>1</td>
</tr>
<tr>
<td>Objection to study being sponsored by a pharmaceutical company</td>
<td>1</td>
</tr>
</tbody>
</table>
Why Do SDMs Provide Consent?

DECLINE GROUP

Fig. 2 SDMs’ reasons for declining consent (N = 27)

- Research has no place in ICU
- The research may affect medical care
- More risk than benefit in a RS
- RS was presented at the wrong time
- SDM did not want to burden the nurse with RS
- Disagreement in the family regarding the RS
- SDM does not trust medicine or research in general
- SDM did not trust the medical team
- SDM had previous bad experience with RS
- SDM did not want patient to receive placebo
- SDM did not want experimental treatment
- SDM disliked the way the RS was presented
- SDM was too worried to consider a RS
- SDM did not want to make decision concerning RS
- Patient is used as a guinea pig in RS
- Patient was not right for RS
- Patient has been enrolled in a RS before
- Patient would not have wanted to be enrolled
Physicians Decline Consent

Methods
• 67 centres (3,764 patients) enrolled in PROTECT trial
• 218 (14.9%) – no consent encounter because attending MDs requested that their patients not be approached

REASONS FOR NOT APPROACHING
• High risk of bleeding (31.2%) - presence of renal failure, epidural, perioperative state
• Preferences for thromboprophylaxis (12.4%)
• Morbid obesity (9.6%)
• Uncertain prognosis (6.4%)
• Discomfort with research (3.7%)
• Unclear (17.0%)
Physicians Decline Consent

FACTORS ASSOCIATED WITH PHYSICIAN DECLINE

<table>
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<tr>
<th>Table 3: Factors independently associated with physicians declining: hierarchical regression</th>
</tr>
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<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Odds ratio (95% CI)</td>
</tr>
<tr>
<td>---------------------</td>
</tr>
<tr>
<td>Years of ICU research experience of the lead consenting research personnel</td>
</tr>
<tr>
<td>0 years versus &gt;10 years</td>
</tr>
<tr>
<td>&gt;0–10 years versus &gt;10 years</td>
</tr>
<tr>
<td>Center size (beds screened for possible PROTECT patients)</td>
</tr>
<tr>
<td>15–20 beds versus &lt;15 beds</td>
</tr>
<tr>
<td>21–25 beds versus &lt;15 beds</td>
</tr>
<tr>
<td>&gt;25 beds versus &lt;15 beds</td>
</tr>
<tr>
<td>Unit type</td>
</tr>
<tr>
<td>Open versus closed</td>
</tr>
<tr>
<td>Formal trials group affiliation</td>
</tr>
<tr>
<td>Yes versus no</td>
</tr>
<tr>
<td>Year of PROTECT</td>
</tr>
<tr>
<td>Year 1 versus pilot</td>
</tr>
<tr>
<td>Year 2 versus pilot</td>
</tr>
<tr>
<td>Year 3 versus pilot</td>
</tr>
<tr>
<td>Year 4 versus pilot</td>
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Other Forms of Consent - Definitions

“Deferred/delayed consent: Consent obtained after the patient has been included in an ongoing research protocol.

- The ‘after the fact consent’ relates specifically to the patient’s continued participation in the study.

“A waiver of consent is present when a given research intervention is initiated without a prospective consent from either the patient or a proxy.”
TCPS2 – Article 3.8 – Deferred Consent

**Article 3.8** The REB may allow research that involves medical emergencies to be carried out without the consent of participants, or of their authorized third party, if all of the following apply:

- (a) a serious threat to the prospective participant requires immediate intervention;
- (b) either no standard efficacious care exists or the research offers a realistic possibility of direct benefit to the participant vs. standard care;
- (c) the risk is not greater than that involved in standard efficacious care, or it is clearly justified by the prospect for direct benefits to the participant;

(d) the prospective participant is unconscious or lacks capacity to understand the risks, methods and purposes of the research project;
(e) third party authorization cannot be secured in sufficient time, despite diligent and documented efforts to do so; and
(f) no relevant prior directive by the participant is known to exist.

When a previously incapacitated participant regains capacity or when a third party is found, consent shall be sought for continuation in the project, and for subsequent examinations or tests related to the research project.
Opinions of Delayed Consent

Research participants’ opinions of delayed consent for a randomised controlled trial of glucose control in intensive care

- Questionnaire involving 210/298 (79%) participants enrolled under delayed consent in the NICE SUGAR trial

- Delayed consent to participate was obtained
  - From patients: 57/210 (27.1%)
  - SDMs: 152/210 (72.4%)
Opinions of Delayed Consent

Results

• Most respondents 195/204 (95.6%) would have consented to participate in the trial *if asked prior to enrolment*
• Most ranked the person who consented on their behalf (163/198; 82.3%) as the *preferred decision-maker* when they were not able to make decisions
• Most (177/202; 87.6%) agreed with the decision made

**Conclusion:** delayed consent is *acceptable* to trial participants
TCPS2 - Article 3.7 – Waived Consent

“Article 3.7 The REB may approve research without requiring the participant’s consent where the REB is satisfied, and documents, that all of the following apply:

✓ (a) the research involves no more than minimal risk to the participants
✓ (b) the lack of the participant’s consent is unlikely to adversely affect the welfare of the participant
✓ (c) it is impossible or impracticable to carry out the research and to answer the research question properly if prior consent is required
(d) whenever possible and appropriate, after participation, or at a later time during the study, participants will be debriefed and provided with additional pertinent information........ at which point they will have the opportunity to refuse consent
(e) the research does not involve a therapeutic intervention, or other clinical or diagnostic interventions.
Participants Perspectives: Waived Consent

Methods

• Interactive interviews nested within the Progesterone for the Treatment of TBI trial (phase 3 RCT)
• N=85 interviews (54 or 64% with SDMs)
• Patients and SDMs enrolled under waiver of consent at 12 sites
Participants Perspectives: Waived Consent

Results

• 71/85 (84%) had positive attitude toward trial inclusion
• 72% found *use of waiver of consent ‘acceptable’ in general*
• 78% found *their inclusion ‘acceptable’ in the trial*
• Only 2/85 (2.4%) disagreed with ‘exception from informed consent’

• 80% were accepting of randomization
• 92% accepting of placebo
• Black respondents were less accepting than white (55 vs 83%, p=0.049)
### TABLE 4. Positive and Negative Reasons for Views of Exception From Informed Consent in Progesterone for the Treatment of Traumatic Brain Injury

<table>
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<th>Reasons for Views of Exception From Informed Consent</th>
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<td><strong>Negative reasons given</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Concerns about consent</td>
<td>22</td>
<td>26</td>
</tr>
<tr>
<td>Other people may not be as accepting</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>Concerned about potential side effects</td>
<td>11</td>
<td>13</td>
</tr>
<tr>
<td>Unsure about balance of risks/benefits in trial</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Believes drug is experimental (guinea pig concerns)</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Concerned about placebo being given</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Lack of medical benefit (or any additional benefit compared to standard)</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>Others disagreed with enrollment (combined: family members or patient themselves had well known negative feelings)</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td><strong>Positive reasons given</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direct medical benefits</td>
<td>75</td>
<td>88</td>
</tr>
<tr>
<td>Unable to get consent</td>
<td>33</td>
<td>39</td>
</tr>
<tr>
<td>Risks of study are low/no harm done</td>
<td>30</td>
<td>35</td>
</tr>
<tr>
<td>Contribute to scientific knowledge/help future patients</td>
<td>27</td>
<td>32</td>
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<tr>
<td>Other people agreed with enrollment (combined: family members/surrogates, medical personnel, patient themselves, religious figure)</td>
<td>22</td>
<td>26</td>
</tr>
<tr>
<td>Trust in researchers/doctors to do what is best</td>
<td>20</td>
<td>24</td>
</tr>
<tr>
<td>In case of an emergency, do what needs to be done</td>
<td>18</td>
<td>21</td>
</tr>
<tr>
<td>Patient so badly injured that it could not hurt/last option</td>
<td>12</td>
<td>14</td>
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<tr>
<td>Research is important</td>
<td>9</td>
<td>11</td>
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Research Participation for Bereaved Family Members

Methods

• Qualitative study; interviews + letters
• Family members who’s loved one died in 41 ICUs in France
• Thematic analysis of 54 narratives, 52 letters, written annotations on 150 questionnaires
Research Participation for Bereaved Family Members

Results

Bereaved family members affirmed several benefits to participation
1. Expression of thanks
2. Help other bereaved family members
3. Express themselves at a distance
4. Not to feel abandoned
5. Share difficult emotions
6. Receive support and care
Research Participation for Bereaved Family Members

Conclusion

• Bereavement research may be beneficial for family members
• Exploring family experiences – help to define specific family needs in this setting
• Bereaved families need an opportunity to voice their feelings about their ICU experiences and give meaning to the end-of-life process
• Families need to feel they are still cared for
• Support may be helpful: condolence letters, phone calls or post-intensive care meetings
Conclusions

1. How we approach SDMs for research consent is very important
   - Risks/benefits of participation
   - Trust in health care team

2. In ‘consent encounter’ – SDMs value most the personality & professionalism of the person approaching them

3. Main reasons for decline consents: fear of harm/discomfort, too anxious to consider participation

4. Physician refusals are more likely with less experienced research personnel and in open (vs. closed) ICUs

5. Study participants amenable to deferred/waived consent

6. Several benefits to involving bereaved family members in research.
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